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Case Report

Conversion of the primary aneurysmal bone cyst into osteogenic sarcoma following treatment with percutaneous sclerotherapy using polidocanol injection

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ABSTRACT

The intralesional injection of sclerosing agents has been identified as a safe method for treating primary aneurysmal bone cysts (ABC). However, to the best of our knowledge, there have been no reported instances in the literature of a primary ABC transforming into osteogenic sarcoma following complete healing facilitated by an intralesional sclerosing agent, such as polidocanol. We present the case of a 20-year-old female diagnosed with a histologically proven primary ABC located at the distal end of the tibia. She underwent a series of 5 intralesional injections of 3% polidocanol (hydroxypolyaethoxydodecan) and achieved complete clinical and radiological healing. However, after 10 years, her symptoms resurfaced, and subsequent histological examinations revealed osteogenic sarcoma. Surgical excision was performed, followed by bone grafting and ankle arthrodesis. This case suggests that intralesional alcohol injections might not prevent the inherent potential for malignant transformation of primary ABCs. To ascertain whether such injections increase the risk of sarcomatous conversion, further long-term follow-up studies are imperative.

Keywords: Aneurysmal bone cyst, Polidocanol, Osteogenic sarcoma, Ankle arthrodesis, Sclerotherapy

INTRODUCTION

Aneurysmal bone cyst (ABC), known as an expansile cystic lesion of bone, primarily manifests during the initial two decades of life and predominantly appears in long bones, notably the femur, tibia, and humerus.[1] Traditionally, ABCs were attributed to heightened venous pressure leading to the escape of cellular and blood components into cyst-like spaces within the bone. However, recent advancements have revealed a genetic driver—an induced translocation that up-regulates the ubiquitin specific protease USP6 (Tre2) gene—defining at least a subset of ABCs as a primary neoplasm.[2]

While both primary and secondary ABCs are generally benign, instances of malignant transformation of primary ABCs have been documented, primarily linked to previous exposure to radiation.[3] Remarkably, this appears to be among the initial occurrences of sarcomatous conversion in a primary ABC subsequent to complete healing facilitated by intralesional polidocanol injection.

CASE REPORT

In 2006, a 20-year-old female presented with persistent pain and swelling on the medial aspect of her left lower leg, symptoms that had developed gradually over the past eighteen months without any prior injury. The pain, a constant dull ache, lacked any daily fluctuations, while the swelling, measuring approximately 5×5 cm above the medial malleolus, displayed uniformity in surface and well-defined borders. The area was tender upon touch, and movements involving the ankle joint elicited pain. An X-ray revealed an expansive lytic lesion at the distal end of

the tibia, characterized by clear margins and a limited sclerotic rim (Figure 1). Subsequent magnetic resonance imaging (MRI) imaging depicted a distinct heterogeneous mass accompanied by surrounding soft tissue edema (Figures 2a and b).

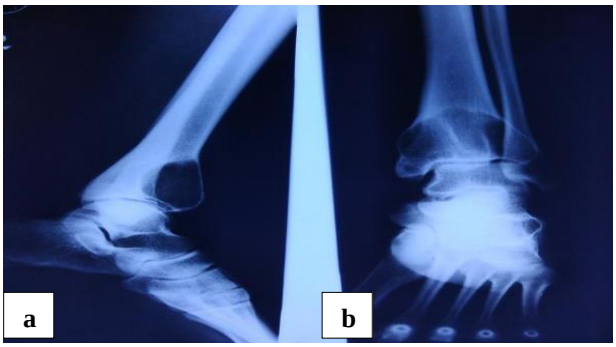

Figure 1 (a and b): A lateral and anteroposterior radiograph of distal tibia showing a well-defined, expansile, lytic lesion with thin sclerotic rim.

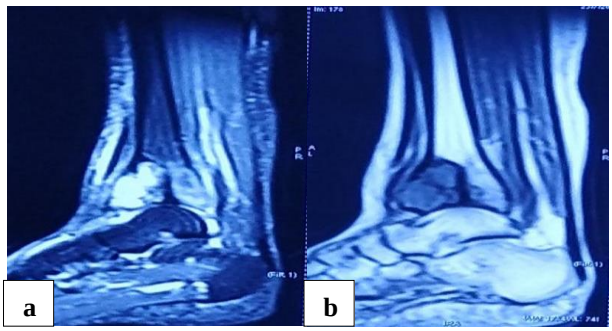

Figure 2: A saggital T2 MRI image shows (a) a distinct heterogenous mass with surrounding soft tissue oedema; and (b) a focal, eccenteric, hypodense lesion without any soft tissue involvement.

To establish a diagnosis, a core needle biopsy guided by imaging was performed, revealing histopathological features consistent with an aneurysmal bone cyst (Figure 3). Treatment involved intralesional alcohol injections (polidocanol injection), which, following five sessions, notably improved both clinical symptoms and radiological observations (Figure 4). Our treatment endpoint, based on previous research, signified the resolution of pain, the initiation of cortical wall reformation within the cyst, and cessation of lesion growth. The patient remained under consistent monitoring for three years post-radiological healing, after which she ceased follow-up.

In 2016, the patient experienced a recurrence of pain and swelling in her left lower leg. Seeking treatment at a local hospital, subsequent X-rays and MRI (Figures 5 and 6) indicated a diagnosis of recurrent aneurysmal bone cyst, albeit without confirmatory biopsy. The patient underwent lesion curettage, followed by bone cement filling to address the void. However, upon histopathological examination at the initial facility and later review at our institute, the findings suggested osteogenic sarcoma (Figure 7).

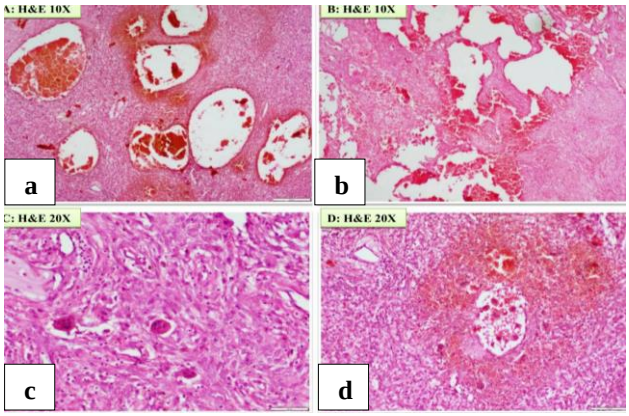

Figure 3 (a-d): Hematoxylin and eosin staining showing solid areas and blood-filled cystic spaces that lack an epitheloid or epithelial lining, separated by cellular septa.

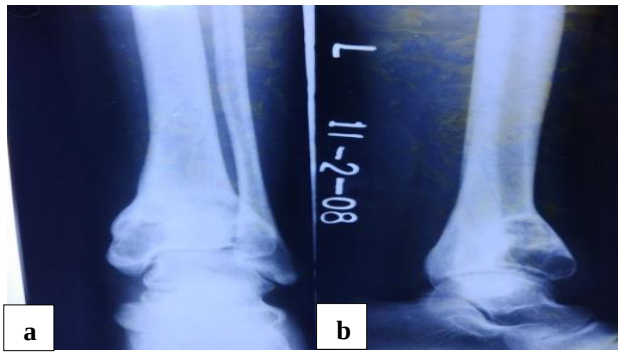

Figure 4 (a and b): A distal tibia anteroposterior and lateral radiograph three years after multiple sessions of sclerotherapy showing complete healing of the lesion.

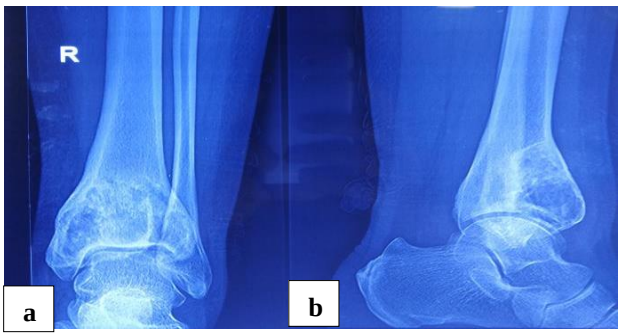

Figure 5 (a and b): The X-ray showing presence of mixed lytic and sclerotic areas in previously healed lesion.

The patient underwent four cycles of chemotherapy before undergoing excision of the lesion, accompanied by fibular bone grafting and ankle arthrodesis (Figure 8). Histopathological examination of the excised segment confirmed the presence of osteosarcoma. Three-months

post-surgery, the patient developed lung metastasis, which was subsequently removed by the cardiothoracic and vascular surgery (CTVS) team. Regular follow-ups have been conducted since then, revealing no signs of new metastatic growth or local recurrence at final follow-up of six years.

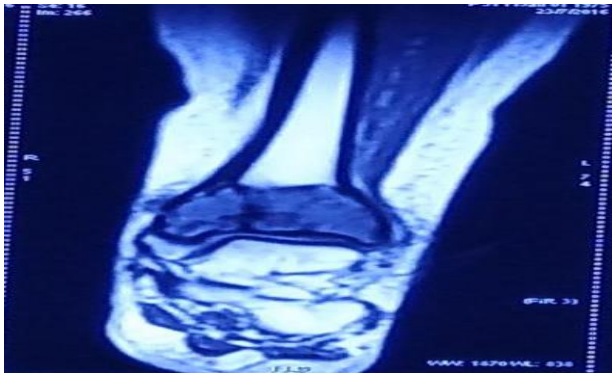

Figure 6: A coronal T1 MRI image showing local recurrence in previously healed lesion.

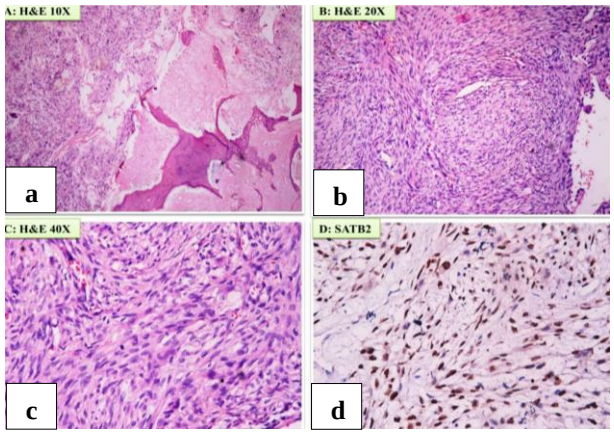

Figure 7 (a-d): Histopathology showing malignant spindle cells positive for SATB2.

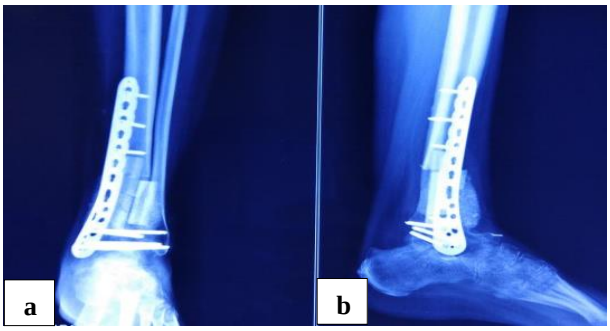

Figure 8 (a and b): Post-operative X-ray after wide excision of tumor and ankle arthrodesis with plate and fibula graft.

DISCUSSION

The ABC is a rare benign lesion often manifests during adolescence, yet its precise cause remains unidentified. ABC displays uncommon characteristics such as expansive growth, tissue destruction, and hemorrhage inside the tumor. Its histology showcases multiple interstitial spaces filled with blood, typically lined by various cell types, including multinucleated giant cells and fibroblast-like cells.[4] Patients commonly experience pain and swelling around the affected bone. Constitutional symptoms are rare due to the tumor's non-malignant nature. As the lesion expands, it can evolve into a palpable or visible mass on the surface.[5]

Radiographically, ABCs appear as lytic, expansive, geographically-shaped lesions with lobulated patterns, typically located at the metaphysis and demarcated by a distinct sclerotic border. Fluid-fluid levels with different signal intensities, more discernible on MRI (especially on fluid-sensitive sequences) than on CT scans, strongly suggest but do not definitively diagnose ABCs.[6] Since aggressive ABC radiologically mimics telangiectatic osteosarcoma, histopathological examination is mandatory.[7]

Histologically, telangiectatic osteosarcoma presents with cystic spaces containing blood, much like ABC. However, in this form of osteosarcoma, the septa harbor malignant stromal cells that display unusual characteristics: hyperchromasia in their nuclei, significant variations in size and shape (pleomorphism), and irregularities in cell division (atypical mitosis). Occasionally, a lace-like pattern of abnormal bone tissue (neoplastic osteoid) may manifest. Moreover, telangiectatic osteosarcoma exhibits genetic mutations commonly associated with osteosarcoma, such as alterations in the P53 and retinoblastoma (RB) genes. Importantly, it differs from ABC by lacking the specific USP6 gene rearrangement, a useful distinguishing feature aiding in accurate diagnosis.[6]

The treatment paradigms concerning ABC have undergone evolutionary changes throughout the years. While resection remains unfeasible in the majority of cases, intralesional procedures like curettage are now considered the gold standard. Owing to local recurrence rates surpassing 50%, diverse adjuvant treatments have been employed. Prominent among these are PMMA bone cement, argon beam, phenol, ethanol, and cryotherapy. Additionally, less intrusive methodologies like Curopsy, selective arterial embolization, sclerotherapy employing ethibloc or polidocanol, as well as systemic therapy involving RANKL inhibitors (Denosumab), have been explored.[8]

Intralesional sclerotherapy for the management of ABC represents a minimally invasive approach offering potential benefits such as reduced surgical duration, limited scarring, and the avoidance of additional procedures for bone harvesting.[9] Sclerosants generally exert their effects through direct damage to the endothelial lining, prompting a series of coagulation events that culminate in the thrombotic occlusion of blood vessels. Potential complications associated with the application of

polidocanol encompass hypopigmentation, localized necrosis due to extravasation, pulmonary embolism, osteomyelitis, and allergic reactions.[10] At our institution, the primary treatment modality for most ABCs involves intralesional polidocanol injection, yielding a favorable success rate. A prior study conducted within our establishment demonstrated satisfactory outcomes in over 97% (70 out of 72) of patients, with recurrence observed in merely two cases (2.8%), both instances occurring within two years following the completion of treatment. Both recurrences were effectively managed through subsequent sclerotherapy sessions.[11]

The transformation from primary ABC into a malignant form is exceedingly rare. Some authors have speculated that previously reported transformations might have actually involved telangiectatic osteosarcomas misdiagnosed as primary ABC.[12,13] However, it's acknowledged that radiotherapy can induce the conversion of ABC into sarcoma.[14,15]

As far as available knowledge goes, there's no documented instance of ABC developing into osteosarcoma subsequent to sclerotherapy. This novel discovery underscores the necessity of appropriately counseling patients and ensuring prolonged monitoring. Sclerosants, such as 3% polidocanol, have been safely utilized in treating varicose veins and bleeding esophageal varices, and no published literature has linked them to neoplasm induction.[16] Whether our case signifies a spontaneous transformation or a polidocanol-related side effect remains uncertain.

CONCLUSION

Based on the aforementioned findings, these conclusions can be drawn: intralesional polidocanol injection might not restrain the malignant potential of this lesion; there exists a distant possibility that the polidocanol injection itself could have induced the malignant transformation, necessitating further extensive, monitored long-term study; and the patient should receive comprehensive information about both the disease's prognosis and the treatment method.

Recommendations

Despite being a benign bone tumor, ABC can be treated with percutaneous injection of aethoxysclerol successfully. Long term follow-up of patients is warranted even after resolution of symptoms. Malignancy conversion of ABC can happen even after a decade. Whether this is denovo conversion of ABC or treatment induced conversion to malignancy needs further study.

Secondary osteosarcoma following ABC conversion can be treated safely using limb salvage surgery.

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