Case Report

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Giant Aggressive Aneurismal Bone Cyst of the Proximal Humerus Unresponsive to Denosumab

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Abstract

Aneurysmal Bone Cyst (ABC) is a destructive lesion. The main treatment is curettage, local adjuvant and grafting. However, it is difficult to apply the optimal surgical procedure in aggressive lesions. In these cases, the use of denosumab prior to surgery has been shown to reduce bone destruction and facilitate surgical treatment. A 22-year-old woman was referred for limited shoulder movement and pain complaints. Physical examination and radiological findings were interpreted in favor of ABC. The biopsy was also found to be consistent with the ABC. Since the lesion was aggressive, denosumab was applied prior to surgery. The mass quickly became calcified and patient's pain complaint decreased. After stopping denosumab treatment, lesion progressed rapidly and destructive character became dominant at every part of lesion. The patient underwent proximal humeral resection and prosthesis. A painless limb with limited shoulder movement was achieved. Although denosumab application prior to surgery was initially good in this case, after termination of treatment, lesion progressed rapidly and the gains associated with denosumab use was lost.

Keywords: Aneurysmal bone cyst, Denosumab

Introduction

Aneurysmal bone cyst is a benign local aggressive lesion [1]. It was first described by Jaffe in 1942 [2]. The Lesion generally holds the metaphysis of long bones. It often has subperiosteal origin. As it progresses, it spreads to medulla and expands the bone by thinning the cortex. Those with medullary onset may be confused with simple bone cysts. False septation, lytic appearance, eccentric placement, periosteal reaction and fluid-fluid level can be seen in radiological examination. Aggressive Aneurysmal Bone Cyst behave so destructive and may be confused with malignant bone tumors but no metastases seen and periosteal reaction may not be fully evaluated. Morphologically, in cystic areas fresh blood appearance is seen. Solid areas had a blood-impregnated spongiotic texture. Histopathological examination reveals intense

osteoclastic activity, inflammatory cells and giant cells.

Curettage and grafting are common methods in surgical treatment of Aneurysmal bone cysts [3]. Since, recurrence rate is high with curettage alone, therefore local adjuvant application is also performed just after curettage. Local adjuvant can be performed by phenol, cryotherapy, and cautery and argon gas application. Also en bloc resection, selective arterial embolization, sclerotherapy, embolization and radiation therapy, are among treatment options [4,5]. In recent years, denosumab application is seen as a new approach in aneurysmal bone cyst treatment. Denosumab receptor activator inhibitor nuclear kappa B ligand (RANKL), thereby reducing osteoblastic activity and inhibiting bone destruction [6]. Especially, in aggressive lesions, denosumab can be applied before surgical treatment in cases where curettage and grafting are difficult.

In this case report, an aneurysmal bone cyst, which was decided to be treated with denosumab, was evaluated before surgical treatment planning but a very aggressive lesion was observed.

Case

A 22-year-old female patient was admitted to clinic with shoulder pain and motion limitation complaints twenty-three months ago. Physical examination revealed that shoulder movements were restricted and painful, and proximal humerus was swollen. A completely lytic and expansile lesion and pathologic fracture with a weak periosteal reaction around proximal humerus was detected at patient's shoulder radiography (Figure 1). On MRI, lesion was cystic and there were occasional fluid levels. Radiological findings were evaluated in favor of aneurysmal bone cyst (Figure 2). However, because of the aggressive appearance, a closed biopsy under imaging was recommended to confirm the diagnosis. Histopathological examination revealed a large fibrohistiocytic appearance involving numerous osteoclast-type multinuclear giant cells among large fibrin masses. The findings were evaluated in favor of aneurysmal bone cyst. Surgical treatment (curettage and bone grafting) was recommended to the patient. The patient did not accept surgical treatment. After five months the patient's complaints increased, and the patient referred to our clinic again. Bone destruction was seen in her radiography (Figure 3). Surgical treatment was postponed and it was decided to apply denosumab before surgery. On days 1, 8 and 15, 120 mg loading dose was administered, following that, monthly 120 mg Denosumab was administered for one year. After denosumab treatment, the patient's complaints decreased. Three months later, it was seen in radiography that the cyst had started to calcify. Intensive calcification was observed in cystic structure in the radiograph taken after 1 year of denosumab treatment (Figure 4). During this time, while patient had no pain, limited range of motion in shoulder continued? After Denosumab was discontinued, the patient's pain started again 3 months later, and the lytic character of the lesion started to come to foreground again in radiography. Five months after denosumab was stopped, lytic appearance spread over the lesion. The patient was scheduled for wide resection and tumor resection arthroplasty. (PENTA) During surgery, the lesion seemed to be bleeding much. The bone was thin like a paper. It was also seen that surrounding muscle structures were atrophic. Neurovascular structures were preserved and the wide resection and tumor resection arthroplasty was applied. The shoulder belt muscles were fixed to the prosthesis using attachment tube (IMPLANTCAST)

(Figure 5a, 5b, 5c and 6) No postoperative complications developed. She as 10 point of pain according to the visual analogue scale (VAS) and it has reached to zero after operation. She had no range of motion before operation due to the pain. Although active shoulder range of motion was limited due to prosthesis, a painless limb and life comfort was provided.

Figure 1: X ray at the first admission.

Figure 2: MRI sections of the lesion.

Figure 3: X ray after 5 months without treatment.

Figure 4: X ray after 1 year of denosumab treatment.

Figure 5: Intraoperative pictures.

Figure 6: Postoperative x-ray of the left humerus of the patient.

Discussion

Surgery is the basic approach in the treatment of aneurysmal bone cysts. In many cases the application of curettage and local adjuvant is sufficient for total cure. In aggressive cases though, it is difficult to obtain the desired result with only surgical treatment. The biggest problem with these patients is local recurrence. In these cases, applications for mass reduction before surgery provide convenience during surgery and increase success rate of the surgeon. Denosumab is one of the prominent agents in this field in recent years [7].

The cause of bone destruction in aneurysmal bone cyst is osteoclastic activity. Osteoclasts are giant cells that are brought by mononuclear cell fusion. RANKL is a molecule that plays an important role in this process and increases osteoclast activity. Denosumab blocks RANKL activity. This reduces bone destruction and allows new bone formation immediately [8]. Denosumab is used to stop this activity in the diseases where osteoclastic activity present, such as giant cell tumor. In aggressive cases where the Periosteum turns into blood bags, it re-establishes ossification and hardens the mass.

Pelle et al. [9] reported that they achieved good results in an aneurysmal bone cyst case placed in sacrum, which they treated with denosumab for 12 months. Denosumab administration was an effective alternative in cases where surgical treatment is difficult. Patel et al. [10] reported that after denosumab administration, rapid ossification occurs and cortical thickening becomes apparent, and there was no evidence of recurrence after 12 months of follow-up. Lange et al. [11] reported that they have achieved successful results with 2 spinal aneurysmal bone cyst they treated with denosumab after surgery. Ghermandi et al. [12] have demonstrated efficacy of denosumab in 2 spinal cases on which selective arterial embolization was carried out with no results, and denosumab has proven to be an alternative to selective arterial embolization. Ntalos et al. [13] reported that they achieved successful results in case with pelvic placement.

In literature denosumab application in cases of aneurysmal bone cysts placed at long bones. Pauli et al. applied denosumab prior to surgery in a case with proximal radius placement. The authors have reported that well-ossified mass is easier to remove with extensive resection and denosumab application is also useful in aneurysmal bone cyst as it is in giant cell tumors.

When literature is evaluated around denosumab application; Although some authors [9,11] underline that it should be used with caution in pediatric patients due to complications such as jaw necrosis, atypical femur fractures, rebound osteoporosis and hypocalcemia, most authors emphasize that denosumab application gave good results in medical treatment of aneurysmal bone cysts. The authors emphasize that it facilitates application of surgery, reduces the amount of intraoperative hemorrhage and recurrence rate. For this reason, it is emphasized that it is a very good option especially for tumors that cannot be surgically treated. Shortly after we applied denosumab to our case, we saw that the patient's pain stopped, functions improved, and that the tumor was ossifying radiologically. Although we saw a very successful outcome at the beginning, after the treatment was stopped, the tumor progressed in a short time and rapidly reached pre-denosumab state. For this reason, we concluded that the application of denosumab in this case was not effective enough.

In conclusion, this case showed us that denosumab is not a good option for the aggressive aneurysmal bone cyst. Of course; there is need for large series for an evidence based result.

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