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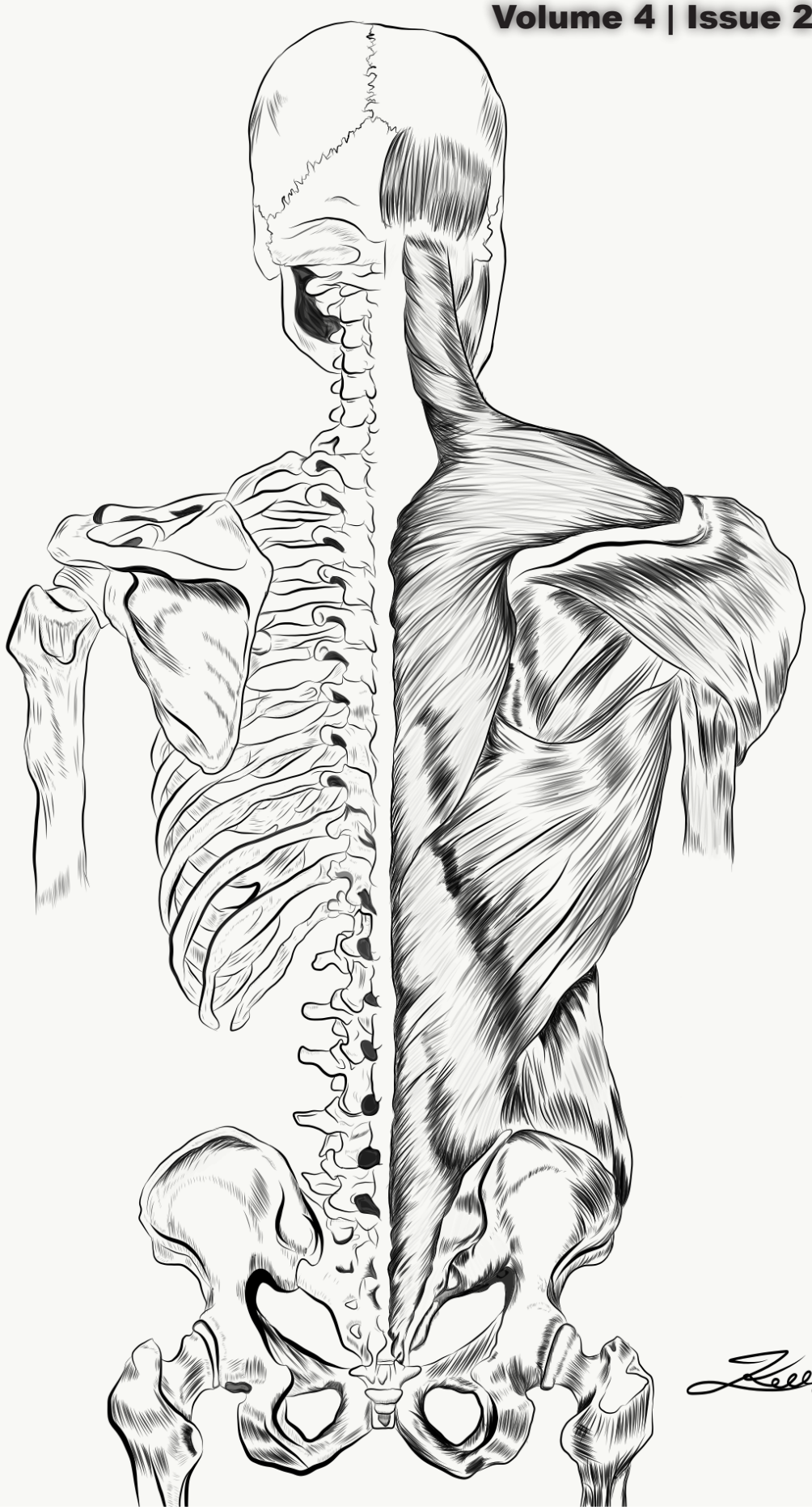

MISSION STATEMENT

What's emerging in medicine today? The Sackler Journal of Medicine – a forum where trends in medicine including translational research, the economics and policy of healthcare, and clinical experiences are explored, analyzed and discussed. SJM is a peer-reviewed journal for medical students to discuss and learn about the latest medical breakthroughs and the fundamentals of medicine.

We encourage student and physician collaboration to bring you literature reviews, case reports, original research, reflective pieces, and short commentaries on published papers. Take the opportunity to contribute your work, experiences and voice to the conversation.

SUBMISSIONS INFORMATION

Submissions from students, faculty, and individuals are welcomed. For more information please visit the "Submissions" page on the Sackler Journal of Medicine website at sacklerjom.org

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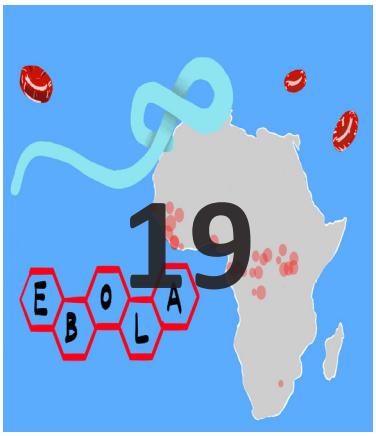
Table of Contents


3


9


11


15


19
E
B
O
L
A


22


26


28


SIM

Letter From the Editors

Melissa Bendayan and Micah Iticovici
Editors-in-chief

Dear Reader,

If this is your first time picking up the journal, or if you are a regular reader, we would like to thank you for taking the time to read our publication. Enclosed is a collection of original research, reflections, and art work done by the students at the Sackler School of Medicine.

This last year has been a significant one for the journal as well as for the school. This edition in particular is special because it is the first in the transition of the Sackler Journal of Medicine from an annual publication to a biannual publication. We hope this change will allow us to showcase an even wider spectrum of student work, ranging from more artistic publications like poetry, to personal reflections on the difficulties of being a medical student. Given the growing volume of submissions by students we decided that it would be best to give students more opportunities to publish their work.

Recently, the Sackler Journal of Medicine Blog has been revitalized and since the beginning of this academic year, we have had weekly updates and commentary on high impact medical publications from our blogging team. The goal of the blog is to provide keep readers informed on advancements in medicine, as well as creating a space for discussing the controversial aspects of these publications.

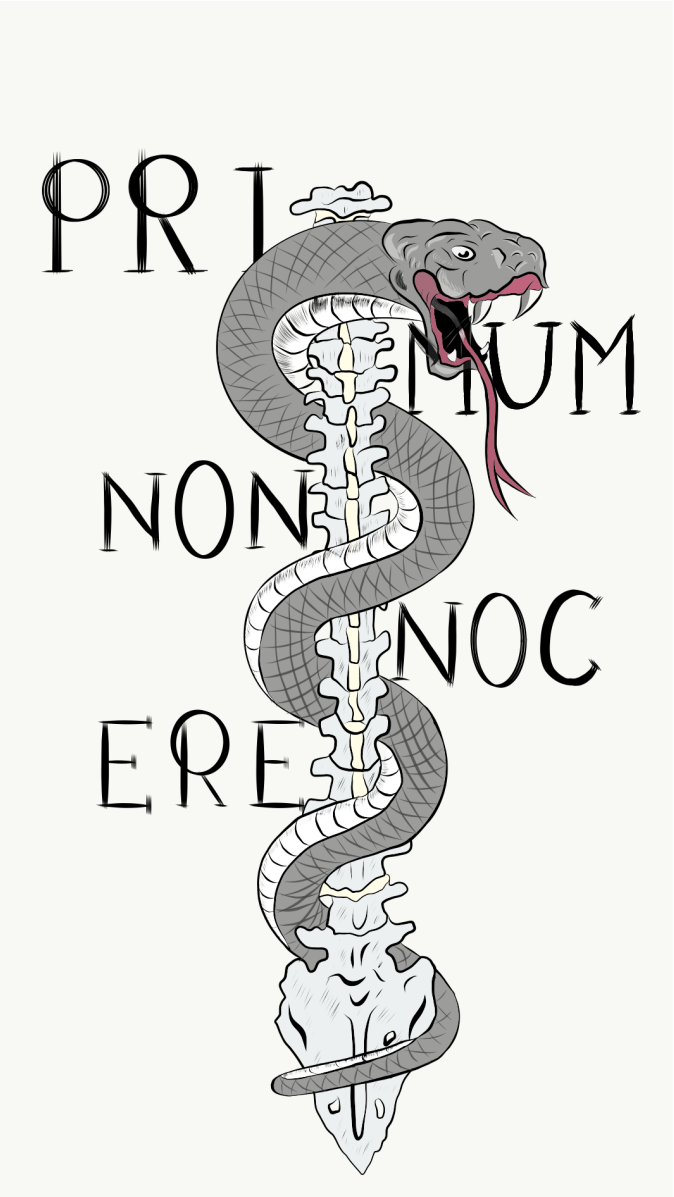
We would also like to bid farewell to the to the previous Editors and Chiefs, Amanda Katz and Madhu Govindaswamy, and thank them for all their hard work in helping prepare this issue as well as running the journal for the past year.

Finally, we would like to wish all the best to Dr. Sheryl Shoham in her retirement from the Sackler School of Medicine this year. Her efforts in creating the first- and second-year curriculum and her dedication to shaping our institution will surely be remembered for years to come.

Best,

Melissa Bendayan and Micah Iticovici

Editors-in-Chief



Artist: *Olivia Keller-Baruch*

Letter From Dr. Allen

Aaron Allen M.D.
Faculty Adviser- SJM

Dear SJM Readers,

Erna Bomberk once wrote, "never go to a doctor whose office plants have died."

While the line above is certainly humorous, its underpinnings are anything but. Let us find the truth beneath these words as they emphasize the importance of empathy, compassion and attention to living beings- both plants and patients alike.

So much of what makes a good physician is attention to detail: how many times have we seen an astute physician unravel a complex diagnosis based on a single detail alone? It is not only physiological details that make the best physicians, but also emotional or personal details that are critical. How much must we be observant of the patients entire lifestyle and values, from diet to home life- in addition to clinical findings- to know what truly ails our patients?

The importance of attention to detail is as critical for the researcher. Today, with focus on genetics and careful study of molecular biology, any experiment in any lab is only as good as the protocol and investigation. The old adage "garbage in, garbage out," asks us to consider results only in the light in which the data has been obtained.

Those of you who excel at this, always making sure to check their answers 4-5 times for mistakes, are probably feeling quite good about yourselves. But what about everyone else, who, like most of us, has a hard time remembering every detail and might have even let a house plant let alone a goldfish pass away from lack of attention? What should we do then?

Fortunately, not all hope is lost. Medicine and research are crafts. Just like an apprentice in any trade must work and perform his craft over and over again to achieve perfection, so too must the medical student and researcher work adamantly to hone their skills, gradually but progressively improve their craft, and ultimately become more proficient and precise.

While it is true that the articles in this issue may not be have reached the New England Journal of Medicine, the feat of a medical student to produce such professional work does not go unnoticed. The editors, and authors and reviewers deserve tremendous credit for all of this. On a larger scale, this journal and all of your exciting work in your medical school journey serves as training for each of you to improve and refine your skills to a level where you can achieve your M.D. and far beyond.

Do not accept your current level of proficiency: not in making a differential diagnosis, not in connecting to a patient and not in your research. Medicine is a lifelong quest; make sure that you enjoy every minute.

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Dietary Fish Consumption During Pregnancy: A Risk-Benefit Analysis

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Neurocognitive function is essential to a child's development. For new parents, it is a major factor to consider as early as the prenatal period given that a mother's diet and health during pregnancy can influence fetal development[1]. Two nutrients, omega-3 fatty acids and methylmercury, have long been associated with beneficial and detrimental effects, respectively, on neural development during gestation and early childhood[1]. However, for humans, these two nutrients come tangled together as they are most commonly consumed through dietary fish. As a result, parents inevitably must weigh the benefits of omega-3 fatty acids to the risks of methylmercury, which has recently been revisited in the public eye[2]. The following article aims to clarify where the science and economics currently stand in this risk-benefit analysis. Based upon omega-3s in the human diet, the cycle of mercury into aquatic life, an expert FAO/WHO panel evaluating the data available, and tuna's role economically and in health, it seems that benefits outweigh the risk; as such, it would suggest that women should be encouraged to eat fish during pregnancy.

Learning Points

- Fish contains omega-3 fatty acids, which is beneficial to neurocognitive development, and methylmercurly, which is detrimental. Since both can cross the placental barrier, this makes it confusing for pregnant women as to whether or not they should consume fish.
- Many studies show that the benefits likely outweigh the risks, and that maternal consumption of any fish with a methylmercury content below 0.5 µg/g (most fish), even up to seven servings a week, is more beneficial for a child's IQ than detrimental.
- The FAO/WHO panel evaluated the literature and created a chart with fish types, methylmercury, and DHA + EPA levels.
- Tuna is the most widely consumed fish in the United States. Fresh tuna has a very high methylmercury level, but canned tuna (especially light tuna) is likely safe for pregnant women.

Building Omega-3 Fatty Acids

Omega-3 fatty acids are synthesized in plants, algae, and phytoplankton[3]. Animals lack D15-desaturase, an enzyme that makes the defining double-bond between the n-3 and n-4 carbon on a fatty acid chain, making the fatty acid an omega-3 family member[4] and an essential fatty acid (i.e. must be consumed through the diet because it cannot be made endogenously). However, after the initial synthesis of an omega-3 fatty acid, animals (i.e. humans, fish) do have enzymes that can modify omega-3s, notably into eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). There is an increasingly strong body of scientific evidence suggesting significant health benefits as a result of the consumption of EPA and DHA. In adults, some of the more notable health benefits include a reduction in coronary death by 36%, a reduction in overall mortality by 17%, and an overall protective effect against coronary heart disease (CHD)[5], the number one killer in the United States (U.S.)[6].

For humans, the easiest way to consume a substantial amount of these fatty acids is through fish. This is because omega-3 producers (phytoplankton, algae) make up a substantial portion of the diet of many fish, and as a result fish accumulate high levels of omega-3s. In turn, humans are able to acquire enough omega-3s, with a relatively low fish consumption (250-500 mg/day EPA/DHA[5], or 2-3 servings of fish per week), to receive positive benefits[5].

Interestingly, in regards to CHD (which has been the most extensively studied and where there is the strongest evidence), a threshold effect has been seen. Therefore, more than a modest amount is not necessarily better[5].

Tangled: DHA and Methylmercury

As research evolves in the area of omega-3s, the associations are mostly with a slew of positive health benefits[1]. However, one particularly controversial topic is in regards to pregnancy. Omega-3s cross the placental barrier[7] and DHA is directly incorporated into the grey matter of the fetal brain[5]; it is reasonable to believe that DHA influences early neural development. Furthermore, many studies agree, although on different measures and to different degrees, that maternal DHA intake is positively correlated with improved childhood cognition[5].

So where is the controversy? It primarily lies in the issue of methylmercury, a potent neurotoxin that also crosses the placental barrier[5] and at high levels has been shown to have severe neurological consequences[5]. Methylmercury is the product of atmospheric (elemental) mercury (largely from industrial pollution) picked up in natural water cycles, and rained down into the oceans and lakes[5]. In oceans and lakes, the elemental mercury, which cannot cross the placental barrier, and inorganic mercury, which is not absorbed well by tissues, is converted by microbes into methylmercury, which then is actively absorbed into tissues[5] and is a dietary health hazard. In other words, elemental and inorganic mercury are relatively benign. When people talk about the dangers of "mercury in fish," they refer to an organic form of mercury that was created by aquatic microbes.

As a result, the packaged source of omega-3s in fish comes with varying degrees of methylmercury. The degree is important and based upon the type of fish, its diet and lifespan, and the level of methylmercury exposure in its environment. In regards to the general population's diet, the question arises – do the benefits of omega-3s outweigh the consequences of methylmercury? This question is hardly easy to answer, but much of the literature suggests that eating fish in limited amounts, and more importantly fish that are known to have less bioaccumulation of methylmercury, is the best compromise. A general rule of thumb for dietary fish consumption is that fish with less bioaccumulation of methylmercury are at a lower trophic level (not eating other contaminated fish) and have shorter lives (less time to accumulate methylmercury).

A Closer Look: Pregnancy and Fish

For pregnancy however, the question is arguably much more important due to omega-3's positive role and methylmercury's negative role in fetal brain development. Herein follows a brief review of where the literature stands on the issue.

One prospective cohort study[8] looked at maternal second trimester fish intake and developmental scores at age three of the child. The final cohort included 341 mothers living in Massachusetts and the mothers were comparable on many potential confounders, including similar weekly fish intake preceding conception; most were non-smokers, white, educated, and not under significant socioeconomic stress. At the end of the second trimester, fish consumption of the previous three months was taken through a Food Frequency Questionnaire (FFQ) with an extended fish section and methylmercury was measured in red blood cells. Fatty acids were measured through further analysis of the FFQs, as well as the fatty acid content of the red blood cells. The children's cognitive outcomes were measured at three years old through a PPVT (vocabulary test) and WRAVMA (visual-spatial, visual-motor, and fine-motor test). Mothers were grouped and analyzed based upon eating >2, <2, or no servings of fish per week during the second trimester of pregnancy. There were at least 40 mothers in each group, although the majority fell in the middle (<2). Outcomes of the study showed that rising methylmercury levels, as wells as EPA and DHA levels, correlated to rising fish consumption. In other words, if a mother ate more fish she also accumulated more methylmercury. Ten percent of mothers accumulated >1.2 ppm, which although seen in both fish-eating groups, was 2.5 times more likely to occur in the high-

intake group; in this 10% of mothers, cognitive scores for their children were below the scores of children born from mothers who never ate fish. However, for the other 90% of mothers who accumulated only some mercury (<1.2 ppm), there were clear cognitive benefits in their children, surpassing the children of mothers who never ate fish. The authors concluded that the benefits of fish consumption outweigh the risks; however, eating fish with lower mercury content was advised.

In 2010, an expert panel was assembled by the Food and Agriculture Organization of the United Nations (FAO) and World Health Organization (WHO) to weigh in "on the risks and benefits of fish consumption" and specifically address the "benefits of [long chain n-3 polyunsaturated fatty acids] with risks of methylmercury among women of childbearing age"[1]. The panel reviewed many landmark studies, including the two largest longitudinal studies from the Faroe Islands and Seychelles, and literature reviews. Interestingly, the two longitudinal studies had somewhat contradicting results. In the Faroe Islands (n=approx. 900 mother-child pairs), which included a follow up at seven years[9] and fourteen years after birth[10], methylmercury in the cord blood, hair of the children, and hair of the mother at parturition, was positively correlated with decreased cognitive function in the children, specifically in measures of attention, language, and memory[1]. However, these associations, while stronger at age seven, at age fourteen arguably lacked significance because the association of poor neurocognitive test performance was the same to gestational mercury exposure as it was to time of day the child was tested (both were $p<0.001$)[10]. Although the results suggested a statistically significant relationship between methylmercury exposure and poor neurocognitive function test performance, the results were confounded by a strong association that was also seen between poor neurocognitive function test performance and time of day that the tests were administered.

Meanwhile, the Seychelles Child Development Study (n=779 of mother-child pairs), which analyzed children at nine years old, found only one measure of decreased cognitive function (a motor function test for the non-dominant hand), which was associated with high maternal mercury exposure (approximately twelve servings of fish per week)[11]. Yet, they found improvement on a measure of hyperactivity associated with increased mercury levels, so the authors declared the overall effects a wash; there was not enough substantial data to associate maternal fish consumption as more detrimental

Table 1. Relative mercury versus DHA+EPA content of different fish species. Adopted from 2010 FAO/WHO Report 1.

		EPA + DHA			
		$x \leq 3$ mg/g	$3 < x \leq 8$ mg/g	$8 < x \leq 15$ mg/g	$x > 15$ mg/g
Mercury	$x \leq 0.1$ µg/g	**Fish:** butterfish; catfish; cod, Atlantic; cod, Pacific; croaker, Atlantic; haddock; pike; plaice, European; pollock; saithe; sole; tilapia **Shellfish:** clams; cockle; crawfish; cuttlefish; oysters; periwinkle; scallops; scampi; sea urchin; whelk	**Fish:** flatfish; John Dory; perch, ocean and mullet; sweetfish; wolf fish **Shellfish:** mussels; squid	**Fish:** redfish; salmon, Atlantic (wild); salmon, Pacific (wild); smelt **Shellfish:** crab, spider; swimcrab	**Fish:** anchovy; herring; mackerel; rainbow trout; salmon, Atlantic (farmed); sardines; sprat **Fish liver:** cod, Atlantic (liver); saithe (liver) **Shellfish:** crab (brown meat)
	$0.1 < x \leq 0.5$ µg/g	**Fish:** anglerfish; catshark; dab; grenadier; grouper; gurnard; hake; ling; lingcod and scorpionfish; Nile perch; pout; skate/ray; snapper, porgy and sheepshead; tuna, yellowfin; tusk; whiting **Shellfish:** lobster; lobster, American	**Fish:** bass, freshwater; carp; perch, freshwater; scorpion fish; tuna; tuna, albacore **Shellfish:** crab; lobster, Norway; lobsters, spiny	**Fish:** bass, saltwater; bluefish; goatfish; halibut, Atlantic (farmed); halibut, Greenland; mackerel, horse; mackerel, Spanish; seabass; seabream; tilefish, Atlantic; tuna, skipjack	**Fish:** eel; mackerel, Pacific; sablefish
	$0.5 < x \leq 1$ µg/g	**Fish:** marlin; orange roughy; tuna, bigeye	**Fish:** mackerel, king; shark	**Fish:** alfonsino	**Fish:** tuna, Pacific bluefin
	$x > 1$ µg/g		**Fish:** swordfish		

than beneficial[11]. To note, a significant portion of the Faroe Islander's sea diet was mammalian, and the diet and lifestyle of Seychelles' islanders is considered to be more comparable to the U.S.[11]. Additionally, researchers involved in both studies suggest that there are beneficial effects of fish consumption that may have negated some of the consequences of methylmercury exposure[10,11].

The FAO/WHO panel ultimately gathered data from many studies and came up with estimated quantitative associations for gestational methylmercury exposure and maternal DHA intake and IQ. They decided upon a central limit of -0.18 and upper limit of -0.7 IQ points per microgram of methylmercury per gram of hair. For DHA, the panel decided to use an average of 4.0 IQ points per 100 mg of DHA per day, and estimated that 27.8 grams of fish provided 100 mg of DHA[1]. There was an upper threshold to the beneficial effects seen by DHA intake in many studies, so the panel decided that a maximum of 5.8 IQ points could be attributed to maternal DHA consumption, although they admitted that there was much variation and this was a difficult number to assess[1]. The panel used five different databases from various parts of the world to assemble a list of 103 fish species with the average methylmercury content and EPA+DHA content of each species (Table 1). They used the quantitative estimates of the negative methylmercury IQ associations and the positive DHA IQ associations to assemble corresponding tables based upon frequency of maternal fish consumption, accumulation of each variable, and potential decrease or increase in IQ as a result (Tables 2 and 3).

In Table 1, fish in the top right are considered the best choices, as they have high EPA + DHA with low methylmercury; conversely, the lower left box is high in methylmercury and low in EPA + DHA. Table 2 is best understood if imagined overlaying Table 1; each box in Table 2 corresponds to the same box in Table 1. Table 2 shows a scored risk-benefit analysis (scoring outlined above) where the red numbers are a predicted range of potential negative effects, and the green is the predicted positive effect from consuming one serving of fish per week (the type of fish corresponding to the matching box in Table 1). The yellow shaded boxes in Table 2 suggest that these fish types should be avoided because overall the consequences of the methylmercury levels outweigh the benefits of the EPA + DHA levels. Finally, Table 3 is designed the same as Table 2, except it uses the measure of seven servings of that fish per week, versus Table 2 is for one serving per week. The boxes that were not yellow in Table 2 but became yellow in Table 3 suggest that these fish are okay to eat once a week but, as one eats more of it, the consequences outweigh the risks. Overall, the analysis reaches the point that maternal consumption of any fish with a methylmercury content below 0.5 µg/g (most fish), even up to seven servings a week, is more beneficial for a child's IQ than detrimental.

Table 2: Estimated IQ risks (red) and benefits (green) associated with maternal fish intake (one serving a week) in different fish categories (Table 1). Boxes shaded in yellow suggest that, if using the upper limit of methylmercury risk (-0.7), the risks may outweigh the benefits if fish in these categories are consumed once per week during pregnancy. Serving size is 100 grams. Adopted from the 2010 FAO/WHO Report 1.

			EPA + DHA			
			$x \leq 3$ mg/g	$3 < x \leq 8$ mg/g	$8 < x \leq 15$ mg/g	$x > 15$ mg/g
		Median	2	5.5	11.5	20
Methylmercury	$x \leq 0.1$ µg/g	0.05	−0.02, −0.08 +0.77	−0.02, −0.08 +2.1	−0.02, −0.08 +4.4	−0.02, −0.08 +5.8
	$0.1 < x \leq 0.5$ µg/g	0.3	−0.12, −0.47 +0.77	−0.12, −0.47 +2.1	−0.12, −0.47 +4.4	−0.12, −0.47 +5.8
	$0.5 < x \leq 1$ µg/g	0.75	−0.30, −1.2 +0.77	−0.30, −1.2 +2.1	−0.30, −1.2 +4.4	−0.30, −1.2 +5.8
	$x > 1$ µg/g	1.5	−0.60, −2.3 +0.77	−0.60, −2.3 +2.1	−0.60, −2.3 +4.4	−0.60, −2.3 +5.8

			EPA + DHA			
			$x \leq 3$ mg/g	$3 < x \leq 8$ mg/g	$8 < x \leq 15$ mg/g	$x > 15$ mg/g
		Median	2	5.5	11.5	20
Methylmercury	$x \leq 0.1$ µg/g	0.05	−0.14, −0.5 +5.4	−0.14, −0.5 +5.8	−0.14, −0.5 +5.8	−0.14, −0.5 +5.8
	$0.1 < x \leq 0.5$ µg/g	0.3	−0.84, −3.3 +5.4	−0.84, −3.3 +5.8	−0.84, −3.3 +5.8	−0.84, −3.3 +5.8
	$0.5 < x \leq 1$ µg/g	0.75	−2.1, −8.2 +5.4	−2.1, −8.2 +5.8	−2.1, −8.2 +5.8	−2.1, −8.2 +5.8
	$x > 1$ µg/g	1.5	−4.2, −16.3 +5.4	−4.2, −16.3 +5.8	−4.2, −16.3 +5.8	−4.2, −16.3 +5.8

Table 3: Estimated IQ risks (red) and benefits (green) associated with maternal fish intake (seven servings a week) in different fish categories (Table 1). Boxes shaded in yellow suggest that, if using the upper limit of methylmercury risk (-0.7), the risks may outweigh the benefits if fish in these categories are consumed seven times per week during pregnancy. Serving size in 100 grams. Adopted from the 2010 FAO/WHO report 1.

Tuna as the Economical Choice

In the U.S., tuna is "the most commonly consumed fish"[12] and it is important, on a public health level, that government recommended dietary guidelines take accessibility into account. For instance, if the dietary guidelines are that pregnant women should eat fish, then it seems that 1) fish should be somewhat accessible to the entire population and 2) before making such a recommendation, the most accessible and widely consumed fish be taken into consideration with this recommendation. It is unreasonable to expect the public, especially those that may have little education, access, and literacy, to know the inclusions and exclusions of a particular health recommendation. Thus, a national health recommendation should not propagate a message that is highly specific and complicated. Therefore, it should be considered if the most commonly consumed and widely available food in a given category, which in this case is canned tuna, qualifies under a proposed recommendation.

It is of concern that some tuna fall into the yellow-shaded boxes, indicating that seven (Tables 1 and 3), or even one serving of this fish (in the case of big-eye tuna) (Tables 1 and 2), can be more detrimental than beneficial if consumed during pregnancy. However, it is well established that fresh tuna contains more methylmercury than canned tuna[12,13] and the aggregated database of the FAO/WHO did not make this differentiation[1]. Furthermore, a study investigated the mercury content in commercially canned tuna (n=168) from a New Jersey grocery store over a five-year period (1998-2003) and found that the mercury content varied by year, and depended upon the type of canned tuna: solid white (0.429 ppm), followed by chunk white (0.355 ppm), and finally light tuna (0.118 ppm)[12]. Light tuna, which is usually skipjack, never had a sample that exceeded 0.5 ppm; solid and chunk tuna is restricted to albacore[12]. Of note, neither of these tuna species fall into the hazardous yellow-shaded boxes in Tables 2 or 3, and the mercury averages of all three canned tuna types fall below the FAO/WHO limit (0.5 µg/g) that would recommend restricting consumption of these fish types to less than seven times a week during pregnancy. Furthermore, based off of current Walmart prices, light tuna is cheaper than solid tuna[14].

After reviewing the evidence, and given the strong stigma against eating fish during pregnancy, should the U.S. dietary guidelines recommend pregnant women to eat more fish? Although there is agreement among the studies reviewed that it is safer to consume fish lower in mercury content, canned tuna is currently the most accessible option for the general population. Tuna is controversial because it is on a high trophic level and thus can accumulate high levels of methylmercury. However, the species of tuna used in canning have been shown to have lower levels of methylmercury compared to fresh tuna species. Based upon the studies of methylmercury levels in canned tuna, combined with the benefits and risks assessment of the FAO/WHO expert review committee, there is reasonable evidence to suggest that the

benefits of eating several servings of canned tuna per week during pregnancy likely outweigh the risks of forgoing fish altogether.

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Artist: *Olivia Keller-Baruch*

From Marine Corps special operations to medical entrepreneur: Derek Herrera and the Connected Catheter

Zachary Lundby
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In 2012, Derek Herrera was on a patrol in Afghanistan when he was critically wounded. A bullet fired from an insurgent bypassed Derek's body armor by entering near the shoulder and lodged itself in his spine. As a result, Derek lost all function below his T7/T8 vertebrae leaving him paraplegic and with trunk stability issues but retaining control of his chest and arms. Although he survived his wound, this was a particularly tragic event for a young man in the prime of his life, or anyone for that matter, due to the loss of independence. Things that he used to take for granted were permanently lost. However, Derek, ever the fighter, decided he would do something to address these issues. Derek noted that, "I didn't know that manning my bladder would be the most challenging task I faced on a daily basis" and used this as motivation to start his company called Spinal Singularity[1].

After receiving numerous sources of crowd and seed funding, Spinal Singularity developed a "smart catheter" called the Connected Catheter that allows the user to empty their bladder on command by manipulating a duckbill valve at the base of the penis[2]. This eliminates the need for Foley Catheters (the classical type of catheter that allows urine to drain into a waste bag attached to the user), and is a saving grace for all of those suffering from neurogenic bladder. Neurogenic bladder is a condition wherein the individual is unable to feel the fullness of their bladder and thus, cannot control the voiding process. The Connected Catheter is extremely valuable in this regard because of the logistics surrounding the condition which involve frequent bathroom visits, always knowing where the nearest bathroom is located, and completely dehydrating before a plane or car ride to avoid an embarrassing accident. This has relevance for anyone suffering from multiple sclerosis, amyotrophic lateral sclerosis, Alzheimer's, certain types of strokes, spinal cord injury, and more.

Derek's Connected Catheter is unique because it lasts up to a month and has the ability to tell the user when the bladder is full via wireless technology.

Image: *thenewsrep.com*

Learning Points

- Patients with thoracic level spinal cord lesions often lose the capability to perform tasks we take for granted such as going to the bathroom unassisted, having sex, and walking
- Neurogenic bladder is when an individual is unable to feel the fullness of their bladder and thus, cannot control the voiding process
- Derek's Connected Catheter can tell the patients with neurogenic bladder when their bladder is full using wireless technology
- Patients with neurogenic bladder using Derek's Connected Catheter are no longer incontinent and do not need an indwelling catheter

Current catheters must be inserted and removed on a daily basis and drain passively. Furthermore, the catheter is fully internal and is activated by compressing a valve at the base of the penis. The Connected Catheter can be inserted and removed at home by the user and seeks to decrease instances of trauma and UTIs as a product of the long lifetime of the catheter.

Derek Herrera's Connected Catheter has the capability to revolutionize catheter technology, which has remained largely stagnant since the introduction of the Foley Catheter. Individuals with nerve injuries that still retain use of their arms will be able to go to the bathroom and urinate like any healthy person. Although they will not be able to feel the fullness of their bladder, they will still be able to monitor its distension by checking the application on their smartphone. Individuals with nerve injuries that do not suffer from any gross motor dysfunction but still have urinary incontinence will no longer have to worry about embarrassing accidents or carrying around a waste bag. The valve built into the catheter will allow these individuals to choose when to relieve themselves. Owing to these many factors, should the device be brought to market it will be a great boon for individuals suffering from nerve injuries and for the medical field as a whole.

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Artist: *Olivia Keller-Baruch*

Healthcare access in the Israeli refugee population: My experiences at the Tel Aviv Terem clinic

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Background and Research

Refugees are "people whose lives or freedom are endangered in their country of origin"[1]. As of October 2014, Israel contained 47,000 refugees, mostly from Eritrea but with a significant population also from Sudan[1]. The journey to Israel for the refugees is 20,000 difficult and dangerous kilometers, but many have decided it is worth the risk[2]. Eritrea is a country led by ruthless dictatorship and Sudan is also a "dictatorial republic"[1]. In Eritrea, army service is harsh, mandatory, and indefinite, while in Sudan, people are killed in civil war, by the hundreds of thousands in ethnic cleanings that destroy villages[3]. However difficult life may be for refugees in Israel, and as much as some people may want them gone, these groups are determined to stay. They remain under the protection of deferred deportment; even with financial incentives to leave to third-party countries, most are determined to stay long term. Leaving their country of origin has already made the Eritreans enemies of their state and liable to torture and imprisonment if they ever return. While Israel recognizes a small fraction of asylum seekers, among Eritrean and Sudanese people, official refugee recognition rates are 88% and 64%, respectively[1].

A single office in Tel Aviv processes refugee applications, which limits and often even derails the speed of the recognition process[4]. While waiting for an application appointment, these individuals cannot legally work, but must to survive, and almost all risk arrest overstaying their visas while waiting for necessary appointments. Meanwhile, they all also need healthcare as their status hangs in limbo.

Policies by international organizations provide the legal guidelines on how healthcare should be provided to refugee populations in all places[5]. While the reality is widely varied, most countries at least as developed as Israel manage to uphold the basic human rights tenants, because physicians generally treat all their patients through the lens of secular medical ethics. Financial and security concerns remain significant issues, so, while not a perfect solution, non-governmental organizations fill in where the government fails to provide for the refugee populations[6]. Changes to the geopolitical scene in Africa, and increased Israeli border security, portends a dramatic fall in African migration, lending credence to the argument for ensuring the wellbeing of the relatively small population of those who have landed themselves in Israel[2]. Whether motivated by humanitarianism, political ideals, symbolism, or notions of power dynamics, people of a multitude of perspectives – none of which are mutually exclusive – dedicate themselves to this work. Over the course of my volunteering at the Terem clinic, I thought extensively about my motivations and what ends could be met while working on this project.

The Israeli Ministry of Health and Terem urgent care network runs the Terem clinic[2]. Though Israeli emergency rooms treat everyone regardless of status or insurance, most people in the country without proper documentation still live with inadequate medical care. Therefore, in 2008, Michael Dor, once the Deputy Director of the Medical Services Division of the Israeli Health Ministry, created the Public Clinic in the Tel Aviv Central Bus station, where police and immigration services are verboten[2]. The refugees congregate largely in South Tel Aviv near the Central Bus Station because, upon release from detention, each one receives a ticket to the Central Bus Station; many stay there because several of the relevant organizations are located nearby[1]. What started as a three-times-per-week operation grew to a now fully

functioning all-week free clinic with desperately needed grant from the Ministry of Health in 2013[2]. The clinic boasts volunteers from all over the world, including full time Eritrean employees that help bridge language and cultural barriers, and 20,000 patient visits per year.

Personal Connection and Goals

When selecting this project, I was motivated by education, political, and ideological factors. My goals for this project were to see and learn things that would make me a better doctor and to fulfil a moral ideal of giving time towards equalizing healthcare access for a marginalized group of peoples. I was interested in being exposed to a new population of patients and the unique challenges posed by them. We do not encounter refugees in the hospitals, therefore it was a fresh experience to learn about their healthcare issues. These concerns included financial obstacles, a need for translation, a lack of fundamental health knowledge, and uncertain follow up due to a variety of unknown variables in their future. While not many of my future patients are likely to be refugees, each of these challenges are certain to arise within any patient population, and the more experience I have with dealing with them now, the better I will be able to assist my patients in the future.

I also have a strong belief that healthcare is a fundamental right that should be provided to every individual in a country. This is a statement strictly on the role of a government in providing healthcare to everyone within its borders, regardless of how they ended up there and how long they will stay. The important and complex matters of border control and deportation can be addressed separately. Because Israel is a fundamentally Jewish country, its leadership should feel further compelled to ensure the refugee population has access to medical resources. Jews are commanded in scripture to not allow fellow humans to suffer without acting, and to treat foreigners well because the Jewish people were also once strangers in an unfamiliar land. These ideas are close to my heart and called me to this project which exemplified an opportunity to fulfill the values they express.

Volunteering Experience

My first introduction to the Terem clinic was an orientation session on a Friday in November 2017. Two Eritrean clinic workers showed

Artist: *Anais Di Via Ioschpe*

us around, explained the services provided, and introduced us to the electronic records system used there. I found the most important part of this day was when they then took us to an authentic Eritrean restaurant in the area to eat lunch. This exposure to the area, where African refugees live in Tel Aviv, was the best possible introduction to the patient population of the clinic. The people living there have created a mini version of their countries of origin, so much so that I felt as if I had actually travelled there. In my brief visit, my sympathy towards the community grew. I think it is a valuable use of time for anyone working with a specialized population to see how they live outside the medical environment to appreciate the rich and complex context of their lives and health problems.

In the end of December, I came to Terem to assist a physician conducting an asthma clinic. I was struck primarily with the critical utility of the Eritrean translator and impressed with his linguistic skills as someone who proficiently spoke five languages. I also got the strong impression that what was translated to the patient was a reduced version of what was said in English and there still seemed to be a lack of comprehension on the part of most of the patients. This indicated to me an absence of basic relevant knowledge that we expect of most patients in developed countries. While in a busy clinic like this, it became necessary in the conclusion of the appointment to give simple instruction to the patients of how to manage their asthma and use medications correctly. Ideally, clinicians would have the time to educate their patients, but with the language barrier and many waiting patients, it was not feasible. I felt satisfied that we accomplished the essential goal of following up and providing these patients with important medications, but it was frustrating that many came to the appointment having already run out of their previous prescriptions risking a serious medical event. Throughout the rest of my experience at Terem, I became acutely aware that regular follow up is a standard hard to meet in these conditions.

On a subsequent visit in January, I was put to the task of contacting a list of patients to participate in a project following patients with a history of high blood pressure for the next year, providing them with free visits and medications, as long as they agreed to regular visits. My job was to contact some of the clinic's most regular high blood pressure patients and schedule them for initial tests, at which point we could obtain their signed agreement to the arrangement. This proved a daunting and challenging task. I was shy to make these calls and often unsure whether to speak in Hebrew or English. By looking up their patient profiles, I was able to make some educated guesses. Even with a common language, I felt there was some breakdown of communication in these conversations. Maybe it was too much information to explain on the phone, but some seemed confused even by the clinic name. This led me to consider a language, accent, or hearing problem over the telephone. Certainly, in this instance, it could not have been an educational gap. In the end, I was successful at booking several patients and I later met some of the project participants at their first doctor visit.

While later volunteering in February, I assisted high blood pressure patients in their visits with the doctor. I took blood pressure measurements and brief medical histories ahead of patients' meetings with the doctor. A handful of patients had not yet been signed on to the project, so we introduced it to them and set them up to continue. In a clinic full of refugees, the volunteers and employees stand out by dress, attitude, and frankly, skin color. I was uncomfortable with the level of deference and respect I was given by the patients despite reiterating that I was not a doctor. One noteworthy experience was when one man was not comfortable with me taking his blood pressure in the waiting room as I had been doing, and so from then on, I began doing it in an empty exam room. I thought I was being efficient, but I had not been considering privacy, and this reminded me that it is an important component in all patient interactions. Just because something would not make me uncomfortable does not mean that everyone else feels the same way. This was also my most fulfilling visit in terms of having maximal patient interaction and feeling like I had a significant impact in the care provided to them.

A week later, I was there again in continuation of the blood pressure project. I found, like in my initial exposure at Terem, that lack of health literacy is a theme for this population of patients. The blood pressure appointments

are essentially medication counseling sessions in which the doctor tries to prescribe based on patient reports of what they are taking, side effect complaints, and disease control. Like initially noted, one of the greatest challenges is that the patients frequently come after finishing their medications, so current readings do not tell us if the condition is controlled on current prescriptions. This makes it challenging to make appropriate adjustments to their regime. Timely follow up is one of the biggest obstacles and is complicated by the uncertainty in these individuals' lives. It can be encouraged by the physician, but we must rely on the patients to prioritize their medical treatment and be available to receive the care at appropriate intervals.

Conclusions and Implications

Providing healthcare to the refugee population in Israel is a tricky task. Well-intended providers must surmount political, infrastructural, and financial limitations, and the obstacles of reaching sufficient understanding with a patient from a very different background. The complexity and instability of these patients' lives adds to the chaos that is often out of the hands of the clinic and patients. Nonetheless, being part of the effort to provide necessary healthcare to a community that would not otherwise receive it is a worthy and rewarding task. Aligned with my political and moral beliefs, it was a productive and emotionally satisfactory experience. It was also indubitably educational to meet and contend with a new range of patients and issues. It was not always easy, but I overcame personal insecurities and gained unexpected experience. Certainly, some of my new skills and knowledge gained while volunteering at Terem will make me a better physician for my future patients who may share common ground with those I encountered there.

I know the state of healthcare for this population can still be improved. Terem is only one clinic in one city with limited resources. A reallocation of funds and real societal discussion about the future of the refugees would go a long way towards improving their outcomes. The only solution I see is to create a possibility of these people receiving access to the same quality of care as Israelis. This would require a restructuring of the refugee recognition process and infrastructure and cannot be discussed without touching on national security and budgetary issues, topics beyond the scope of this paper but important and necessary components of the greater dialogue. I do not see this level of systemic overhaul happening any time soon, but it is nice to imagine this becoming a tangible solution to the ongoing problem I tried to address with my small contribution volunteering at Terem.

This reflection was written in Spring 2018, following a span of volunteering at Terem in Winter 2017-2018.

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A 23-Month Old with Acquired Unilateral Abducens Palsy

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Abstract

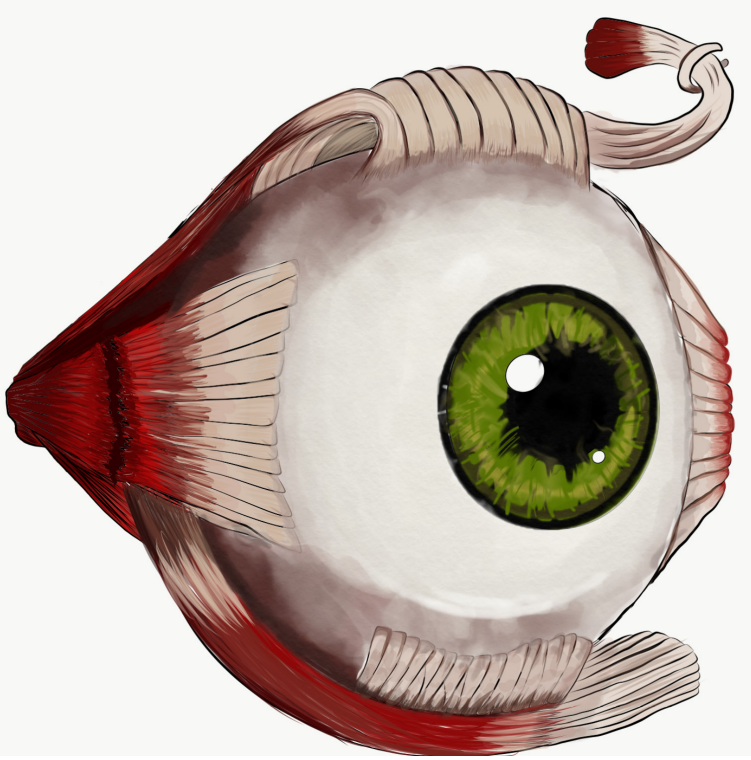
The following report brings to light an unusual case of an acquired, isolated abducens nerve palsy. While abducens palsy can be congenital, acquired palsies are far more common and often arise as a result of trauma or an underlying neoplasm. Thus, not surprisingly, patients with such palsies often present with various other neurologic manifestations. When no other such symptoms are evident, and the palsy is an isolated finding, one of the rarer causes of acquired abducens dysfunction must be investigated. It is crucial to obtain a detailed patient history, perform a thorough physical exam, and implement the correct workup in order to uncover the underlying etiology and treat accordingly.

Introduction

The abducens nerve (cranial nerve six) courses from its nucleus in the caudal portion of the pons through the subarachnoid space to innervate the lateral rectus muscle responsible for eye abduction. It has the longest subarachnoid course of any of the cranial nerves and is thus most susceptible to injury. The case concerns a 23-month old male who presented with a difficulty of left eye abduction on attempted left lateral gaze. An etiology of the palsy is explored and he is treated appropriately.

History of Present Illness

The patient is a 23-month old, generally healthy male. Three days prior to his arrival on our unit, his parents noticed that whenever he wished to look to the left, he would fully rotate his head to the left to do so. He was seen at an emergency clinic where he was given ibuprofen for suspected sternocleidomastoid tightness. Following a day of no improvement, he was seen at the emergency department where he was found to have a normal neurologic exam except for slightly brisk patellar reflexes. An ophthalmologist also examined him, and he found no evidence of papilledema with normal light refluxes. The patient was discharged home with a referral to be seen at the hospital's strabismus clinic the next day. At the clinic, he was found



Artist: *Olivia Keller-Baruch*

to turn his head to the left on attempted left lateral gaze. When looking straight ahead, he was unable to abduct his left eye, though no esotropia (inward turning of the eye) was evident. His neurologic exam that same day revealed a positive Babinski reflex on the right. In light of these findings, he was admitted and referred for an MRI of the brain.

The patient had no complaints of restlessness, nausea, vomiting, loss of consciousness, lethargy, or involuntary movements. There was no history of a fall or any sort of trauma. He had no recent unusual exposures or sick contacts and had not experienced a similar episode in the past.

One-week prior to his arrival on our unit, his family vacationed in the south of Israel where he suffered from slight congestion and a cough, though no fever.

Past Medical History-Birth and Development

The patient's mother experienced an uncomplicated pregnancy. She underwent all proper prenatal screenings and experienced no fever,

diabetes, or marked hypertension throughout. Genetic screenings and amniocentesis (performed because the mother was thirty-eight years old at the time of pregnancy) revealed no abnormalities. Our patient was born via normal vaginal delivery at term (forty-one weeks) and weighed 3.1 kg. He was circumcised at eight days. He is currently at the 65th percentile for weight, 50th percentile for height, and 48th percentile for head circumference. He has reached all of his developmental milestones on time—runs, jumps, ascends and descends stairs, possesses appropriate language skills, and attends nursery school. He was diagnosed with hyper-reactive airway disease at six months, for which he takes albuterol and fluticasone inhalers as needed. He has no known allergies and all immunizations are up to date.

Family History

The patient's mother is forty-one years old and generally healthy, though scheduled to undergo a lumpectomy soon. She is of Moroccan and Syrian descent. She has an aunt who suffers from Familial Mediterranean Fever, Behcet's, and is allergic to milk and eggs. The patient's father is forty-eight and generally healthy. He is of mixed Ashkenaz and Sefardi descent and has a non-contributory family history. The patient has a half sister from his father's previous marriage who is healthy.

Physical Exam

The patient's vitals on arrival to the unit were as follows: temperature 36.5 C, pulse 125, BP 125/80, and saturation 99% in ambient air.

The patient appeared well-developed, well-nourished, and in no apparent distress. There were no signs of dehydration or meningeal irritation. His skin displayed no rashes, bruises, or signs of discoloration. His head was normocephalic with no evidence of trauma. There was no discharge from his eyes, and no evidence of conjunctivitis or scleral icterus. Otoscopy was not performed but his outer ear appeared normal and there was no evidence of discharge. His nose displayed normal pink mucosa with no discharge or blood visible. His mucous membranes were moist, he possessed normal dentition, and there was normal movement of the soft palate. No cervical lymphadenopathy or thyromegaly was palpated. The lungs were clear to auscultation bilaterally and no stridor, wheezes, or crackles were appreciated. Cardiovascular exam revealed a quiet precordium without heaves or thrills. A normal S1 and S2 were heard, without any murmurs or gallops. Pulses were 2+ in all extremities and capillary refill time was normal. The abdomen was soft, non-tender, and non-distended, with bowel signs present in all four quadrants. There was no evidence of hepatomegaly, splenomegaly, or appreciable masses. Genitourinary exam was normal and extremities revealed no gross deformities.

On neurologic exam, the patient was fully alert and oriented. His pupils were equal, round, and reactive to light and accommodation. He displayed no eye deviation at primary gaze but difficulty with abduction of the left eye on left lateral gaze. His eye movements were otherwise normal with appropriate convergence and no evidence of ptosis. His facial sensation was intact to pinprick and his face symmetric with normal eye closure and smile. His hearing was normal to finger rubbing. His palate displayed symmetric elevation and uvula was midline. Head turning and shoulder shrug were intact and his tongue was midline. Based on an assessment of the patient's walking and jumping, he possessed normal muscle bulk and tone and his motor strength was deemed 5/5 in all extremities. He displayed 2+ and symmetric patellar and ankle reflexes and negative Babinski bilaterally. His posture was normal with a steady gait and normal step, base, arm swing, and turning. Romberg sign was absent.

Workup

Fundoscopy was again performed to rule out any evidence of papilledema. A complete blood count with differentials and metabolic panel were also obtained. Results were unremarkable and as follows:

- **CBC:** Hb 12.6 g/dL, Hct 26.3%, MCV 81.3 fl, RBC 4.5 M/micl, WBC 10.89 M/micl, PLT 205 K/micl, Neutrophils 69.3%, Lymphocytes 21.1%
- **CMP:** Na 134 mEq/L, K 4.3 mEq/L, Cl 94 mEq/L, Ca 9.6 mg/dL, albumin 4.4 g/dL, phosphorus 5.0 mg/dL, glucose 47mg/dL (after fasting in preparation for MRI), creatinine 0.26 mg/dL, urea 29 mg/dL, CRP 0.37 mg/dL

An MRI with gadolinium was then obtained which revealed no evidence of intracranial or orbital lesions. A lumbar puncture was performed which revealed normal cell count, glucose and protein levels, and opening pressure.

- **Cell count:** WBC 2/mm^3
- **Chemistry:** glucose 38 mg/dL, WBCs, protein 17 mg/dL
- **Opening Pressure:** 20 cm H_2O

Differential Diagnoses

The etiologies of acquired abducens palsy are rather varied. The most common cause in the pediatric population, accounting for 45% of cases, is an intracranial neoplasm. Whether benign or malignant, neoplasms can compress the abducens nerve anywhere along its lengthy path. Posterior fossa tumors such as medulloblastomas or brainstem gliomas are the most feared culprits. Our patient's normal MRI, however, ruled out either of these etiologies. The second most common cause of acquired abducens palsies, accounting for 42% of cases, is trauma, often due to a base of skull fracture. This too, however, was ruled out based on our patient's lack of history and/or evidence of trauma as well as the normal imaging findings. Elevated intracranial pressure (e.g. due to pseudotumor cerebri or hydrocephalus) is also a potential cause of abducens palsy, however a normal opening pressure on lumbar puncture ruled out this etiology. An infectious process such as meningitis could also contribute to the findings, however our patient's unremarkable lumbar puncture and lack of fever make this unlikely. Finally, isolated, acquired sixth nerve palsy may follow a viral infection. Given that our patient suffered from what seemed like a viral infection one week prior to admission, this etiology seems plausible.

Spasm of the near reflex (known as convergence spasm) is also associated with an abduction deficit and should be included in the differential. However, miosis of the pupil upon attempted lateral gaze, which was absent in our patient, is an important differentiating factor. Additionally, myasthenia gravis can present similarly but is unlikely in the absence of other signs such as ptosis or fatigability. Orbital floor fractures as well as thyroid opthalmopathy should also be considered but would be accompanied by proptosis, conjunctival edema, and conjunctival injection—all of which were absent in our patient.

While the literature differs slightly, it is estimated that only 9% of all abducens nerve palsies in children are isolated, and of these, less than half are idiopathic. Given these statistics, idiopathic abducens palsy is a diagnosis of exclusion. However, following our patient's very thorough workup, which revealed no significant findings, our patient was eventually diagnosed with an idiopathic, though possibly post-viral, left abducens nerve palsy.

Management

Our patient was placed on a month of PO prednisolone drops with a taper (15 mg x1/day for days 1-10, 12 mg x1/day for days 11-15, 9 mg x1/day for days 16-20, 6 mg x1/day for days 21-25, 3 mg x1/day for days 26-30) with instructions to follow up with a neuro-ophthalmologist in a month's time. He spent a total of four days on our unit and we witnessed a significant clinical improvement throughout. He was also given a patch for his normal eye in order to prevent amblyopia.

Discussion

In children presenting with acquired strabismus, the abducens nerve is the most commonly affected. The nuclei of the abducens nerve are located in the dorsal pons. Fascicles originating in the nucleus travel within the pontine tegmentum to exit at the pontomedullary junction. From there, the nerve traverses along the subarachnoid space, eventually reaching the posterior cavernous sinus. After exiting the cavernous sinus, the abducens nerve then travels through the superior orbital fissure and enters the orbit to innervate the lateral rectus muscle. As a result of this lengthy path, the abducens nerve is particularly susceptible to traction forces produced by trauma or by elevations in intracranial pressure.

When evaluating a sixth nerve palsy, it is important to determine whether difficulty in abduction is an isolated finding or if other signs and symptoms are present. If there is a history of trauma, if the patient presents with headache, nausea, vomiting, or papilledema, or if the palsy is bilateral, urgent neuroimaging should be obtained. MRI is the preferred modality due to its excellent capability in visualizing posterior fossa structures. However, even in isolated sixth nerve palsies, the American Academy of Ophthalmology currently recommends obtaining an MRI in all children with acquired sixth nerve palsy. This is due to the fact that recent studies have shown neoplasms to be the most underlying cause of abducens palsies, even when no other signs of neurologic involvement are present. As discussed previously, tumors—whether benign or malignant—can compress the abducens nerve anywhere along its path. If imaging is normal, a lumbar puncture should be performed to assess for other etiologies such as pseudotumor cerebri or aseptic meningitis. Trauma and viral infections are the second and third most common causes of abducens nerve

palsies, respectively.

Treatment surrounds addressing the underlying cause as well as careful follow-up by a pediatric neuro-ophthalmologist. While isolated, unilateral abducens nerve palsy often resolves spontaneously, patients are often still treated with steroid therapy if inflammation is suspected, e.g., with a suspected post-viral etiology, as seen in our patient. Alternate patching, which involves patching of the normal eye, is often employed to prevent amblyopia, also known as lazy eye. Prism lens correction has also been used as an effective treatment. Finally, botulinum toxin injected to provide temporary paralysis of the medial rectus—the antagonist of the lateral rectus—has been shown to be an effective treatment option in adults, however, its efficacy in the pediatric population has been debated. If clinical improvement is not seen within six months, strabismus surgery may be indicated.

Summary

A 23-month old, generally healthy male presented with difficulty abducting his left eye and turning of his head to the left on attempted left lateral gaze. He had no complaints of restlessness, nausea, vomiting, or loss of consciousness. There was no history of trauma. His past medical history is unremarkable and his family history non-contributory. He had no unusual exposures or sick contacts, though did experience a brief episode of cough and congestion one week prior to symptom onset.

On physical exam, the patient was found to have difficulty abducting his left eye, but no esotropia noted on primary gaze. As neoplasms are the most common cause of abducens nerve palsies, an MRI was ordered to rule out any tumors that could potentially compress the sixth cranial nerve. Though there was no history of trauma, MRI also ruled out any possible base of skull fracture, another possible cause of abducens palsies. A lumbar puncture was then performed to rule out other etiologies such as meningitis or pseudotumor cerebri. When results from the lumbar puncture returned normal, it was determined that the etiology was idiopathic, or possibly post viral given the history of what seems like a viral infection a week prior to presentation. This truly was a diagnosis of exclusion as just 9% of all cranial nerve palsies are isolated, and of these, less than half are due to non-neoplastic or non-traumatic processes.

The patient was given a course of steroids with instructions to be followed up by a neuro-ophthalmologist. Throughout his hospital stay, a significant improvement was noted, and he experienced a full recovery over the course of the month.

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Report on the Ebola Epidemic in Central Africa

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Introduction

Ebola Virus Disease (EVD), a viral hemorrhagic fever, is caused by four strains of ebolaviruses, members of the *Filoviridae* family. While there is a fifth proposed strain of ebolavirus (native to the Philippines), only the four African species are known to be pathogenic in humans[1]. Two of these African strains were discovered in 1976, when outbreaks of EVD occurred in Sudan and Zaire, lending the names *Sudan ebolavirus* (SEBOV) and *Zaire ebolavirus* (ZEBOV). ZEBOV was recognized as the deadliest, with a fatality rate of almost 90%[2].

The last major epidemic in West Africa was caused by ZEBOV (2014-2016): similarly, the current outbreak of EVD in the eastern Kivu and Ituri provinces of the Democratic Republic of the Congo is also caused by ZEBOV. The symptoms of EVD typically begin 4-10 days post-exposure, although the actual incubation period may range between 2-21 days[3]. The initial symptoms are usually flu-like, accompanied by diarrhea and vomiting. As the virus progresses, the initial symptoms eventually lead into severe hemorrhagic fever, which may result in multiple organ failure and shock, ultimately leading to death. Symptom progression is very rapid, with untreated patients dying 6-16 days after initial symptomatology.

Disease is spread via bodily fluids (including fluids of bats, as well as from several species of primates believed to be a reservoir for ebolavirus species) and thus preventative measures have focused on: isolating infected patients; decontamination efforts; and attempts to trace persons with whom infected patients have encountered. Since ebolavirus strains are still infectious in corpses, safe burials have been provided for patients who have succumbed to EVD[4].

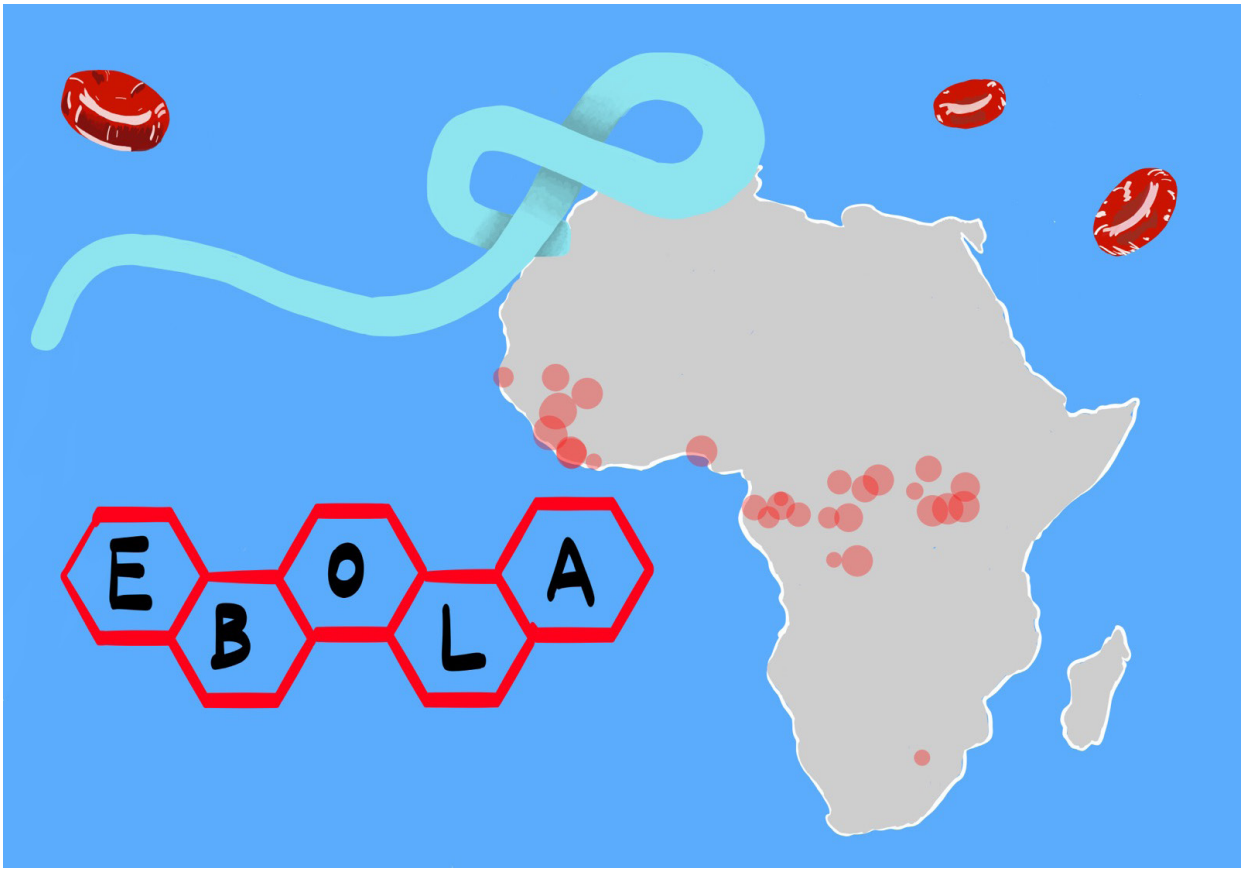
Current Epidemic

The current epidemic in Central Africa began on August 1st, 2018, and at the time of this writing, the World Health Organization (WHO) has reported that there have been 2,831 cases and 1,892 deaths[5]. Continuous efforts have been made to vaccinate all people who may have come in contact with infected individuals in Goma city, the capital of the affected Kivu province. It is believed that 98% of persons who may have encountered infected individuals have been vaccinated (included in this number are those who may have secondary exposure to infected persons and healthcare workers providing medical aid). Other efforts have been made to limit the spread of the disease including, but not limited to: registration of patients in order to monitor them; establishment of eight diagnostic laboratories; decontamination of infected areas; and providing education on disease-prevention and necessary precautions in at risk communities. Additionally, the DRC Ministry of Health in conjunction with the WHO is distributing a new package containing decontamination materials, training manuals, and procedures to workers involved in infection prevention[6].

Treatment

In the past, treatment has been mainly supportive, focusing on the loss of hemostasis caused by hemorrhagic fever of EVD. To this end, fluid replacement therapy has been employed and has been associated with a marked increase in survival for patients, especially if treatment was begun early in disease course[7]. Similarly, comprehensive treatment includes managing the patient's fever, renal issues, and keeping secondary infections under control[8]. However, due to rapid symptom onset and progression, if patients do not receive treatment immediately, their prognosis is very poor.

Because of the high level of severity and lethality of EVD, the WHO, during the 2014-2016 West African outbreak, ethically supported the use of experimental drugs on infected patients[9]. This is remarkable since the only known effective drug that works against viral hemorrhagic fevers, Ribavirin, is ineffective against EVD. Therefore, current interest is high in attempting to develop a new antiviral effective against ebolaviruses[10]. Also, it appears that with this new outbreak of



Artist: *Anais Di Via Ioschpe*

EVD in Kivu and Ituri, there may also be a new breakthrough in developing such an antiviral.

The Pamoja Tulinde Maisha (PALM) study has been investigating four experimental drugs in treating this current EVD outbreak: ZMapp; remdesivir; mAb114; and REGN-EB3. As of early August 2019, the study enrolled 681 patients, and it is being considered by many to be a possible breakthrough in the treatment of EVD. It has recommended that testing be stopped with ZMapp and remdesivir, and instead that all future treatment be conducted with mAb114 and REGN-EB3 due to their potential to increase the chances of survival of infected patients[11]. mAb114 is a monoclonal antibody that was originally isolated from an EVD survivor in 1995. REGN-EB3 is a combination of three monoclonal antibodies, also of human-derivation[12,13]. Monoclonal antibodies like mAb114 work by binding to different sites on the glycoprotein core of the ebolavirus, a key mediator of viral entry, and thereby preventing ebolavirus entrance into human cells[14]. The trial continues, with results expected in the fall; it is hoped that by switching to the exclusive use of these two drugs, the overall prognosis of the disease in those infected will be significantly better.

Conclusion

The nature of EVD transmission means that any outbreak can turn into an epidemic of unmanageable proportions. Yet, through the collaboration of multiple regional governments in the Central African region with several international health organizations, in conjunction with the possibility of new, more effective treatment protocols and preventative measures, it is hoped that this current epidemic will remain contained, and, that treatment will prevent the already high mortality rate from climbing. Depending on the success of the current monoclonal antibodies, future research should focus on isolating other antibodies from current ebolavirus survivors, as well as developing synthetic antibodies that target the glycoprotein core of virus.

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Sexual Transmission of HSV Bronchitis in an Immunocompetent Adult

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Abstract

A 60-year-old MSM patient presented in an outpatient clinic for consultation after an abnormal chest X-ray and hospitalization for hemoptysis. He was seen previously for COPD and is a current, two pack a day smoker. A bronchoscopy showed abnormal white plaques in both the anterior segment of the left upper lobe and in the right lower lobe bronchus. Samples of the right lower lobe lesion showed squamous cell dysplasia and Herpes virus inclusions. The lesions resolved after treatment with oral famciclovir. This report details a very rare disease process in the immunocompetent with a novel route of infection: unprotected oral sex.

Introduction

Herpes Simplex Virus (HSV) infections of the lung are extremely uncommon in the immunocompetent[1]. While they remain rare, cases of Herpetic lung infection are often nosocomial and associated with mechanical ventilation[1]. In cases of HSV infection of the lung, treatment with antiviral medication, such as famciclovir or acyclovir, can be effective in clearing the infection[2,3]. In the context of chronic tobacco use, symptoms such as hemoptysis and shortness of breath can point increasingly towards cancer. Detection remains difficult and symptoms can be non-specific, often leaving cancer high on the differential diagnosis. Though this patient's symptoms and cytopathology closely mimicked squamous cell carcinoma, meticulous history taking and attention to detail spared this patient from undergoing lung resection and from recurrent infection. Using this case, we also propose a route of transmission that has been previously unreported in the clinical literature: unprotected oral sex.

Case

A 60-year-old man presented in outpatient for consultation after a recent hospitalization for pneumonia and an abnormal chest X-Ray. History was notable for COPD, hemoptysis, and tobacco use of two packs per day. Two months prior to this visit, he noted increasing frequency of lung infections and a productive cough with brown sputum and blood. A CT performed during his hospitalization showed dense lingular infiltrate with an area of cavitation. The patient was treated with antibiotics in hospital for three days, improving his symptoms. A four-week follow-up CT was ordered to ensure clearance of the infiltrate. However, this follow-up CT still showed suspicious changes, resulting in a bronchoscopy to elucidate these changes and an alpha-1 antitrypsin blood level test to understand the patient's multiple recent bouts of infection. Highly probable differentials at this time were scarring, atelectasis, alpha-1 antitrypsin deficiency, or cancer.

While the patient had symptomatically returned to baseline, his bronchoscopy revealed abnormal white plaques in the anterior segment of the left upper lobe and right lower lobe bronchus. During the bronchoscopy, the patient had a persistent cough, making biopsy impossible. Brushing and bronchoalveolar lavage (BAL) samples of the right lower lobe lesion were obtained and their cytopathological interpretations were suspicious for squamous cell carcinoma/carcinoma *in situ*. A second bronchoscopy, delayed due to increased shortness of breath and wheezing, was completed 6 weeks later under general anesthesia. Cytology samples were collected again via brushings and BAL from the lesion in the right lower lobe. These samples were interpreted as squamous cell carcinoma *in situ* with one sample noted to have HSV cytopathic effect.

The patient was diagnosed with squamous cell carcinoma. A PET and Ventilation Perfusion scans were ordered, and an aggressive treatment for carcinoma began, including resection of the right lower lobe. However, due to his advanced COPD, it was unclear if the patient would tolerate the latter intervention. Pathology samples were sent to SUNY Upstate Medical University for a second opinion. At this time, an addition to this patient's history revealed

that he had participated in unprotected oral sex with other men. An HIV screen was ordered and came back negative, and a likely route of transmission was predicted to be aspiration of HSV-infected semen.

Pathologists at SUNY Upstate confirmed that tissue samples showed ulcerous exudate consistent with the white plaques. Elsewhere, the mucosa showed dysplasia of squamous epithelium and Herpes viral inclusions. The patient began treatment with oral famciclovir 500mg twice a day. A follow up bronchoscopy was scheduled after a full course of antiviral treatment to ensure the lesion had resolved. This bronchoscopy showed decreased inflammation and decreased mucus. A final tissue biopsy showed no signs of herpetic infection and no squamous carcinoma *in situ* at the site. The patient confirmed that there were no new respiratory issues at that time and he was counseled on safe sexual practice.

Discussion

The similar presentation of HSV bronchitis and lung cancer was particularly salient in this case. It is common knowledge that smoking can lead to lung cancer, with ubiquitous symptoms including persistent cough, hemoptysis, shortness of breath, and recurrent infections, all of which this patient experienced. Analyzed lung lesion biopsies showed squamous dysplasia, which can also be seen in Herpes-infected cells[4]. Resulting from progressive genetic instability and change, the pathogenesis by which smoking can lead to squamous cell carcinoma is step-wise[5]. Histologically, these changes are described as hyperplasia, squamous metaplasia, dysplasia and carcinoma *in situ*[5]. These dysplastic foci disrupt the normal structure and function of the lung's parenchyma. Predisposition to lower respiratory tract HSV infection has been reported to increase with smoking[6] and, as observed in this case, the common risk factor of smoking has a nearly identical presentation of these lesions, complicating the patient's diagnosis. However, pulmonary HSV lesions are lesser known as HSV classically infects squamous epithelial cells[6]. Perhaps most importantly for this patient, the correct diagnosis eliminated risky surgery as a possible treatment.

Though infrequent in the immunocompetent, many have characterized HSV bronchitis before[1-6], but its route of infection via oral sex is unusual. Several cases of immunocompromised[1,7,8] and elderly[2] patients have been previously reported to contract HSV bronchitis. Presentations of immunocompetent HSV bronchitis often are linked to aspiration of saliva[4,7]. While there are many anecdotal cases of bronchitis resolution with antiviral therapy, the efficacy of antiviral therapy remains relatively unstudied and contested[1]. More research is needed to discern the most efficacious treatment in HSV-caused bronchitis.

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Artist: *Olivia Keller-Baruch*
Adapted from SketchyMicro

Localized Vitiligo Occurring on Old Biopsy Scar: A Case Report

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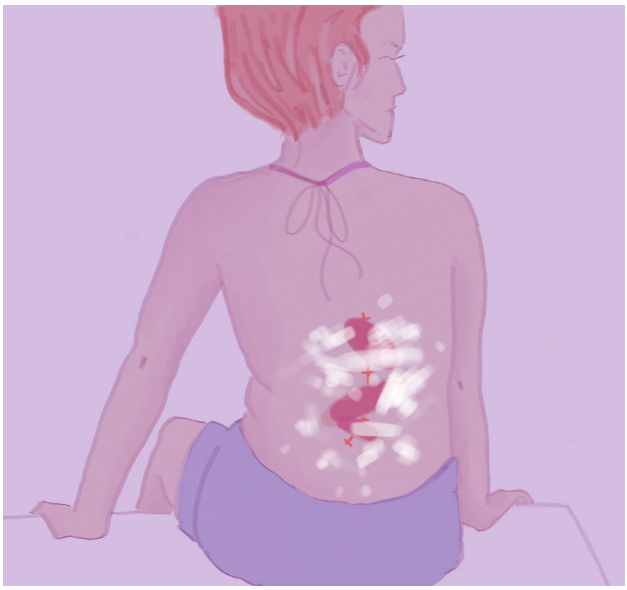
Abstract

Vitiligo is a depigmentation disorder, which involves the interplay of genetic, environmental, and self-destructive mechanisms in its pathogenesis. It results in destruction of pigment-producing melanocytes, which may reveal white macules or patches. A triggering environmental event is thought to cause substantial stress in an already susceptible melanocyte, which elicits an autoimmune response in genetically predisposed individuals. In this report, we describe a novel case of localized vitiligo occurring in an old biopsy scar from 24 years prior.

A 33-year old male presented with tenderness and rapid depigmentation over several weeks of an old biopsy scar on his back. At age 9, the patient had a mole biopsied in the exact location, which led to scarring. The patient denied a change in scar pigmentation until recently when the area turned white. There is a history of excessive sun exposure and sunburns in the area, as well as a family history of malignant melanoma and basal cell carcinoma of the skin. Physical examination revealed a non-scaly depigmented patch occurring in an old biopsy scar involving medial scapular back. A differential diagnosis of halo nevus was made, and a biopsy was performed. Following biopsy results, the patient was clinically diagnosed with recent vitiligo occurring in an old biopsy scar.

Background

Vitiligo is a depigmentation disorder of the skin, hair, or mucosa, which reveals white macules or patches due to destruction of pigment-producing melanocytes.[1,2] This response is generated by a complex interaction of genetic, environmental, and self-destructive factors.[3] An initiating environmental event such as severe sunburns is thought to cause substantial stress in an already susceptible melanocyte, which elicits an autoimmune response in genetically predisposed individuals.[4]



Artist: *Niko Morozov*

A diagnosis of vitiligo is known to confer a higher risk of disease to immediate relatives. Vitiligo affects 1% of the general population, whereas the risk of an affected patient's sibling and identical twin for developing the disease is 6% and 23% respectively.[5,6] The risk of developing other autoimmune diseases, like diabetes, autoimmune thyroiditis, pernicious anemia, and Addison's disease is also subsequently increased.[1] This suggests that vitiligo is best-classified as an autoimmune disease.[7]

Oxidative stress poses a potential environmental risk which may play a role in the disease pathogenesis. Stress may result from overproduction of pro-oxidant species, and/or creation of antioxidant chemicals via reduction reactions.[8] Melanocytes are constantly exposed to stressors, including ultraviolet radiation and harmful chemicals, and pathologic conditions such as inflammation and cancer that also increase the production of reactive oxygen species (ROS). Healthy melanocytes are capable of responding to these stressors, whereas melanocytes in patients with vitiligo are more vulnerable.

Decreased levels of catalase have been found in melanocytes of patients with vitiligo.[9,10] Catalase is a key enzyme in the degradation pathway of hydrogen peroxide (H_2O_2) and in the catalyzation of other antioxidants that protect melanocytes from self-destructive ROS, like

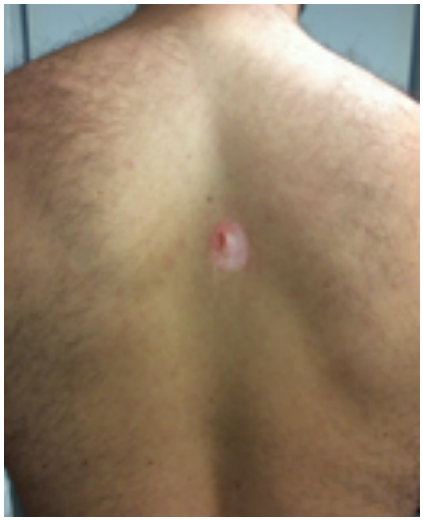


Fig. 1: *A clinical photo of a non-scaly depigmented patch occurring in an old biopsy scar in the medial scapular back*

glutathione peroxidase and glucose-6-phosphate dehydrogenase. This suggests the involvement of oxidation-reduction defects in the disease. Experimental evidence supports the idea that patients with vitiligo initially experience some form of stress, triggering the immune system to attack the body's own melanocytes. Many people report first noticing vitiligo symptoms following traumatic events, periods of stress. or severe sunburns.[11] We report the case of localized vitiligo occurring in an old biopsy scar from 24 years prior.

Case Presentation

A 33-year old male presented with a painful hypopigmented scar which he reported developing a few days prior to consultation. At age 9, the patient had a mole biopsied in the same location, which led to scarring. The biopsied mole was determined to be benign. The patient denied a change in scar pigmentation until recently when the area lost pigmentation and turned white. This change in pigmentation and pain concerned him. When questioned, he denied itching. The patient reported a history of excessive sun exposure and sunburns in the area. There is a family history of malignant melanoma in an aunt and basal cell carcinoma of the skin in his biological mother.

Physical examination showed a non-scaly depigmented patch occurring concordant with the biopsy scar on the medial scapular back. No other halo nevi or evidence of vitiligo noted in the area. A careful inspection and palpation of the area was performed, and skin was of normal temperature, turgor, and texture. There were no suspicious skin lesions, rashes, or depigmented areas noted on a total skin examination.

A differential diagnosis of halo nevus was initially made, and a confirmatory shave biopsy of the patch was performed. Bacitracin and a bandage were applied to the site. The patient was instructed to apply Bacitracin BID for 2-3 days, and to begin clobetasol propionate cream BID once biopsy site had healed. The patient was subsequently lost to follow up.

The shave biopsy was received in 10% buffered formalin and measured 9x5x1 mm in one cassette. There was a proliferation of fibroblasts aligned parallel to the skin surface interposed among linearly arranged thickened collagen bundles and small blood vessels. Most notably, there was an absence of melanocytes and melanin pigment within the epidermis extending over and slightly beyond a zone of fibrosis. Consequently, the clinical diagnosis was updated to new-onset vitiligo occluding an old biopsy scar.

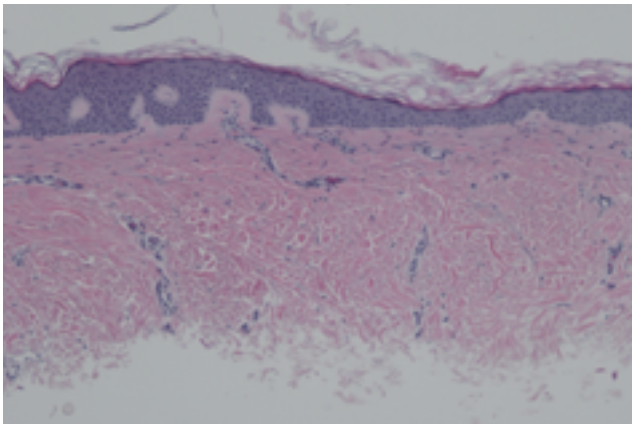


Fig. 2: *There is an absence of melanin pigment and melanocytes within the epidermis overlying a zone of fibrosis.(H&E, 10x objective)*

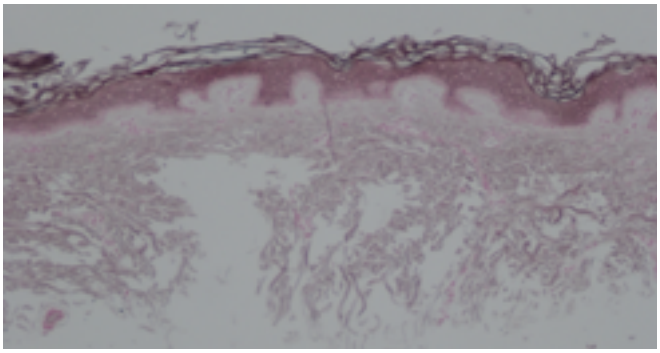


Fig. 3: *The absence of melanin pigment within the epidermis is highlighted with a Fontana-Masson stain for melanin pigment. (Fontana-Masson, 10x objective)*

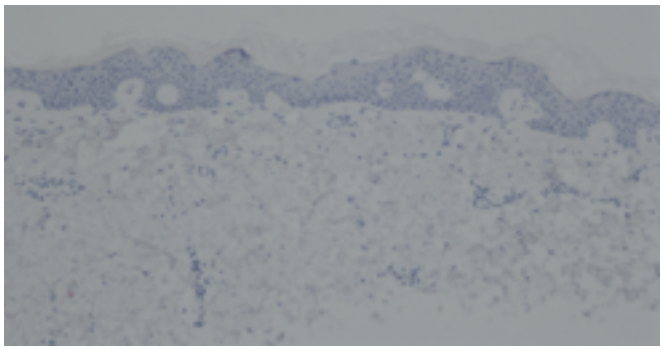


Fig. 4: *The absence of melanocytes within the epidermis is highlighted with a Melan-A immunoperoxidase stain. (Melan-A, 10x objective)*

Discussion

Current evidence suggests that vitiligo is an autoimmune disease with a genetic predisposition that may be triggered by environmental stressors. Increased prevalence among immediate relatives has been established. Additionally, environmental risk factors including ultraviolet radiation and harmful chemicals are known to increase the production of harmful ROS. This finding, when combined with decreased catalase levels in susceptible melanocytes found in patients with vitiligo, leads us to posit a pathogenic mechanism. Deo *et al.*[11] showed that many patients initially notice vitiligo following severe sunburns. This supports our theory that vitiligo may be caused by decreased catalase and severe sunburns. However, an established scar (such as one due to a twenty-five-year-old biopsy) coinciding with later instance of vitiligo has not been reported in the literature. Yet, we may consider the biopsy as a potentially triggering environmental event. It must be considered that the patient has a family history of melanoma and basal cell carcinoma of the skin, but not one of autoimmune disease.

In conclusion, although a genetic predisposition of autoimmune disease or catalase levels could not be established, we theorize that a local autoimmune attack on melanocytes could have been precipitated by a recent history of excessive sunburns in the area and excessive scar tissue from the biopsy, leading to vitiligo formation in this patient.

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Median Arcuate Ligament Syndrome and its Associated Conditions

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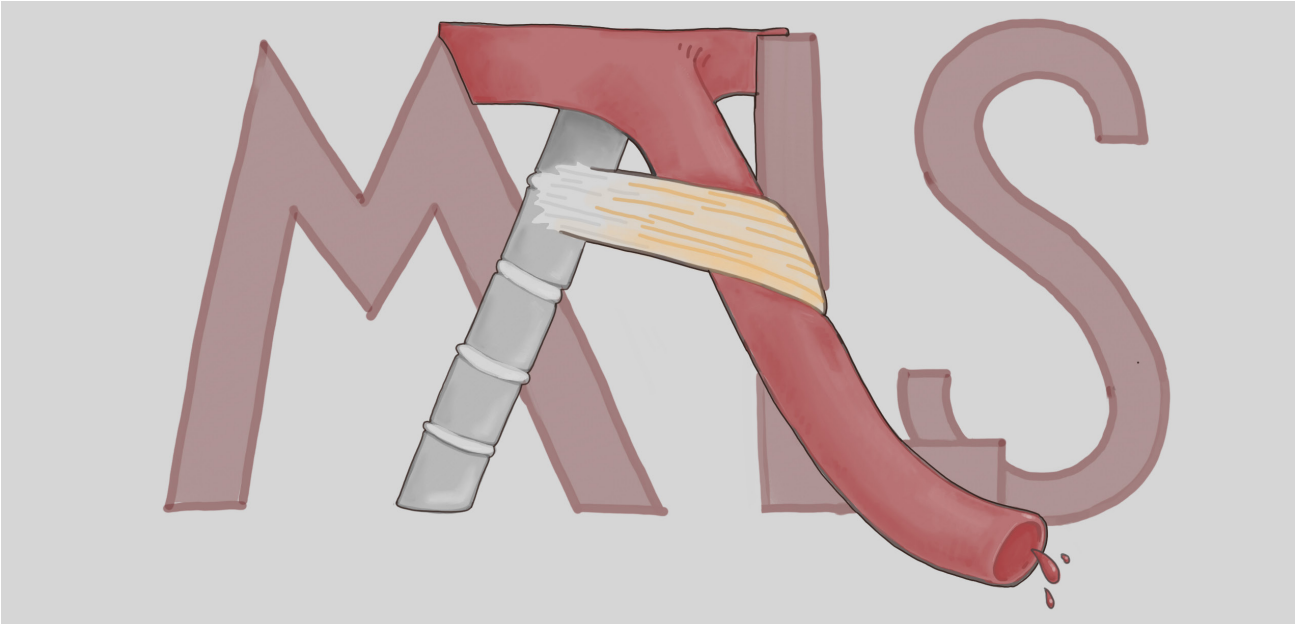

Abstract

The risk factors and associated conditions of median arcuate ligament syndrome (MALs) have not been well characterized in the literature. In this study we aim to investigate the presentation and outcomes of MALS patients, with an emphasis on the prevalence of other uncommon disorders. Data from patients with MALs who underwent surgery between 2013 and 2018 were collected and compiled into a retrospective database and analyzed. Eleven patients were identified, and seven among them underwent diagnostics to evaluate gastric emptying. Five of these seven patients (71.4%) had radiographic evidence of delayed gastric emptying. Four of the eleven patients (36.4%) were found to have anatomic abnormalities of their visceral vasculature. Two of the eleven patients (18.2%) were found to have connective tissue disorders; both had Ehlers-Danlos syndrome. Three of the eleven (27.3%) had a diagnosis of postural orthostatic tachycardia syndrome, a condition characterized by large changes in blood pressure when going from a supine to a standing position. This is the first case series to report on an association between MALs and delayed gastric emptying. We also explored the relationship between MALs and other disorders, including visceral vascular abnormalities, Ehlers-Danlos syndrome, and postural orthostatic tachycardia syndrome. It is notable that these conditions are more prevalent in the MALs population than in the general population, suggesting a possible pathophysiologic relationship.

Introduction

Median arcuate ligament syndrome is a rare disorder characterized by anatomic compression of the celiac trunk and plexus by the median arcuate ligament. The anatomic variant leading to MALs was first described by Lipchitz et al in 1917.[1] This anatomy is thought to be present in 3.5% of the population,[2] but it was not until 1963 that Harjola et al[3] described a clinical manifestation of this variant anatomy; a patient suffered chronic post prandial pain, which resolved following surgical release of the median arcuate ligament and division of the celiac ganglion. This disorder has been described in the literature as causing a constellation of symptoms, including postprandial abdominal pain, sitophobia or the fear of eating, nausea, vomiting, diarrhea, and unintentional weight loss.

Diagnosis of median arcuate ligament syndrome is one of exclusion, as the symptoms

are varied, vague, and may mimic other conditions. Patients being evaluated for median arcuate ligament syndrome should therefore undergo a complete gastrointestinal evaluation to rule out other pathologies.[2] If MALs is still suspected following these diagnostics, patients should undergo angiography and either CT or MR to evaluate celiac anatomy, as well as dynamic duplex ultrasound in order to functionally assess celiac trunk velocity. During expiration, the course of the celiac trunk moves superiorly, which may increase the degree of compression by the median arcuate ligament and thereby increase duplex velocity. This functional variation is useful in further identifying patients with MALs.[4]

While surgical release remains the mainstay treatment for MALs, the pathophysiology is not fully understood. The primary theories proposed are related to vascular insufficiency and neuropathic pathology. Some propose that compression of the celiac trunk by the MAL and subsequent alimentary ischemia result in the aforementioned constellation of symptoms. The neuropathic theory postulates that compression of the celiac plexus leads to overstimulation of the ganglion, leading to irritation of the sympathetic pain fibers, splanchnic vasoconstriction, and ischemia.[2,5]

Given the rarity of this condition and the unclear mechanism, the risk factors, associated conditions, and sequelae of MALs have not been well described. Here we present a single center experience with MALs, with a focus on the possible association between this syndrome and other rare disorders. These include gastroparesis, Ehlers-Danlos syndrome, postural orthostatic tachycardia syndrome, and visceral vascular anatomic variants.

Materials and Methods

All cases of median arcuate ligament releases were collected from between 2013 and 2018 from a single tertiary care center by three attending surgeons. Patients were preoperatively evaluated using CT and MR angiography, and dynamic duplex ultrasound to make the diagnosis of median arcuate ligament syndrome. To make a diagnosis of exclusion, patients also underwent extensive preoperative evaluations to rule out alternative causes of their symptoms. As part of these pre-operative evaluations, most patients underwent gastric emptying studies and upper gastrointestinal studies. Patient demographics, symptomatic, imaging, operative, and outcomes data were compiled into a retrospective database and analyzed. Statistical analysis was performed using SPSS v20.

Results

There were 11 patients identified in this study. The median age of the cohort was 37 and the median BMI was 23. The majority of patients (10) were female. Two of the 11 (18.2%) patients had diagnoses of Ehlers-Danlos syndrome. Three of the 11 (27.3%) were found to have postural orthostatic tachycardia syndrome. Patients were followed for a median of 6 months. Diagnoses of MALs were made based on preoperative symptoms and angiography. All patients had preoperative symptoms, with 11 (100%) endorsing epigastric pain. Preoperatively, 10 (90%) patients reported post-prandial pain, 5 (45%) reported sitophobia, and 7 (63%) reported nausea. Seven patients (63%) presented with weight loss, with a mean weight loss of 9.31 kg (6.8-20).

Eight patients were evaluated preoperatively with studies to evaluate gastric emptying, upper GI series (4), and nuclear medicine gastric emptying studies (7), and 3 patients were evaluated for both. Of these 8 patients, 5 (62%) were found to have delayed gastric emptying on either upper GI series or nuclear medicine gastric emptying study. Four patients were evaluated with upper GI series, and 2 (50%) showed delayed gastric emptying. Seven patients underwent nuclear medicine gastric emptying studies, with 3 (42%) showing delayed gastric emptying as defined by >60% retained contents at 2 hours or >10% retained content at 4 hours.

All patients were evaluated with CT or MR angiography preoperatively (8 and 3 respectively), demonstrating celiac trunk stenosis. Four (36%) patients were found to

Table 1: Demographic Characteristics

	n=11
Age (y) (mean±SEM [median])	43.3±5.93 [37]
BMI (mean±SEM [median])	25±2.7 [23]
Female (%)	10 (90.9)
Comorbid Conditions	
Ehlers-Danlos Syndrome (%)	2(18.2)
Postural Orthostatic Tachycardia Syndrome (%)	3(27.3)
Diabetes	1 (9.09)

Table 2: Preoperative Symptoms

	n=11
Post-prandial pain (%)	10 (90.9)
Sitophobia (%)	5 (45.5)
Nausea (%)	7 (63.6)
Weight loss (%)	7 (63.6)
Weight lost (kg) (mean±SEM [median])	10.8±3.91 [7.9]

have abnormal mesenteric vasculature. These variants included: acute angulation of the superior mesenteric artery, gastroduodenal artery aneurysm, replaced right hepatic artery, and variant hepatic artery anatomy with the left hepatic artery arising from the left gastric artery, as well as the right hepatic artery arising from the gastroduodenal artery. Patients were additionally evaluated using dynamic duplex ultrasound, which showed mean celiac trunk expiratory systolic velocity of 320 (152-473) cm/s and a mean expiratory diastolic velocity of 99.9 (36-211) cm/s.

Table 3: Imaging Findings

Angiography (CT:MRI)	**n=11(8:3)**
Celiac trunk stenosis	11
Abnormal mesenteric vasculature	4 (36.4)
Dynamic duplex ultrasound	**n=9**
Systolic celiac trunk velocity (cm/s) (mean [range])	320 (152-473)
Diastolic celiac trunk velocity (cm/s) (mean [range])	99.9 (36-211)
Nuclear medicine gastric emptying study	**n=7**
Delayed gastric emptying (%)	3(42)
Upper GI study	**n=4**
Delayed gastric emptying (%)	2(50)

Table 4: Postoperative findings

	n=10
Length of Stay (d) (median [range])	8 [2-64]
100% resolution of symptoms	4 (40.0)
75% resolution of symptoms	1 (10.0)
50% resolution of symptoms	2 (20.0)
0% resolution of symptoms*	3 (30.0)

*2 of 3 patients with symptoms refractory to MAL release had history of prior foregut surgery prior to MAL release

Median arcuate ligament release was performed both laparoscopically and robotically (7 and 4 respectively). Dissection of the celiac artery was performed in an inferior to superior fashion in 7 patients, and in a superior to inferior fashion in 4 patients. Intraoperatively, all 11 patients demonstrated compression of the celiac trunk by the median arcuate ligament. The mean length of division of the median arcuate ligament was 4.5 cm (range 2.5-6). The celiac ganglion was divided in all cases.

There was one complication of bleeding from a small arterial branch of the aorta, which was sufficiently controlled by applying pressure. There were no reoperations. Median length of stay was 8 days (range 2-64).

Four patients had complete resolution of symptoms as defined by denying continuation of all noted preoperative symptoms after MAL release. One patient reported a 75% resolution of symptoms, with resolution of preoperative nausea, abdominal pain, and sitophobia, but continuation of abdominal bloating. Two patients reported 50% improvement of their symptoms and 3 reported no symptom improvement post-operatively. Of note, 2 of the 3 patients with recalcitrant symptoms had undergone prior foregut surgery; one underwent a gastrojejunostomy and the other a gastric sleeve. One patient was lost to follow up.

Discussion

Based on the existing literature, our cohort was consistent with the demographics and symptoms typical of MALs. MALs has been reported in the literature as a disease that is predominantly found in women (with a ratio of 4:1 in the literature, 10:1 in our cohort), and in patients 30-50 years old.[6] In the literature, pain from MALs was most commonly localized to the epigastrium,[7,8] a finding which was present in all of our patients.

The association between MALs and gastroparesis was first suggested in the literature in a 1997 case report by Balaban et al;[9] a patient with gastroparesis was diagnosed with MALs and experienced resolution of symptoms following surgical release of the median arcuate ligament. This association was further explored by Trinidad Hernandez et al[6] in a 3-patient series. Our study represents the largest investigation of the relationship between MALs and gastroparesis to date, as well as the only study to evaluate this association in a general cohort of MALs patients. Of the MALs cohort who underwent studies of gastric emptying, we found that 62% of patients showed delayed gastric emptying in functional imaging. This prevalence of delayed gastric emptying in the MALS population is much greater than in the general population, where prevalence is estimated to be 6.3 in 100,000 patients (<0.01%).[10] While our series is too small to draw a statistically significant association between MALs and gastroparesis, we hypothesize that this delay in gastric emptying may be a neurogenic sequela of celiac ischemia from compression by the median arcuate ligament. This mechanism is supported by the reversibility of the associated gastroparesis after MAL release.[3]

Similarly, Ehlers-Danlos Syndrome is

thought to affect 1 out of every 5000 live births (<0.01%),[11] however in this MALs cohort 2 of the 11 (18.2%) patients carried a diagnosis of this disorder. While we cannot draw conclusions with regard to an association between these conditions, a shared etiology in disorders of connective tissue/collagen production and processing is in line with the hypothesis of MALs as a fundamentally vascular issue.

One to three million Americans (<0.01%) are thought to carry the diagnosis of postural orthostatic tachycardia syndrome (POTS),[12] a much lower incidence than was found in our MALs cohort (27.3%). While the series size is limited, this could suggest that there may be a connection between these two conditions. This suggestion of a link between POTS and MALs is a novel one and to date there has been no description in the literature of a connection between the two disorders.

Four (36%) patients in the cohort had variant vascular anatomy. While there was not a common variant amongst these abnormalities, the increased incidence of these abnormalities is in line with the theory that MALS is fundamentally an expression of a disorder of the vasculature.[2] Another theory proposes that abnormal collateral vessels may form with more frequency in patients with MALs, secondary to the relative ischemia from compression of the celiac trunk.[13]

Intraoperatively all surgeons elected to both perform release of the median arcuate ligament and transection of the celiac ganglion, addressing both the possible vascular and neuropathic component of the disease, as has been recommended in the literature.[5] Of these patients, 4 (40%) had complete symptomatic relief and 7 (70%) had relief of the majority of their symptoms. This is in line with the data from Reilly *et al*,[14] which suggests a curative rate of 56% in patients who undergo operative vascular release alone, and a rate of 77% of those that receive a release along with vascular reconstruction or dilation. Similarly, Grotemeyer *et al*[15] reported a 73% cure rate in their patients who underwent vascular release as well as selective additional vascular interventions. It is important to note that the operative management of both Reilly et al and Grotemeyer et al focused on vascular pathology and did not address the celiac ganglion. In the series by Kohn *et al*,[16] both vascular release and division of the celiac ganglion were performed with a reported 100% cure rate; however, the sample size of this series was limited at 6 patients.

This study is limited by its small population size and retrospective nature. The small sample size was attributed to using the patients of only three attending surgeons at a single tertiary care center. A better powered study is required to resolve statistically significant differences between the proportion of patients with these rare conditions in MALs population, as well as compared to the general population.

Overall, MALS is a rare disorder that has been relatively overlooked. It is associated with many conditions, most commonly delayed gastric emptying and visceral vasculature abnormalities. We were able to determine that these conditions occur at higher rates than in the normal population, but our small sample size hinders us from determining if this is statistically significant.

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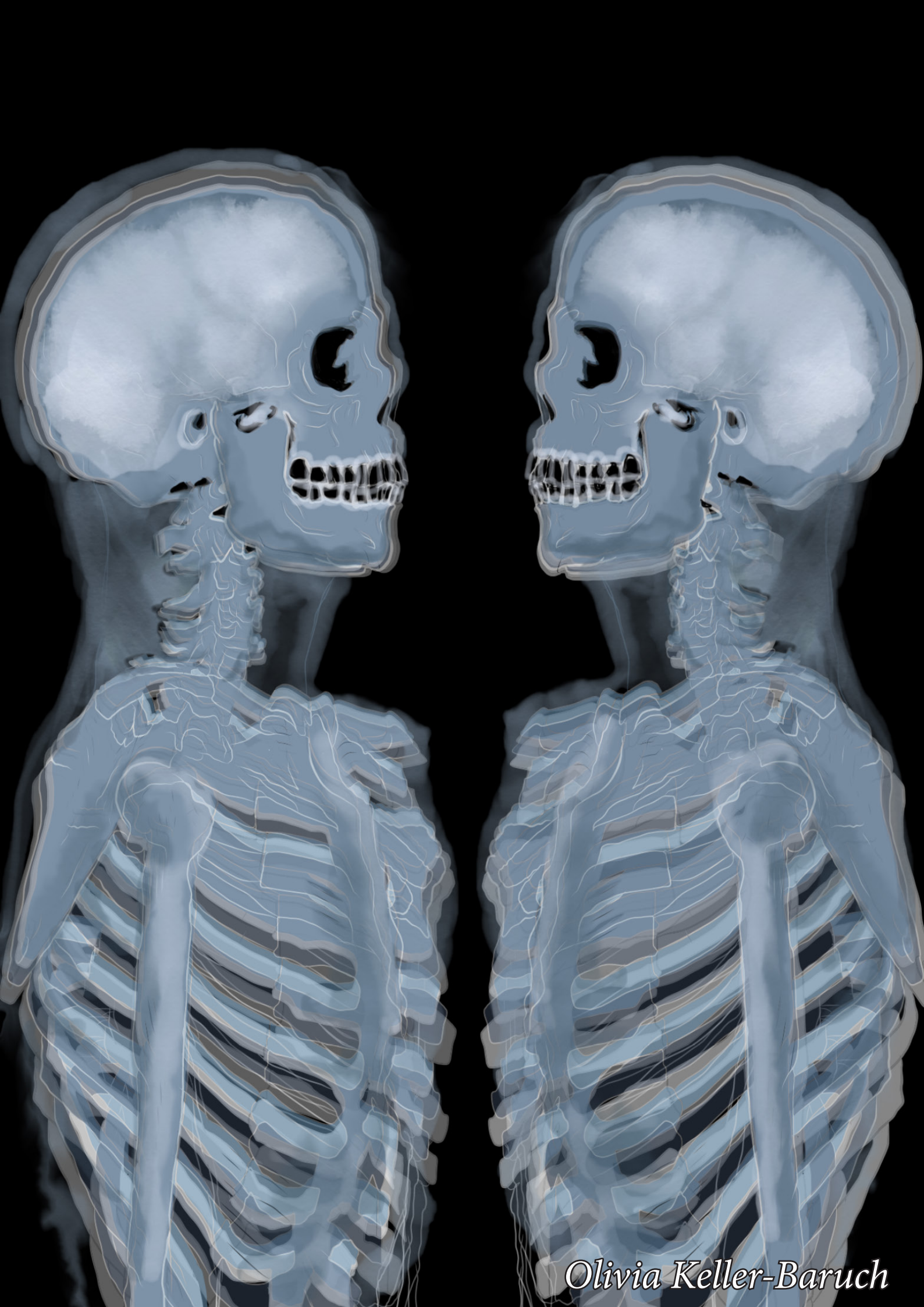
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