CASE SERIES

UNDERSTANDING THE RARE BONE TUMOR "ADAMANTINOMA"

Badaruddin Sahito[1], Nadia Nazir Jatoi[2], Dileep Kumar[1], Ameema Asad[2], Syed Saboor Hasan[2], Maratib Ali[3]

[1]Dr. Ruth KM Pfau Civil Hospital Karachi, [2]Dow Medical College, Dow University of Health Sciences, Karachi, [3]Department Orthopaedic Surgery, Dow University of health sciences, Karachi-Pakistan

Adamantinoma is a rare neoplastic bone tumor that has the potential to metastasize. The classic presentation is in the tibial region however; cases involving other bones of the body have been noticed. The tumour is very likely to be mistaken for other bone diseases and therefore it is important to investigate and study about its nature and thus differentiate it from other differentials. Nevertheless, literature on the presentation, findings, investigations and treatment options of adamantinomas are limited. In this case series, we report four cases from a local hospital in Karachi who were diagnosed, treated and followed up for adamantinoma. Studies regarding the disease will help us understand more about its features.

Keyword: Adamantinoma; Orthopedic; Pakistan; Wide-local resection; Fibula bone graft

Citation: Sahito B, Jatoi NN, Kumar D, Asad A, Hasan SS, Ali M. Understanding the rare bone tumour "Adamantinoma". J Ayub Med Coll Abbottabad 2021;33(Suppl. 1):835–40.

INTRODUCTION

Adamantinoma is a rare, low-grade malignant bone tumor that accounts for 0.1–0.5% of all bone tumors, with potential to metastasize.[1,2] The pathogenesis of the tumor is debatable but recent histology indicated towards an epithelial origin.[3] The most likely sites involved are the anterior metaphysis or diaphysis of the tibia. Other sites include the fibula, ulna, femur, humerus, and radius.[4] It mostly affects people in adolescence to middle age (20-40 years) and has slight preponderance in males compared to females (1.3:1).[5]

Adamantinomas have an insidious onset which may produce unspecific symptoms such as pain, swelling and tenderness depending on the extent and site of the neoplasm, where a patient may tolerate pain for considerable periods before seeking medical help.[1] Statistically, 23% of patients present with a corresponding fracture at the affected site, while in several cases there may be deformity resulting in bowing of the anterior tibia.[2] Despite the rarity of this tumour, it has an excellent prognosis if diagnosed and treated early. Due to the sparse data on adamantinomas from this region, this article will represent a series of cases from the Department of Orthopaedic Surgery, Civil Hospital Karachi (CHK). The patients and/or their families were informed that data from the case (including the pictures represented) would be submitted for publication, and gave their consent.

CASE-1

22-year-old female university student presented to the OPD of CHK, with complaints of pain and swelling on the right leg for five months. The pain was progressive and non-radiating. Analgesics significantly improved the condition but walking aggravated the pain.

On examination, a well-defined non-tender swelling was noticed at the mid-shin level on the right leg. The distal neurovascular architecture, from the lesion, was intact. For investigation, X-ray was initially advised and showed an osteolytic bone lesion on the mid tibial region with narrow zone of transition (Image 1.1). Bone scan showed high uptake in the mid-shaft region of the right tibia.

Further investigation with MRI revealed a hypo-intense lesion on T1-inverted image while on T2-inverted image; a heterogeneous lesion was noted after contrast enhancement. CT scan was performed to show the extension of the bone and did not show metastasis. For diagnosis, biopsy was advised. The histopathology results showed classic adamantinoma findings. The patient was scheduled for a wide local resection with reconstruction from the contra-lateral fibula and iliac bone graft and likewise, consent was obtained by the patient for the procedure.

The bone was fixed with a 4.5mm dynamic compression plate following the intervention. Post-operative sections of margins showed no signs of viable residual tumour. The patient was allowed little mobilization on the first day. On the third postoperative day, walking on the contra-lateral limb was encouraged. She was allowed to do partial weight bearing after six weeks and full weight bearing was allowed after four months. She was followed monthly for six weeks and then every three months thereafter. X ray findings three-month post operatively are shown (Figure-1.2).

Fibula completely united one year post-operatively. She was completely free of the disease five year following the wide resection with reconstruction. The X-ray shows the findings noticed five years post operatively (Figure-1.3).

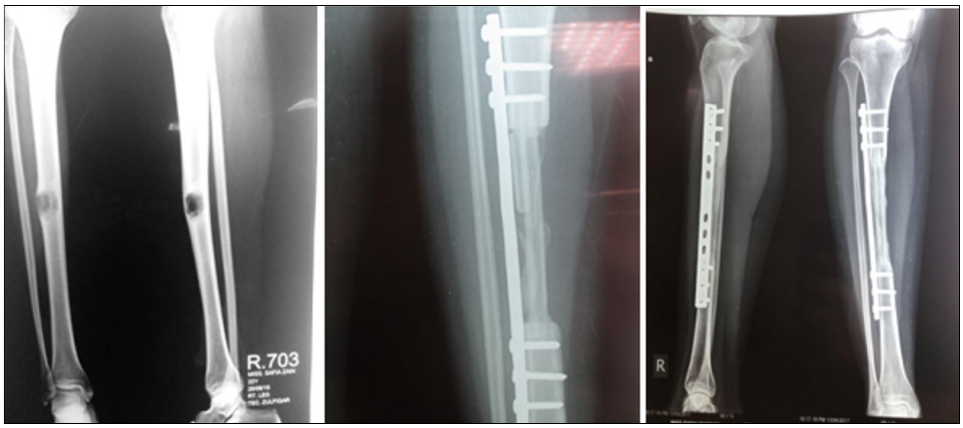

Figure-1.1: Osteolytic bone lesion on the mid tibial region with narrow zone of transition
Figure-1.2: After 3 months post-operatively
Figure-1.3: 5 years post-operatively

CASE-2

18-year-old female student was referred to CHK from another local hospital, with complaint of pain in the mid-shin region of the left leg for four months. The pain was mild, dull and associated with burning sensation. It was aggravated with walking however, analgesics relieved it.

On examination, slight bowing of the anterolateral region in the mid-shin level of the left leg was noted. Distal neurovascular architecture of the surrounding tissue was intact. The baseline and haematological investigations were unremarkable. An X-ray of the left leg showed osteolytic changes at the site of the lesion. Whorls with thinning of the tibial cortex and a narrow zone of transition were noticed (Figure-2.1).

Bone scan showed high uptake at the lesion site. MRI scan of the right leg showed a hypo-intense lesion on T1-inverted image (Image 2.2) while on T2-inverted image; a heterogeneous lesion was noted after contrast enhancement. An incisional biopsy of the tumour and the specimen sent for histo-pathological investigation. The biopsy specimen showed findings of adamantinoma bone tumour. The sections revealed fragments of cortical lamellar bone exhibiting a fibro-osseous lesion. The osseous component was composed of irregular bony trabeculae with osteoblastic rimming. There was a band of fibrous stroma with scattered clusters of epithelial cells around compressed vessels. Immunohistochemical stain cytokeratin AE1/AE2 highlighted clusters of epithelial cells in the stroma. CT chest showed no signs of metastasis. Wide-local excision of the lesion with reconstruction was planned. The patient was counselled and consent obtained for the intervention. After wide local resection, bone graft from iliac and contralateral fibula was used for reconstruction (Figure-2.3).

This was followed by stabilization provided by a 4.5 dynamic compression plate. Partial weight-bearing was allowed with the use of sand shoes. She was followed every eight-week and was then allowed full weight bearing. Post-operative X-ray is shown (Figure-2.4).

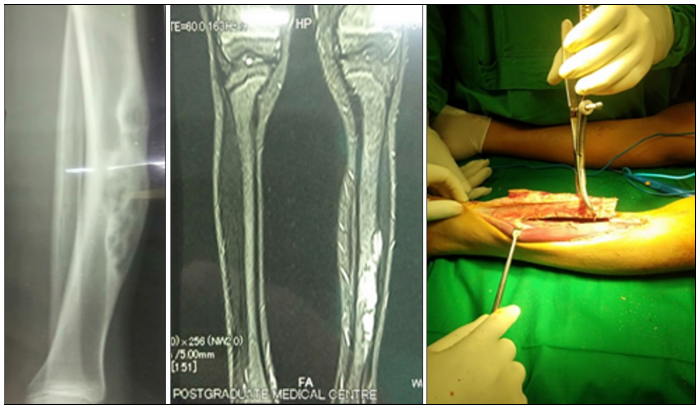

Figure-2.1: Osteolytic changes at the site of the lesion. Whorls with thinning of the tibial cortex and a narrow zone of transition are also evident.
Figure-2.2: MRI scan of the right leg showing a hypo-intense lesion on T1-inverted image.
Figure-2.3: Bone graft from iliac and contralateral fibula used for reconstruction.

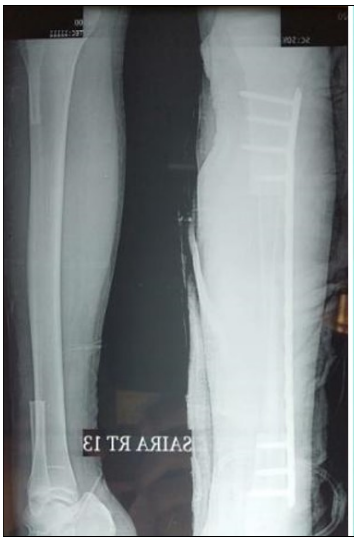

Figure-2.4: X-ray performed at 8 months post-operatively

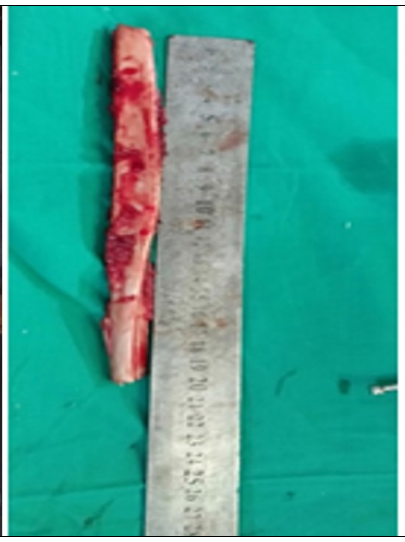

Figure-2.5: Fibular graft

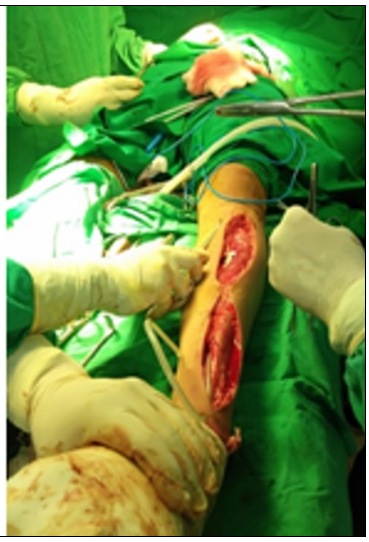

Figure-2.6: Closure

CASE-3

A 34-years old female, presented in the OPD of CHK, with complaints of pain, swelling and deformity in her right leg for the past 16 months. The pain was gradual in onset, dull in character, mild to moderate in intensity and was non-radiating. Additionally, she complained of swelling which was gradual in onset and was associated with deformity for the past 16 months. Upon investigations done at a private hospital in Karachi, non-ossifying fibroma was diagnosed in her proximal right tibia and consequently, she was managed surgically using curettage and bone graft there. However, after 1 year, she returned with the same complaints and investigations revealed recurrence, surgery was performed at the same hospital where she was diagnosed, this time curettage was performed along with fibular bone grafting along with plating. It recurred after 6 months, and this time she was referred to CHK. Rest of the history was unremarkable with no known comorbidities.

On examination, she was unable to bear weight on her right leg. A healed surgical scar was seen approximately 10cm proximal tibia on the lateral side and varus deformity was noted. Distal neurovascular structure was intact. Following up on investigations; an x-ray showed an osteolytic lesion in her proximal tibia, a reabsorbed bone graft and a T-plate which was associated with her previous surgery (Figure-3.1).

It further revealed no clear demarcation of the lesion and supported the examination finding of varus deformity. Furthermore, CT scan of tibia delineated the lesion. However, MRI was not advised due to the plate. CT chest was performed to rule out metastasis. Bone scan showed uptake only at proximal tibia. A biopsy was then finally performed confirming our provisional diagnosis of adamantinoma. Grossly, the specimen appeared as multiple grey white to yellow irregular tissue. The cut surface was homogeneously grey white, firm and fibrous. However, no areas of necrosis or haemorrhage were noted. Histological findings exhibited fibro-osseous tissue with infiltrating nests of epithelial cells in a loose fibrous stroma. Scattered keratin pearl formation was also noted. Moreover, immunohistochemical stains were positive for p63, cytokeratin AE1/AE3 and cytokeratin 19. Thus, the findings established the confirmed diagnosis of a classical adamantinoma.

After patient counselling and consent, surgical management was proceeded with. Wide marginal resection of proximal tibia was done with mega-prosthesis being used for reconstruction (Figure-3.2 and 3.3). 12cm of proximal tibia was resected. Medial head of gastrocnemius was used as a flap to cover the implant and a skin graft was applied over the flap (Figure-3.4).

Postoperatively, she was managed with analgesics and mobilization started in bed, the next day. After one-week full weight bearing began, the knee was immobilized in an extended position. Stitches reabsorbed in two weeks. Consequently, after six weeks, range of motion of the knee was initiated. She followed up initially every month. She was allowed to use a stick for walking. Thereafter her follow-up was done every three months. She followed-up for 23 months. On every visit her range of motion improved 70–80 degrees in flexion.

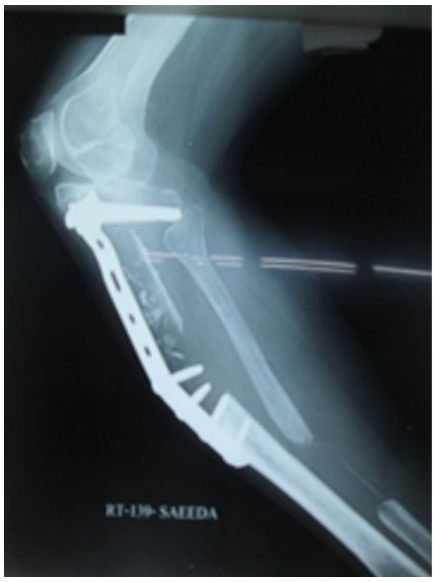

Figure-3.1: X-ray showing an osteolytic lesion in her proximal tibia, a reabsorbed bone graft and a T-plate associated with previous surgery done on the patient

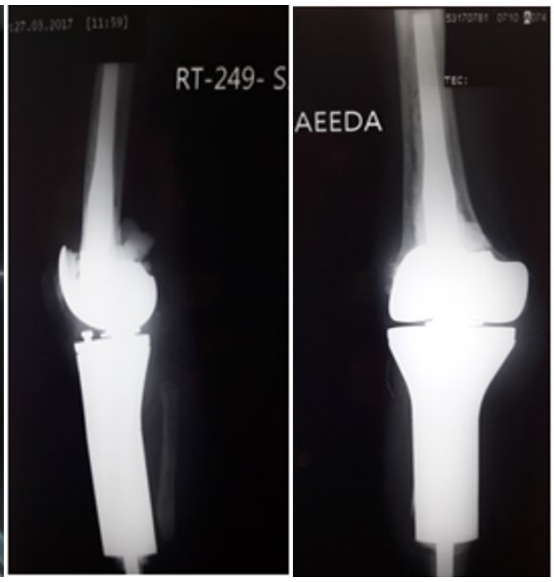

Figure-3.2 and 3.3: X-ray images showing mega-prosthesis was used for reconstruction

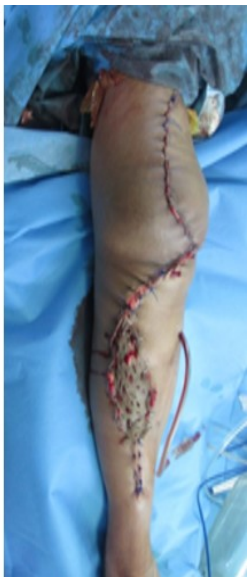

Figure-3.4: Medial head of gastrocnemius was used as a flap

CASE-4

A 27 years old male patient presented to our OPD with complaints of pain and swelling in his left mid-tibial region for the past 8 months. Pain was dull, moderate in intensity and non-radiating. It was not associated with fever, deformity or history of trauma. Pain subsided with paracetamol but walking aggravated the pain. He initially went to a private hospital where a biopsy was performed which revealed characteristic adamantinoma findings.

An x-ray was performed afterwards which reported an osteolytic lesion involving the whole of diaphysis of left tibia. MRI of the left tibia demonstrated hypo-intense signals at T-1, involving the whole of diaphysis-in line with x-ray reports. His baseline investigations were normal.

The case was decided to be managed with left knee disarticulation and consent was obtained after counselling. Postoperatively, he was given broad spectrum antibiotics therapy and once he was stable, he was referred for prosthesis in our hospital.

DISCUSSION

Adamantinoma is classified as a primary low-grade, malignant tumour of the bone with an unknown histogenesis. Although its origin still remains debatable, according to literature the recent opinion has established adamantinoma as a tumour of epithelial origin, based on ultrastructural and immunohistochemical studies. Interestingly, its rarity is evident from the figures: 0.1–0.5% proportion of all primary bone tumours. Literature goes back to 1900, when Maier reported the first case of this rare entity.[7]

Additionally, based on ultrastructural and immunohistochemical studies, the tumour cells are strongly positive with pan-cytokeratin antibodies. Moreover, electron microscopy has revealed crucial histological appearances such as basal lamina, desmosomes, gap junctions, epithelial specific keratin and extracellular composition similar to epithelial tissue.[1] Such findings were seen in our cases as well.

Adamantinoma is broadly divided into two distinctions by Czerniak B *et al*., who presented a review of the clinical, radiologic, and histologic features of 25 cases of long bone adamantinoma. A new type of adamantinoma termed "differentiated adamantinoma" was distinguished from the ‘classic’ long bone adamantinomas. Characteristics of the differentiated adamantinoma include: patient age (first two decades), intracortical location of the entire lesion, uniform predominance of an osteofibrous dysplasia-like pattern, and scattered positivity of epithelial elements for cytokeratin.[8]

Although a vast majority of the studies have associated adamantinoma with slight male dominance globally, with a ratio of 5:4.[9] Interestingly, in contrast to this, our study rendered a 3:1 ratio of female: male incidence. According to the most common observation, tibial diaphysis or fibula[10] and usually involved and accordingly our study found our patients also presented with tumors involving the tibial region. As mentioned previously, the ‘classical’

subtype of the tumour commonly affects patients with ages commonly ranging from 20–50 years old and usually experiencing long-going symptoms.[11] Although all of our patients did fall under the same age range, the duration of pain ranged from only 5–16 months at the maximum, highlighting a moderate chronicity of the symptoms. The tumour is often noticed as a slow growing swelling which is not always associated with pain. However, unfortunately, this slow growing tumour does present with a grave risk to metastasize.[10] Moreover, the classical reasons for the patient to eventually visit an OPD are the pathological fracture or deformity which encourage patients to seek medical help.[12] However, three of the patients came to medical attention early, regardless of mild symptoms only, mainly because the pain hindered their daily routine. It is estimated that nearly 15–20% of the cases present with distant metastases. However, these figures in reality may be falsely low due to the slow growing nature of the tumour and therefore, long term follow up is required to justify its true metastatic potential. Pulmonary metastases are more common than regional nodal metastases. This ability to disseminated decreases the 5-year survival in disseminated adamantinoma to 50–60%. Worthy of mention is that dissemination, in scenarios where the patient reports early is linked with higher incidence in patients with a history of repeated local recurrences due to inadequate primary excision of this lesion. Authors have outlined the risk factors for metastases: male sex, persistent pain, symptoms of less than five years duration, and inadequate initial treatment by biopsy curettage/excision, or resection.[9] Males, should be counselled and followed for as long as fifteen years due to late recurrences of the tumour.[10]

To begin with investigations, X-ray is initially performed; the simplest and cheapest available form of imaging. On x-ray, the tumour appears well-circumscribed, cortical, multi-lobulated and osteolytic. Intra-lesional opacities, septation, and peripheral sclerosis may also be seen. Multifocality within the same bone is also observed and these radiolucencies are surrounded by ring-shaped densities that produce the characteristic "soap-bubble" appearance. The lesion commonly remains intracortical and extends longitudinally, but in some instances also destroys the cortex and invades the medullary cavity or surrounding periosteum and soft tissue. Based on these x-ray findings, clinicians commonly proceed towards CT and MRI findings. It is noted that CT scan successfully demonstrates the soft tissue extension and cortical involvement if present but is not able to depict the intraosseous extension of adamantinoma. It is primarily used to play a role in the routine work-up and to rule out metastases. Moving on, MRI has widely been implemented since it is beneficial for locoregional staging for it very well detects distant cortical foci, intramedullary and soft tissue extension. Added to this, MRI also aids for the determination of tumour-free margins as well as the plan for reconstructive surgery. Classically, two morphological patterns of adamantinoma are described on MRI: multiple small nodules in one or more foci or a solitary lobulated focus.[12]

Gross examination reveals that these tumours are firm and fibrous, and are pink and fleshy, more often in the findings by Unni KK *et al*, the lesion was an admixture of solid areas and small cysts linearly and the bone surrounding the lesion was denser than normal.[13]

The final diagnosis of adamantinoma rests on biopsy. Desai *et al* have highlighted these findings and concluded that the cells in these sparse tumours are arranged in nests, islands, cord, or tubules. The cells may also be arranged in a box car-like pattern and are surrounded by fibrous stroma. Moreover, various patterns seen in adamantinoma have also been reported in literature which includes: (1) basaloid, (2) spindle, (3) tubular (glandular/vascular), (4) squamous, and (5) osteofibrous dysplasia-like. Since the tumour is slow growing, mitotic activity is observed to be low.[6] Our biopsy findings very much followed the same trend.

It is imperative to be distinguished from common benign processes such as bone cysts, giant cells and even some malignant tumours like; chondrosarcomas, angiosarcomas and bone metastases.[12] Of great importance is osteodysplasia which is closely associated with osteodysplasia-like adamantinoma or differentiated adamantinoma. These two lesions have the same histological and radiological appearances and thus, can potentially, create problems in establishing a confirmed diagnosis of adamantinoma. This was also noticed in our case 3, where the patient was misdiagnosed at a different hospital and treated for osteodysplasia with curettage on the tibia in place of en bloc resection of adamantinoma. Since, accurate diagnosis greatly influences the treatment options and owing to its ability to metastasize it is not advisable to treat them with curettage but with wide resection. Recurrences are common with curettage as shown by a study where 100% of the patients who underwent curettage experienced local recurrences.[14] This is further emphasized by case 3, who experienced local recurrence after being treated with curettage. Thus, this confusion can be minimized by making sure the biopsy specimen has been taken from the center because the areas resembling differentiated-

adamantinoma in osteo-dysplasias are present at the boundaries.[15]

As mentioned earlier, adamantinoma are classically treated with wide local resection with clear margins followed by reconstruction which can be performed by distraction bone grafts and metallic segmental replacement.[12] Amputation of the limb, radiotherapy, chemotherapy or adjuvant therapy has not shown superior performance over en bloc resection.[12] Recurrence rates are generally high with a chance of one in every four patients presenting with recurrent disease after ten years after surgery.[11]

REFERENCES

1. Jain D, Jain VK, Vasishta RK, Ranjan P, Kumar Y. Adamantinoma: A clinicopathological review and update. Diagn Pathol 2008;3:8.
2. Mirra JM. Adamantinoma and osteofibrous dysplasia. In: Bone tumors: clinical, radiologic and pathologic correlation, 1989; p.1203–31.
3. Van Rijn R, Bras J, Schaap G, van den Berg H, Maas M. Adamantinoma in childhood: report of six cases and review of the literature. Pediatr Radiol 2006;36(10):1068–74.
4. Szendroi M, Antal I, Arató G. Adamantinoma of Long Bones: A Long-term Follow-up Study of 11 Cases. Pathol Oncol Res 2009;15(2):209–16.
5. Keeney GL, Unni KK, Beabout JW, Pritchard DJ. Adamantinoma of long bones. A clinicopathologic study of 85 cases. Cancer 1989;64(3):730–7.
6. Qureshi AA, Shott S, Mallin BA, Gitelis S. Current trends in the management of adamantinoma of long bones. An international study. J Bone Joint Surg Am 2000;82(8):1122–31.
7. Liman AD, Liman AK, Shields J, Englert B, Shah R. A Case of Metastatic Adamantinoma That Responded Well to Sunitinib. Case Rep Oncol Med 2016;2016:5982313.
8. Czerniak B, Rojas-Corona RR, Dorfman HD. Morphologic diversity of long bone adamantinoma. The concept of differentiated (regressing) adamantinoma and its relationship to osteofibrous dysplasia. Cancer 1989;64(11):2319–34.
9. Tharmabala M, Kandapur V, Senger JL, Kanthan R. Diagnostic pitfalls in tibial adamantinoma: two cases with a clinicopathological review. Clin Pract 2011;1(4):e138.
10. McCarthy E. Adamantinoma. In: Santini-Araujo E, Kalil RK, Bertoni F, Park YK, editors. Tumors and Tumor-Like Lesions of Bone. Springer, London; 2015.
11. Houdek MT, Sherman CE, Inwards CY, Wenger DE, Rose PS, Sim FH. Adamantinoma of bone: Long-term follow-up of 46 consecutive patients. J Surg Oncol 2018;118(7):1150–4.
12. Limaiem F, Tafti D, Malik A. Adamantinoma. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 [cited 2020 Aug]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK538175/
13. Unni KK, Dahlin DC, Beabout JW, Ivins JC. Adamantinomas of long bones. Cancer 1974;34(5):1796–805.
14. Puchner SE, Varga R, Hobusch GM, Kasparek M, Panotopoulos J, Lang S, *et al*. Long-term outcome following treatment of Adamantinoma and Osteofibrous dysplasia of long bones. Orthop Traumatol Surg Res 2016;102(7):925–32.
15. Kuruvilla G, Steiner GC. Osteofibrous dysplasia-like adamantinoma of bone: a report of five cases with immunohistochemical and ultrastructural studies. Hum Pathol 1998;29(8):809–14.

Submitted: August 28, 2020	*Revised: --*	*Accepted: February 2, 2021*

Address for Correspondence:

Nadia Nazir Jatoi, Dow Medical College, Dow University of Health Sciences, Karachi-Pakistan
Email: nadia.jatoi@outlook.com