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EDITORIAL

AXILLARY WEB SYNDROME, THE LOST CORD, AND LINGERING QUESTIONS

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Axillary Web Syndrome (AWS), sometimes also referred to as cording lymphedema, is an unfortunate and frustrating complication that can follow operation and specifically axillary lymphadenectomy for the treatment of breast cancer. Although most lymphologists are familiar with AWS, the mechanism(s) of its origin and development are largely unknown, there is disagreement about what the cords are composed of, and worldwide treatments vary widely. In this issue, the two lead articles focus on imaging the cords and offer insights into their composition.

Olivier Leduc and his team follow up on their 2009 article (1) describing further the clinical features of the cord and reporting (2) images of the cord by both ultrasound (US) and magnetic resonance imaging (MRI). The second article by Linda Koehler and her colleagues looks specifically at US imaging of the cord and uses a blinded radiologist as a mechanism to avoid observer bias in image interpretation (3). Imaging of the cord is not easy with specific techniques described by Leduc et al and lack of identification of the cord using a blinded radiologist reported by Koehler et al. Two other groups worldwide have also found difficulty in imaging the cord using US (personal communication).

What is the cord? Despite the obvious external appearance of the cords to the patient and management team, a clear understanding of what the cord is composed of remains elusive as well as whether all cords are the same (perhaps a complicating factor). Various opinions have been put forth ranging from a lymphatic or vein or a lympho-venous structure with other tissue possibilities such as nerves or fascia. Both Leduc and Koehler with their colleagues demonstrate with their imaging techniques that their findings are inconsistent with an origin from a vein, nerve, or the fascia, and both suggest that the cords are lymphatic in origin. Although they report that normal lymphatic vessels would be difficult to visualize using these techniques, it remains confusing as to why the cords can't be seen despite being clearly visible. A possible answer to this question may be found in studies of cord biopsies. This procedure would raise ethical issues since there is no medical benefit (and possible risk to aggravate the process) to biopsy the cords, which are thought to be self-limiting to the patient. Nonetheless, there are a few reports from tissue biopsies in the literature. One of the earliest is the report by Moskovitz et al (4) who biopsied only 4 patients and found fibrin

within lymphatics and superficial veins and proposed that the lympho-venous damage resulted in thrombosis of the larger veins OR lymphatics. Similarly Reedjik et al (5) proposed that the cords consisted of lymphatic vessels which had recanalized over time, although they also showed confounding histologic features including thrombotic occlusion (lack of blood or elastic lamina negating a venous origin). What is missing from these reports is the knowledge and use of specific lymphatic tissue markers which are now employed by lymphologists. A recent report by long-time lymphologist Gail Gamble and honorary lymphologist Mark Pittelkow and their team at Mayo Clinic (6) reported on a single biopsy from a patient with AWS. They were able to use the lymphatic-specific marker D2-40 to positively identify the structure as containing lymphatic endothelium. This report is only of a single case and possibly more important is that the origin of the AWS was from a furuncle and not the result of an axillary operation (although clinical presentation of the cord was the same and mirrors the first report from Leduc and colleagues). Interestingly, their report reminds us of lingering questions as to the origin/development of the cord by pointing to possible infection and inflam-could these also be a possibility in other AWS cases?

So where does this leave us at the present time? The imaging results do point away from a pure venous origin and confusion with Mondor's disease may be reduced (although some reports on Mondor's disease point more to lymphatic vessels rather than veins). The imaging and histologic reports do not support a nerve origin. The venous system involvement is still possible from histologic features (less supported by imaging), but not likely to be confirmed because of the paucity of biopsies (and no larger series is or is likely to be on the horizon) and possibly more importantly the lack of certainty that all investigators are examining the same structure. Since the pathogenesis is still not understood, could "early" AWS look like an occluded lymphatic vessel and "late" AWS look like a confusingly fibrotic structure that has recanalized into a vessel? The report by Leduc also raises some more interesting questions on the origin of the AWS. They demonstrate with their images that the cords are contiguous with lymphatic structures such as a lymphocele and that the cord runs directly into the lymphadenectomy scar. If AWS is the result of damage to the lymphatic system from operation, why don't we see this in other areas of the body? Is there too much interposed "soft tissue" for these cords to appear on the legs (somewhat supported by reports that patients with higher BMI do not manifest the cord)? Finally, what does it mean if you can "see" the structure with your eyes, but you can only "image" the structure with great difficulty?

What is more important to the patient and also concerning to the treatment team is what to do with the cord after it appears. This is clearly an area with many more questions than answers. One of the more complete examinations on the incidence and course of AWS was performed by Torres Lacomba and her colleagues (7). They carefully followed patients looking for the cord and found an incidence of 48.3% (if all groups were this careful and frequent in examination would the "true" incidence be close to this value?). They briefly described their physical therapy treatment and reported (not in a clinical trial) that a shortening of 6-8 weeks could be achieved over the self-limiting 3 month time frame for resolution. Other groups also report this self-limiting aspect of AWS. So what is the best or most appropriate treatment? In my personal unvalidated and informal survey of physicians, therapists, and patients worldwide, I have found no clear answers. One thing that is obvious from patients on different continents is that despite what the medical world believes and reports, for some patients (exactly how many no one knows!) AWS never goes away. I have personally seen

the cords in patients many years after the operations. Perhaps the patients just stop mentioning it to the medical team? Perhaps it ceases to bother them unless the arm is positioned in full abduction? Treatment at centers worldwide also varies greatly. Some believe that inflammation is a leading factor in the development of AWS and will prescribe anti-inflammatory agents while others add to this antibiotics to reduce the incidence of infection (of course, no studies exist to show infections- but theories are prevalent and some evidence like the furnucle above do exist). Others take a more physical approach to the cord with manual stretching, and both physicians and therapists report hearing the "pop" of the cord as it breaks and then releases. What is this sound? What is "breaking"? Does fibrosis make a noise when it is loosened? Are there pockets of air or fluid in the recanalized vessels? Kepics (8) has proposed a range of possible physical treatment approaches- although none supported by a clinical trial. Finally, some centers just leave it alone with the confidence that it is self-limiting and will go away on its own. Is this the most judicious approach? The treatment clue from Torres Lacomba suggests therapy may be helpful.

Will we ever get these answers and the further questions they will uncover? Till then, patients and their care teams worldwide await definitive information and future discoveries about the "lost cord" of AWS.

REFERENCES

- 1. Leduc, O, M Sichere, T Snoeck, et al: Axillary web syndrome: Nature and localization. Lymphology 42 (2009), 176-181.
- Leduc, O, E Fumière, S Banse, et al: Identification and description of the Axillary Web Syndrome (AWS) by clinical signs, MRI and US imaging. Lymphology 47 (2015), 164-176.
- 3. Koehler, LA, DW Hunter, TC Haddad, et al: Characterizing Axillary Web Syndrome: Ultrasonographic efficacy. Lymphology 47 (2015), 156-163.
- Moskovitz, AH, BO Anderson, RS Yeung, et al: Axillary web syndrome after axillary dissection. Am. J. Surg. 181 (2001), 434-439.
- 5. Reedijk, M, S Boerner, D Ghazarian, et al: A case of axillary web syndrome with subcutaneous nodules following axillary surgery. Breast 15 (2006), 411-413.
- 6. Rashtak, S, GL Gamble, LE Gibson, MR Pittelkow: From furnacle to axillary web syndrome: Shedding light on histopathology and pathogenesis. Dermatology 224 (2012), 110-114.
- Torres Lacomba, M, OM del Moral, JL Coperias Zazo, et al: Axillary web syndrome after axillary dissection in breast cancer: A prospective study. Breast Can. Res. Treat. 117 (2009), 625-630.
- Kepics, JM: Physical therapy treatment of axillary web syndrome. Rehabil. Oncol. 22(2004) 21-22.

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