relationship with the male sex between 40 and 60 years of age.[4] Its etiology has not yet been completely clarified. However, an association has been observed with factors such as prolonged exposure to ultraviolet rays, radiation, smoking, and contact with toxins; some of which are present in our patient. Recurrence was demonstrated in 7 of 12 patients with conjunctival and bulbar UPS, of which 3 ended in exenteration.[2]

Despite the great development of IHC and the categorization and standardization of diagnostic techniques, positive CD68 is only present in 70% of cases.[5] This is due to the great histologic variability of this type of tumor, which, in the vast majority of cases, is benign. Therefore, those with some malignant potential[6] must be differentiated from conjunctival tumors such as carcinomas, melanomas, and lymphomas.[3] Noninvasive techniques such as OCT and UBM are gaining popularity in these pathologies, unlike techniques such as computed tomography and magnetic resonance imaging, which are only useful in cases of suspected ocular or orbital infiltration.[5] Despite a low recurrence in benign cases, up to 60% has been reported in tumors with malignant behavior. In this last group, aggressive management is required, which includes surgical reintervention, associated or not with topical chemotherapy; immunotherapy; radiotherapy; and, in some cases, more radical treatments such as enucleation and even exenteration, due to their metastatic power.[7]

UPS is an extremely rare tumor at the conjunctival level, usually with a perilimbar presentation. Therefore, the histopathologic study associated with IHC will help us provide an adequate and individualized diagnostic and therapeutic approach, which in some cases can lead to radical treatments, as occurred with our patient.

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OPEN

Doxycycline Sclerotherapy of Mandibular Aneurysmal Bone Cysts: A Brief Clinical Study

Megan N. Wong, BS, and James W. Murakami, MD

Abstract: Aneurysmal bone cysts (ABCs) are benign bone tumors typically affecting children. Mandibular ABCs can be difficult to treat surgically, given their sensitive anatomic location and functional and cosmetic impacts. This report presents 3 pediatric patients with mandibular ABCs successfully treated with image-guided percutaneous doxycycline sclerotherapy. The first 2 patients presented with pain and swelling, whereas the third was diagnosed incidentally. Sclerotherapy was the sole treatment for cases 1 and 2, whereas case 3 had sclerotherapy after recurrence following prior surgeries. In all 3 patients, clinical symptoms resolved, and stable bone healing was documented on long-term follow-up. There were no functional or cosmetic complications. Doxycycline sclerotherapy is a safe and viable treatment for primary and recurrent mandibular ABCs.

Key Words: Aneurysmal bone cyst, doxycycline, mandible, sclerotherapy

Aneurysmal bone cysts are benign but locally aggressive lytic bone tumors typically affecting patients in their second decade of life.[1] These lesions predominantly arise in the metaphyses of long bones, but 2% to 6% of cases occur in the face.[1] Surgical resection is the current standard treatment, however, lesions in functionally complex locations are challenging to completely resect while avoiding morbidity.[1] Medical management with denosumab, a monoclonal antibody that blocks osteoclast function, is a proposed alternative, but there are side effects, especially in children.[2] In 2013, doxycycline sclerotherapy was described as a treatment for primarily appendicular ABCs.[3] This technique has been successfully applied in anatomically difficult locations such as the cervical spine.[4] Due to their proximity to sensitive anatomy, mandibular ABCs pose surgical challenges, risking oral function and risking unwanted facial scarring.[5] This study presents 3 patients with mandibular ABCs successfully treated with doxycycline sclerotherapy.

CASE 1

An 11-year-old girl presented with left facial pain and swelling with a magnetic resonance scan demonstrating a 3.5 cm diameter lytic, expansile, left mandibular ramus tumor with internal fluid-fluid levels (Fig. 1A). Given the presumptive diagnosis of an ABC, the patient was referred for image-

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guided biopsy and doxycycline sclerotherapy. She underwent an ultrasound-guided biopsy and doxycycline sclerotherapy under ultrasound and fluoroscopic guidance using technique previously described (Fig. 1B).[4] Doxycycline (40 mg/mL) in normal saline was mixed 50:50 with 25% human serum albumin (Grifols Therapeutics, Clayton) and then agitated with an equal volume of air to generate a stable foam with a final doxycycline concentration of 10 mg/mL. A total of 80 mg of doxycycline was used. In addition, 2.5 mL of calcium triphosphate bone void filler (Vitoss, Stryker) was mixed with the doxycycline and albumin mixture to fill two of the largest bone cavities.

Pathology confirmed the ABC diagnosis, and she underwent 3 more sclerotherapy sessions over 6 months under computed tomography (CT) guidance using 70 to 200 mg of doxycycline without bone void filler as the cavities became progressively smaller (Fig. 1C). By the last treatment, all symptoms had resolved. At 4-year follow-up, she remained asymptomatic, and there was no imaging evidence of a recurrence (Fig. 1D).

CASE 2

A 10-year-old girl presented with right mandibular swelling and pain. Her outside hospital work-up included CT and magnetic resonance scans, followed by a CT-guided needle biopsy yielding the diagnosis of a solid-variant ABC. Four months later, she underwent repeat biopsy and doxycycline sclerotherapy as in case 1. This second biopsy confirmed the ABC diagnosis. The tumor had grown significantly between the two biopsies, nearly doubling in diameter. She underwent 7 more sclerotherapy sessions over 2.75 years (doxycycline dose range was 80–180 mg) with the lesion resolving clinically and by imaging at the last treatment. At her 5-year follow-up, she had no clinical or imaging recurrence. Imaging was like case 1.

CASE 3

A 9-year-old girl had a head CT after trauma which incidentally found a 2.5 cm diameter lytic lesion in the left mandibular ramus. Two months later, she underwent open surgical biopsy and curettage yielding the diagnosis of an ABC. The lesion recurred 7 months later, and she underwent a left segmental mandibulectomy from the mid body through the condyle with repair using a right fifth rib graft. Surgery was complicated by temporary left seventh nerve palsy. At 6-month follow-up, she had no symptoms referrable to the mandible but pain at the bone graft donor site. At 18-month follow-up, she had another ABC recurrence clinically and by imaging (Fig. 2A).

She underwent 4 CT-guided doxycycline sclerotherapy treatments over 9 months using 300 mg of doxycycline each time (Fig. 2B). She presented to the emergency department with injection site pain the day after the third treatment that was conservatively managed. Otherwise, there were no complications. As of last follow-up, 2.5 years after her last treatment, she has no clinical or imaging recurrence (Fig. 2C).

DISCUSSION

Aneurysmal bone cysts are benign, locally destructive, tumors that comprise 9.1% of all primary bone tumors.[1] While most occur in the long bones, 2% to 6% occur in the face and skull, with the majority of those in the mandible. The current standard treatment of mandibular ABCs is surgical resection with reconstruction as needed.[1] Surgery has risks to dentition and nerves and unwanted facial scarring.[5] Surgical resection of pediatric mandibular tumors may require later surgeries to maintain proper function as the patients mature.[5,6] Furthermore, if autografts or other soft tissue flaps are needed for reconstruction, there can be donor site morbidity.[6] Adjuvant radiation therapy and preoperative embolization have been used for challenging resections and/or ABC recurrence, but these approaches have limitations, such as radiation-induced secondary tumors and nerve injury.[1]

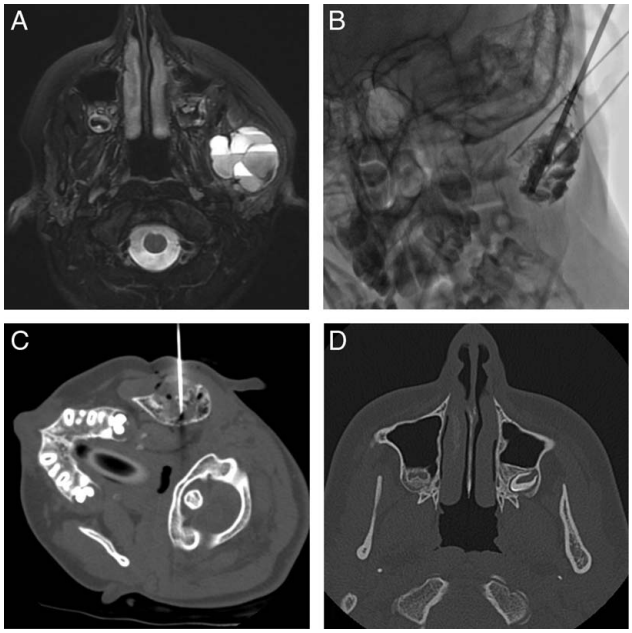

FIGURE 1. Case 1: 11-year-old girl with a left mandibular ABC. (A) Axial T2W MR image shows a multilocular lesion with multiple internal blood/fluid levels. (B) Oblique fluoroscopic image during biopsy and doxycycline injection. (C) Axial CT image from the third treatment shows needle injecting doxycycline. (D) Axial CT image at 4-year follow-up showing complete resolution of the ABC with minimal broadening of the left hemi-mandible. ABC indicates aneurysmal bone cyst; CT, computed tomography; MR, magnetic resonance.

Denosumab and sclerotherapy comprise the primary nonsurgical approaches to treat ABCs.[3,7] Denosumab has demonstrated potential, but the literature cites risks of serum calcium imbalance and bone growth retardation.[2,7] More importantly, the therapeutic effect of denosumab on mandibular ABCs lacks durability, with > 70% disease progression after cessation of therapy.[7]

Doxycycline, in addition to being a caustic sclerosant, is an antibiotic that inhibits matrix metalloproteinases, enzymes responsible for ABC-induced bone destruction.[3] Also, experimental studies in rodents with periodontitis demonstrated antiresorptive and anti-inflammatory properties of doxycycline, suggesting its potential use encouraging maxillofacial bone repair in humans.[8] In clinical practice, percutaneous doxycycline sclerotherapy has shown promise as an ABC treatment.[3,4,9]

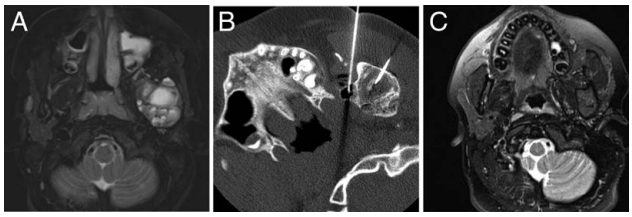

FIGURE 2. Case 3: 10-year-old girl with left mandibular ABC recurrence following 2 prior surgeries. (A) Axial T2W MR image shows ABC recurrence in the bone graft reconstruction of the left hemi-mandible. (B) Axial CT image during the third treatment shows 2 needles injecting different loculations. (C) Axial T2W MR image at 2.5-year follow-up showing resolution of the ABC. ABC indicates aneurysmal bone cyst; CT, computed tomography; MR, magnetic resonance.

CONCLUSION

This study describes successful use of doxycycline sclerotherapy to treat 3 mandibular ABCs. There was one minor complication of postprocedure pain necessitating an emergency department visit in case 3. No sclerotherapy induced facial nerve palsies occurred. Case 2 required more treatments than the others which has been observed to be typical of more aggressive, especially solid-variant, ABCs. At last follow-up, all 3 patients were asymptomatic with no recurrences. There were no complaints of puncture site appearance or scarring. Doxycycline sclerotherapy is a viable treatment for primary and recurrent mandibular ABCs.

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Clinical Treatment Progress for Large Metacarpal and Phalangeal Bone Defects

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Abstract: Large metacarpal and phalangeal bone defects are a hot topic for orthopedic surgeons due to its high clinical incidence, disability rate, and postsurgical amputation rate, along with its difficult treatment, long treatment course, high cost, and poor effect, all of which have a negative impact on the appearance and function of the patient's hands. There are currently a variety of treatment options for large metacarpal and phalangeal bone defects, each with its own benefits and drawbacks. However, there is no treatment method capable of perfectly resolving all the problems of patients with these defects. In this paper, the authors introduce several common plans for and progress of large metacarpal and phalangeal bone defect treatment.

Key Words: Large bone defect, metacarpal and phalangeal bone, progress, treatment

Bone defects are a common clinical condition involving loss of bone substance and large bone gaps caused by a variety of factors. High-velocity trauma, infection, osteomyelitis, tumors, various congenital malformations, and malformation orthopedics can lead to different degrees of bone defects.[1–4] On the basis of clinical experience, some scholars define a bone defect[5] as large if its range exceeds 50% of the bone's circumference or its length exceeds 2 cm. Rimondini et al[6] define a long bone defect as one that exceeds 5 cm in length.

These concepts are broadly applicable to the long bones of the limbs. Schmitz and Hollinger[7] define a large metacarpal and phalangeal bone defect as a defect with a length of 1.5× the metacarpal and phalangeal bone diameter length.

Hands are frequently used to perform delicate tasks, and they are the most vulnerable body parts susceptible to various forms of external violence. Large metacarpal and phalangeal bone defects, particularly, complex metacarpal and phalangeal bone substance defects in addition to a serious soft tissue infection or a skin or soft tissue defect, have a significant impact on the quality of life of the patient. Large bone defects involve complicated treatment, a long treatment course, and a high cost, and they frequently result in numerous complications with high postoperative disability and amputation rates, which can have a significant impact on the appearance and function of the affected fingers and hands.[8]

Therefore, it is a significant challenge for orthopedic surgeons to restore the patient's hand's function while also maintaining the original length and appearance of the metacarpal and phalangeal bone after injury. There are currently various treatment options for metacarpal and phalangeal bone defects, such as autologous or allogeneic bone transplantation, Ilizarov technology,[9] vascularized autologous bone grafting, composite tissue flap technology,[10] Masquelet technology, and bone tissue engineering technology. In this paper, we discuss the large metacarpal and phalangeal bone defect treatments and their progress in recent years.

BONE TRANSPLANTATION TECHNOLOGY

Standard bone transplantation materials include autologous bone, allogeneic bone, and certain synthetic bones. Autologous bone transplantation is the most common method for repairing bone defects and is regarded as the gold standard for bone defect treatment.

This is due to numerous factors. To begin with, the autologous bone has a low risk of immune rejection, infection, or