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Review Article

Adamantinoma: A review of the current literature

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HIGHLIGHTS

- Rare indolent appendicular malignancy with late local recurrences and lung metastases.
- Suspected vascular histogenesis linked to malignant angioblastoma and ameloblastoma.
- Heterogeneous tumour presents challenges regarding diagnosis and treatment.
- Primary resection with wide margins, reconstruction and MDT approach recommended.
- Clinical management, surveillance and follow up guidelines not available.

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ABSTRACT

Adamantinoma is a rare primary low-grade malignant tumour of the appendicular skeleton most commonly found in the tibia. It has an indolent course, with local recurrences and lung metastases occurring over a protracted duration. There have been several suggestions pertaining to a vascular origin in the literature, however, histogenesis remains unclear. Currently, guidelines are not available pertaining to clinical management.

This paper presents an overview of the current literature regarding this unusual malignancy. It also explores disease etiology and acknowledges the benefits and challenges of investigations pertaining to diagnosis. It recognizes a paucity of recommendations regarding appropriate surveillance and follow up. This review aims to assist clinicians in the building of a consensus opinion for optimal adamantinoma case management under current circumstances where formal guidelines do not exist.

1. Introduction

Adamantinoma is a rare primary low-grade malignant tumour of the appendicular skeleton, which contains variable epithelial and stromal (osteofibrous) component [1,2]. There are several subtypes including classic adamantinoma, osteofibrous dysplasia-like (differentiated) adamantinoma and dedifferentiated adamantinoma. Adamantinoma accounts for less than 1% of primary bone tumours, the first example of which was reported by Maier in 1900 [3,4]. It was further reported by Fischer in 1913, who described the histology as being similar in nature to that of ameloblastoma of the jaw, otherwise known as adamantinoma; however, a shared histogenic origin has not been proven [5,6]. Other authors have also historically reclassified the long bone tumour as a malignant angioblastoma [7,8].

1.1. Etiology

The etiology of this tumour has sparked much debate over many years, with a variety of sources suggesting several histogenic hypotheses. These include epithelial, synovial or endothelial origin [1,8,9]. Fischer went on to claim a potential congenital implantation of adamantine epithelial cells in the tibia as well as in the intraoral enamel, whilst others have also speculated over a traumatic implantation of epithelial cells [2,5]. Epithelial origin would also be supported by the

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theory of skin cell basal epithelial displacement during embryological development, as the anterior tibia is found in close proximity to the skin surface [4]. Another suggestion is that of a double nature, with the lesions being created by both spindle cell and epithelial elements. This would be analogous to a synovial sarcoma [1,8].

Changus et al debated against these aforementioned theories, additionally highlighting that sarcomatous tumours usually have a more aggressive natural history. Instead, given the lesions vascular nature, this group presented a new concept of primitive vascular mesenchymal cell primary components. They argued that their designation of angioblastoma presented a better description of a tumour arising from tissue normally present in bone [1,8,10]. This was further supported by LLombart-Bosch and Ortuño-Pacheco, focusing on the differentiation of the mesoderm to form angioblasts, the primary component of blood vessels [7]. Adamantinomas are known to contain varying amounts of epithelial and osteofibrous components. Osteofibrous dysplasia is a benign fibro-osseous lesion in which there are scattered cytokeratin positive epithelial cells (Fig. 1). This has led to some debate regarding the evolution of classic adamantinoma from osteofibrous dysplasia to osteofibrous dysplasia like and classical adamantinoma [3,5]. This mesenchymal-to-epithelial transformation could present yet another histogenic hypothesis within a spectrum of fibro-osseous disease [4].

1.2. Presentation

Adamantinoma most often presents between the second and fifth

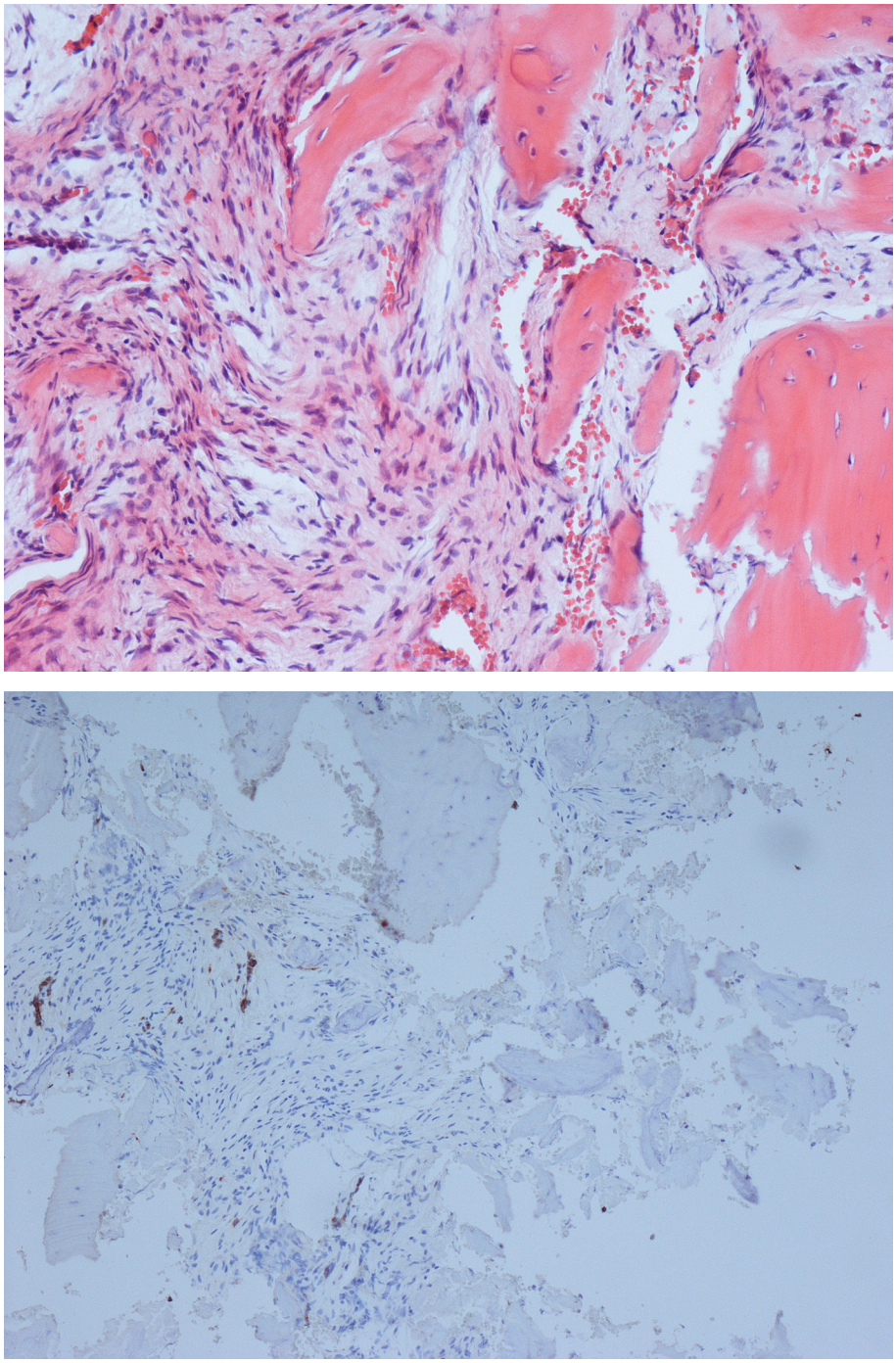

Fig. 1. *(Left)* Osteofibrous dysplasia with haematoxylin-eosin staining. *(Right)* Osteofibrous dysplasia with cytokeratin staining.

decades of life and more commonly in male patients with a male–female ratio of 5:4. It affects the tubular long bones in approximately 97% of cases, with 80–85% occurring in the mid-portion of the tibial diaphysis (or less commonly the metaphysis) and 10–15% concurrently in the fibula [3–5]. Other reported sites include the fibula alone, humerus, ulna, femur, radius, ribs, spine and innominate small bones of the hand and foot [1,11,12].

Beyond the appendicular skeleton, whilst rarer still, adamantinoma can occur in axial locations, with two such cases reported in the ribcage [13,14]. Dini et al provided a summary of a case of spinal adamantinoma alongside five previous reports including two with concurrent mandibular disease [15]. Further still, Mosher reported on a case found in the maxillary sinus and referenced additional cases in the mandible and pituitary gland [16]. These present in addition to several reports of adamantinomas arising exclusively from the soft tissue without any bony involvement. Mills and Rosai, Bambirra, Keeney and Bertoni reported on a total of five cases of histologically identical pre-tibial soft tissue adamantinoma whilst further commenting on possible relationships with this pathology's osseous counterpart [11,17–19]. Whilst remaining controversial in nomenclature, further cases of ameloblastoma have also been reported in the jaw [20,21]. Later in this article, we also comment on one case of metastatic suspected ovarian adamantinoma and two of concurrent unrelated primary tumors [22,23].

1.3. Clinical features

The tumour presents with non-specific slowly progressing symptoms and has an indolent course. These most commonly include pain, swelling, erythema, local sensitivity and bowing deformity; as well as an inability to weight bear and limping [24–26]. Up to 60% of cases will report a previous trauma to the area in question. Severe paraneoplastic, humorally mediated hypercalcemia, hypercalcemic coma, and pancreatitis have also been reported secondary to adamantinoma [3,5].

1.4. Differential diagnoses

In the case of adamantinoma of the long bones, differential diagnoses to consider include Ewing's sarcoma, osteosarcoma, metastatic carcinoma, aneurysmal bone cyst, unicameral bone cyst, eosinophilic granuloma, osteomyelitis, chondrosarcoma, osteofibrous dysplasia, fibrous dysplasia, epithelial metastases, haemangioendothelioma, haemangiosarcoma, non-ossifying fibroma and chondromyxoid fibroma [3,19].

1.5. Radiological diagnosis

Jain et al. noted that a lesion affecting the diaphysis including the anterior cortical bone with extension toward the bone marrow is diagnostic of adamantinoma (Fig. 2). This is based on classic radiographic findings, with approximately 16–23% of cases having a concurrent pathological bone fracture [4,26]. Common features include a central or eccentric osteolytic multilocular lesion with well-circumscribed sclerotic margins indicating slow growth. There is eventual endosteal scalloping and thinning with cortical destruction. Overlapping radiolucencies can create a soap bubble appearance in the middle or distal third of the diaphysis or metaphysis [12]. The mass can be expansile with variable delineation and septations as well as homogenous enhancement and inclusion of the medullary canal. It is usually intra-cortical but invades into the surrounding soft tissue in approximately 15% of cases and a concurrent fracture may produce a periosteal reaction. Lesions can appear in single or multiple nodules in one or more foci [1,5].

Other imaging modalities can also assist in further clarifying the diagnosis. Although computed tomography is useful in assessing cortical involvement and to comment on metastatic disease, Magnetic resonance imaging has been labelled as the gold standard and further delineates distant foci and soft tissue and intramedullary extension margins (Fig. 2). This is particularly useful in order to guide staging and surgical treatment options. Additional use of nuclear medicine scans will likely demonstrate increased blood flow and pooling around the lesion with technetium-99 m methylene diphosphate accumulation (Fig. 3). As an example, positron emission tomography can also identify FDG avid disease across other sites (Fig. 3) [4,5,23].

1.6. Pathological diagnosis

Histopathological diagnosis through the use of biopsies should always be extensive and obtained from the most radiolucent areas. This may additionally include the use of CT or ultrasound guidance. Results should be interpreted in combination with radiological findings and with caution in view of tumour heterogeneity. With this in mind, it is pivotal to highlight the challenging nature of this disease regarding diagnosis, which warrants careful consideration with a full complement of specialist knowledge and expertise. Hence the Multidisciplinary Team approach is required to direct and achieve appropriate management [3,4].

Adamantinoma has been categorized into classical, osteofibrous dysplasia-like (differentiated) and dedifferentiated histological subtypes. Macroscopically adamantinomas are bland pale-colour tumours of variable consistency; they may contain they may contain cystic spaces in which there is straw or blood-like fluid content. Differentiated adamantinoma is distinguished histologically from classical adamantinoma by containing relatively few epithelial cells, some of which lie in small collections or nests (Fig. 4). Osteofibrous dysplasia–like adamantinoma is more commonly seen in the younger population, has a higher proportion of more centrally located osteofibrous stromal tissue and lacks a clear histological epithelial component (Fig. 5) [27,28]. Comparatively, this type tends to be less destructive, multicentric and remains intracortical [3,5,29]. In contrast, classical adamantinomas are seen most commonly and have a prominent epithelial component which cytologically maybe mixed in type [12,30]. Very rarely there may be dedifferentiation of a classical adamantinoma to a sarcoma containing pleomorphic or round tumour cells (Ewing sarcoma-like). Rare reports of high-grade cancerous transformation to squamous cell cancers within adamantinomas have been reported [31].

Microscopically, epithelial tumour cells vary in size and have finely dispersed chromatin with few mitotic figures. The osteofibrous component has a storiform pattern of spindle cells and there are woven bone trabeculae with varying amounts of lamellar bone transformation at the peripheries and foam cell or myxoid change. The spindle cell component is more commonly seen in recurrences and metastases [1,4].

In a series of 195 cases, Moon and Mori used ultrastructural and immunohistochemical (IHC) studies to further the argument for an epithelial origin. These epithelial cells may represent the active neoplasm within adamantinomatous lesions, as the fibrous component shows little comparable expression, suggesting a potential reactive surrounding growth. Several authors have demonstrated there to be epithelial cell basal keratin, growth factor and fibrous vimentin staining regardless of lesion subtype, which has also been seen in recurrences and metastases. Other features include epithelial-like microvilli and tonofibrils forming the desmosomes, which are indispensable for cell-to-cell attachment. Electron microscopy has additionally shown cells to have further epithelial characteristics including basal lamina, gap junctions and extracellular composition [1,2,4]. Llombart-Bosch and Ortuño-Pacheco, however, contradicted these findings in a previous paper. Instead, they reported a lack of desmosomes and evidence of pinocytic activity with bundles of filaments resembling hyperplastic endothelial cells. In addition, there was noted to be fibrolipoblastic lipid-laden mesenchymal cells within the stroma [7].

More recently, further IHC investigation has shown adamantinomas are positive for cytokeratins 5, 14 and 19. There is variable expression of cytokeratins 1, 13 and 17 but virtually no expression of cytokeratins 8 and 18 [4,32]. The stromal component is positive for vimentin.

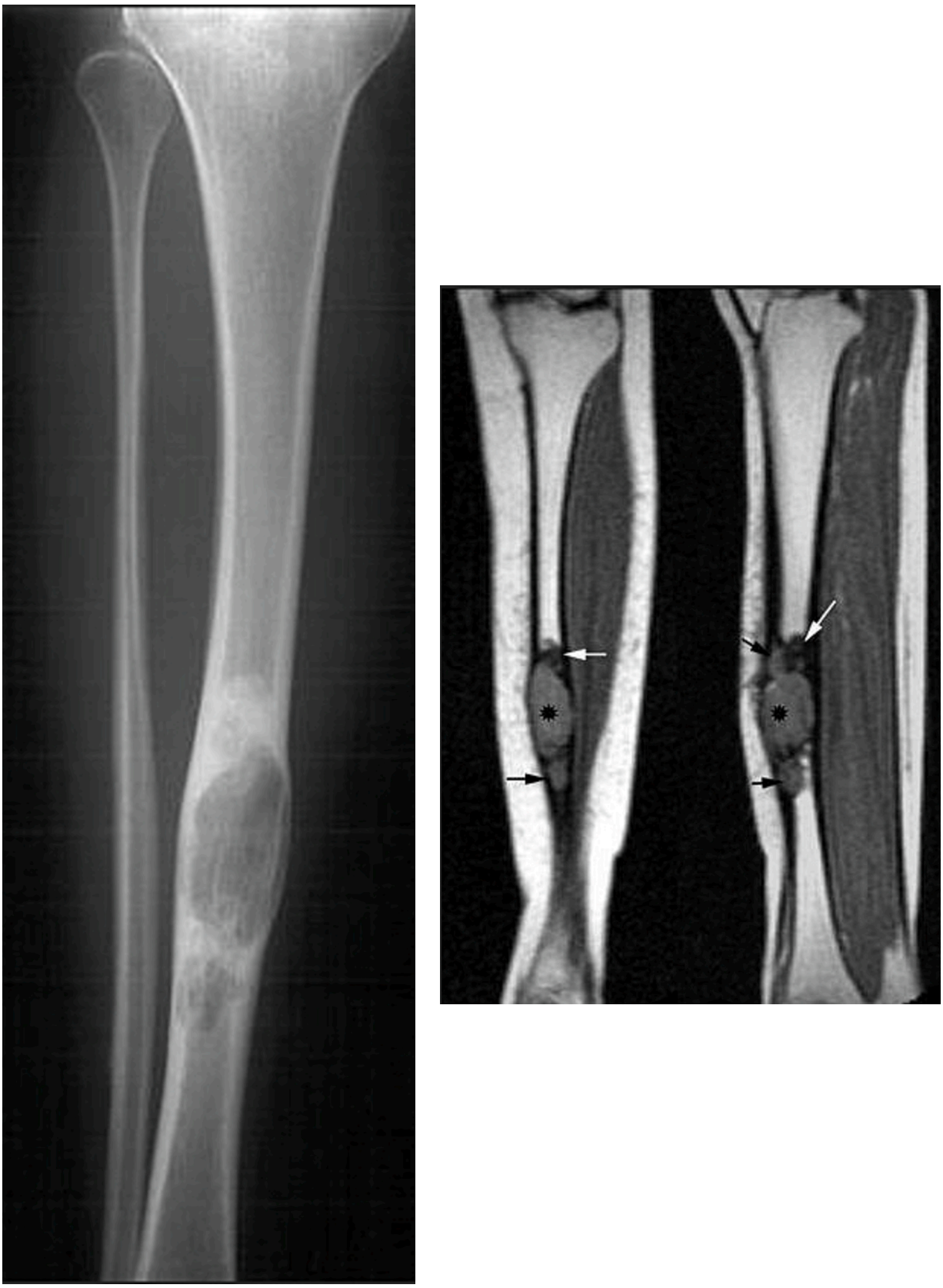

Fig. 2. *(Left)* Anteroposterior radiograph of the left tibia shows a sharply delineated expansile osteolytic lesion at the middle third of the diaphysis with reactive bone sclerosis and small satellite radiolucent foci in direct continuity with the major lesion. *(Right)* Coronal and sagittal SE-T1 weighted images demonstrate a central well-defined expansile lesion of homogeneous intermediate signal intensity (asterisk) with small satellite foci (black arrows) and decreased signal in the periphery of the lesion consistent with sclerotic changes (white arrows) [49].

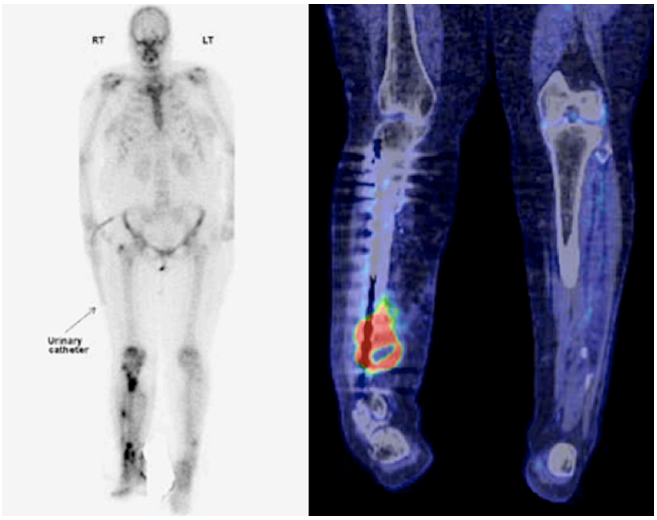

Fig. 3. *(Left)* Technitium-99 nuclear medicine scan demonstrating multi-focal uptake within the right tibia. *(Right)* PET scan demonstrating an FDG avid mass enveloping the anteromedial aspect of the right distal fibula.

Examining flow cytometry and p-53 expression, IHC studies demonstrated up to 48% expression of p53 proteins in all classical subtypes [33,34]. P-63 is also a reliable marker in adamantinomas [35]. E-, P- and N- cadherin, as well as osteonectin are expressed in classical subtype whereas in OFD adamantinoma expression of nuclear factor kB ligand, macrophage cerebrospinal fluid and osteoclastogenic factors are seen [29,36]. Trisomies of chromosomes 7, 8, 12, 19 and 21 have been demonstrated through GTG-banding in both classical and OFD adamantinomas substantiating the common histological origins, findings of translocations, deletions and inversions are only present in adamantinomas [1,8,33,37]. In literature, a rare variant adamantinoma-like Ewing sarcoma is described; however, this is now known to be molecularly distinct and is in fact an Ewing sarcoma that exhibits some histological features of adamantinoma. It can be differentiated on the basis of the classical translocation characteristics of Ewing sarcoma t(11; 22) and t(21; 22) using reverse transcription polymerase chain reactions [38].

The angioblastoma theory has further been supported through microscopic findings by Huvos and Marcove; and a series of 85 cases reported by Keeney et al, which commented on an unusually prominent vascular pattern with regards to the lesions histologic appearance [10,11]. Structures that are similar to endothelial Weber-Palade bodies and alkaline phosphatase have also been demonstrated. In further support of the nomenclature of malignant angioblastoma of the bone, Changus et al went so far as to achieve review and histological reclassification of 25 cases of adamantinoma of the long bone on the basis of the authors' descriptions. They also highlighted the abnormal vascular channels seen within these tumours and focused on a similar histochemical reaction seen when compared to normal blood vessels.

2. Metastatic disease

Metastases occur in the region of 15–30% of patients through lymphovascular routes. Common sites of metastases include the regional lymph nodes and lungs, with cases seen less frequently in the bone and abdominal viscera and even less so in the retroperitoneum [22,26]. We noted a wide variation in the reported rate of lymph node metastases, with Keeney et al. documenting a 7% risk, whilst Moon and Mori described up to 28.6% in their post mortem examinations [2,11]. Less common still, Schowinsky et al commented on a patient with a potential 'secondary' metastasis to the brain from a metastatic lung nodule, 32 years following surgical excision of adamantinoma of the tibia [5,23,39].

Recurrences and metastases can occur over vast periods of time, with cases reportedly occurring up to 36 years after initial treatment. Such an example from Giannoulis et al reported on a 46-year-old patient who developed both multiple early recurrences in the tibia and late metastasis to the lung and ribs 13 years later. However, this protracted course of recurrence and reported overall low-grade malignant potential is not always the case. Binesh et al highlighted such an example in 2012 – here a 19-year-old male died within weeks of diagnosis and initial surgery to eradicate adamantinoma of the pelvis due to acute liver failure secondary to widespread metastases [3,25,40].

It is also important to remain vigilant for potential diagnoses of incidental unrelated primary concurrent cancers. Such a case has been reported only twice in the literature, with a chromophobe-type renal cell carcinoma diagnosed following partial nephrectomy for presumed adamantinomatous metastasis and a case of metastatic adamantinoma alongside primary concurrent breast cancer [22]. This consideration further emphasizes the role of the MDT in decision-making regarding the diagnosis and management of such lesions. When considering potential metastases, there are significant challenges regarding the interpretation of investigations pertaining to the disease site and origin. In such patients, clinicians might also consider ruling out a genetic predisposition to cancer [4,23].

2.1. Surgical management of primary and recurrent disease

Patients are often under the clinical management of the sarcoma MDT with primary management input from orthopaedics and management of pulmonary disease by thoracic surgery, amongst other specialties. The standard treatment for adamantinoma of long bones is en-bloc resection with wide surgical margins, aiming for complete excision in an effort to reduce chances of local recurrence of this locally aggressive tumour [2,11,40,41]. Limb salvage with intercalary resection and reconstruction either with bone transport, free vascularized fibular graft, allograft or endoprosthetic reconstruction can be attempted [1,3,42]. More rarely the treatment to get adequate resection margins would require limb ablative surgery followed by the use of limb prosthesis. Locoregional lymph node dissection should also be considered at the time of primary tumour resection. Intralesional surgery such as curettage and cementing is not recommended.

Whilst most patients are treated with limb salvage, it should be acknowledged that the need for reoperation was significantly high at 39% in one review; and mostly due to surgical complications [9]. A case series by Qureshi et al across 23 cancer centres in a ten-year period reviewed 70 patients; 91% of whom had attempted limb salvage and 51% of whom had an intercalary allograft reconstruction. The final preservation rate was 84%, as 8% later required amputation, with wide operative margins achieved in 92%. Reconstruction related complications occurred in 48% of cases, with allograft fracture and non-union occurring in 24% and 23% of cases respectively. Further minor rates occurred with infection (10%), unspecified soft tissue complications (3%) and delayed union (3%). Adamantinoma is known to be locally aggressive (Fig. 6). Local recurrence was documented with Kaplan-Meier analysis at a rate of 8.6% at 5 years and 18.6% at 10 years, which was not statistically significant regarding relationship to stage [3,9,42]. Houdek documented 10-year disease specific and recurrence free survival of 92 and 72% respectively [9]. Local recurrence is more common still in cases of incomplete resection, as with sarcomatous tumours. Amputation is not felt to improve outcomes in primary tumours, but is, instead, reserved for such instances of local recurrence [5,40]. Care should be holistic and should also include physiotherapy, prosthetic and cancer nurse specialist allied healthcare professionals [4].

More recently, the European Musculoskeletal Oncology Society (EMSOS) published a further large international multicentric study spanning 30 years and 22 tertiary centres. This included 190 cases of adamantinoma, which we believe is the largest case series to date. In this

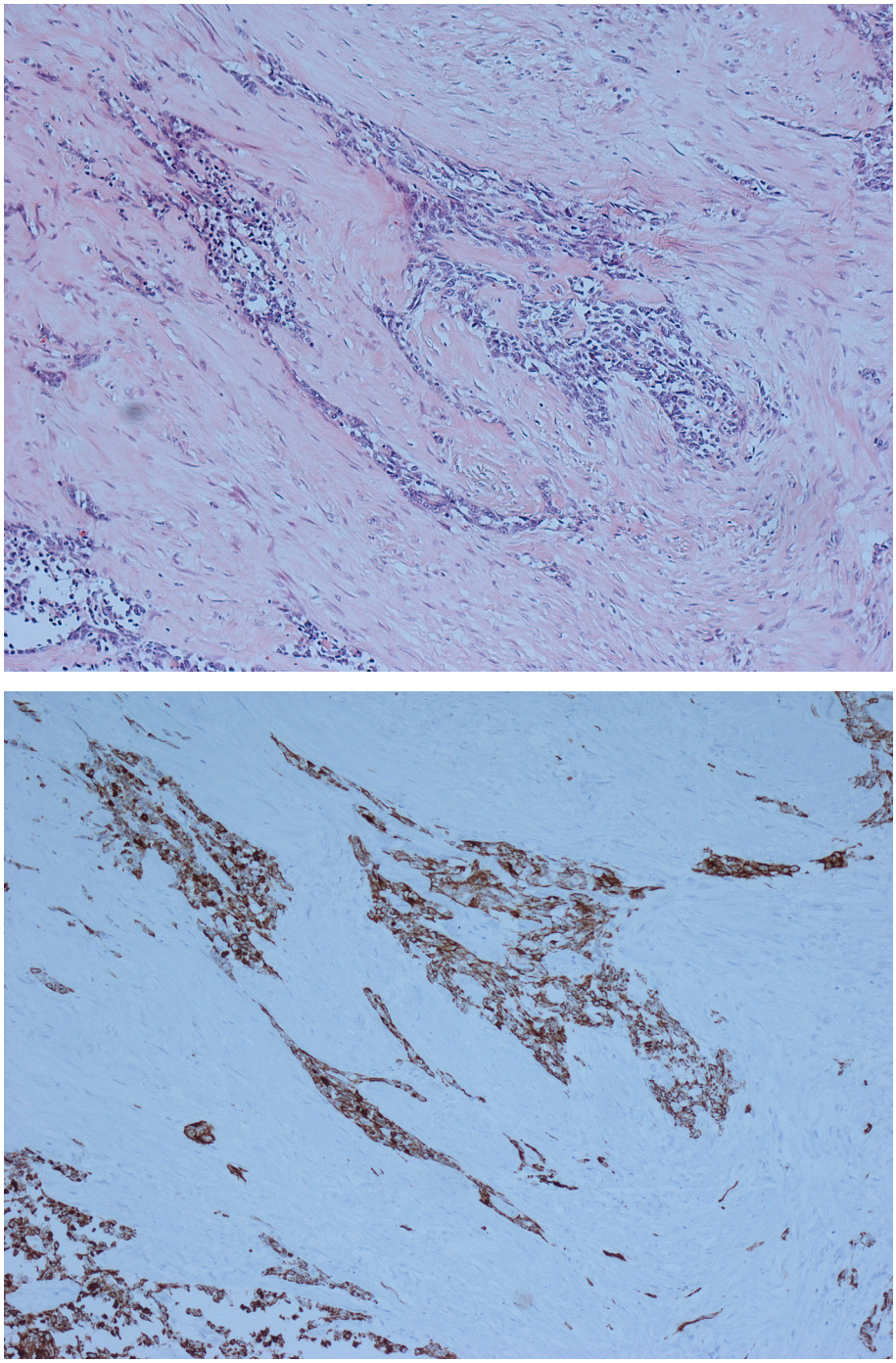

Fig. 4. *(Left)* Classical adamantinoma with haematoxylin-eosin staining. *(Right)* Classical adamantinoma with cytokeratin staining.

article focused on surgical outcomes and oncological survival, the authors further acknowledged the limitations of available data to support current treatment strategies. Local recurrence was recorded in 24% of cases and felt to be multifactorial. A proportion were felt to be due to undetected skip lesions as well as the possible presence of periosteal disease, further highlighting the need for aggressive wide surgical excision with clear margins [26].

2.2. Adjuvant therapy

There has been no demonstrated role for the use of adjuvant therapies (as in metastasizing ameloblastoma), however, there is still significant merit in obtaining input from both medical and clinical oncology specialists. The authors acknowledge that this information is based on a summary of case series and report findings noted whilst conducting their literature review and does not appear to have been investigated in clinical trials; owing to the rarity of this pathology [10,26]. Hazelbag reported on three patients with metastatic disease receiving chemotherapy who did not achieve any benefit regarding tumour volume or survival and three other authors reported disease stability at best with chemotherapy and radiotherapy followed by subsequent progression across a mere matter of months in three further cases [43–46]. In fact, J. Lokich reported the only discernable case of disease regression; where on two separate occasions a patient with metastatic adamantinoma of the bone to the lung responded to combinations of etoposide with cisplatin and then carboplatin. The same patient responded once again

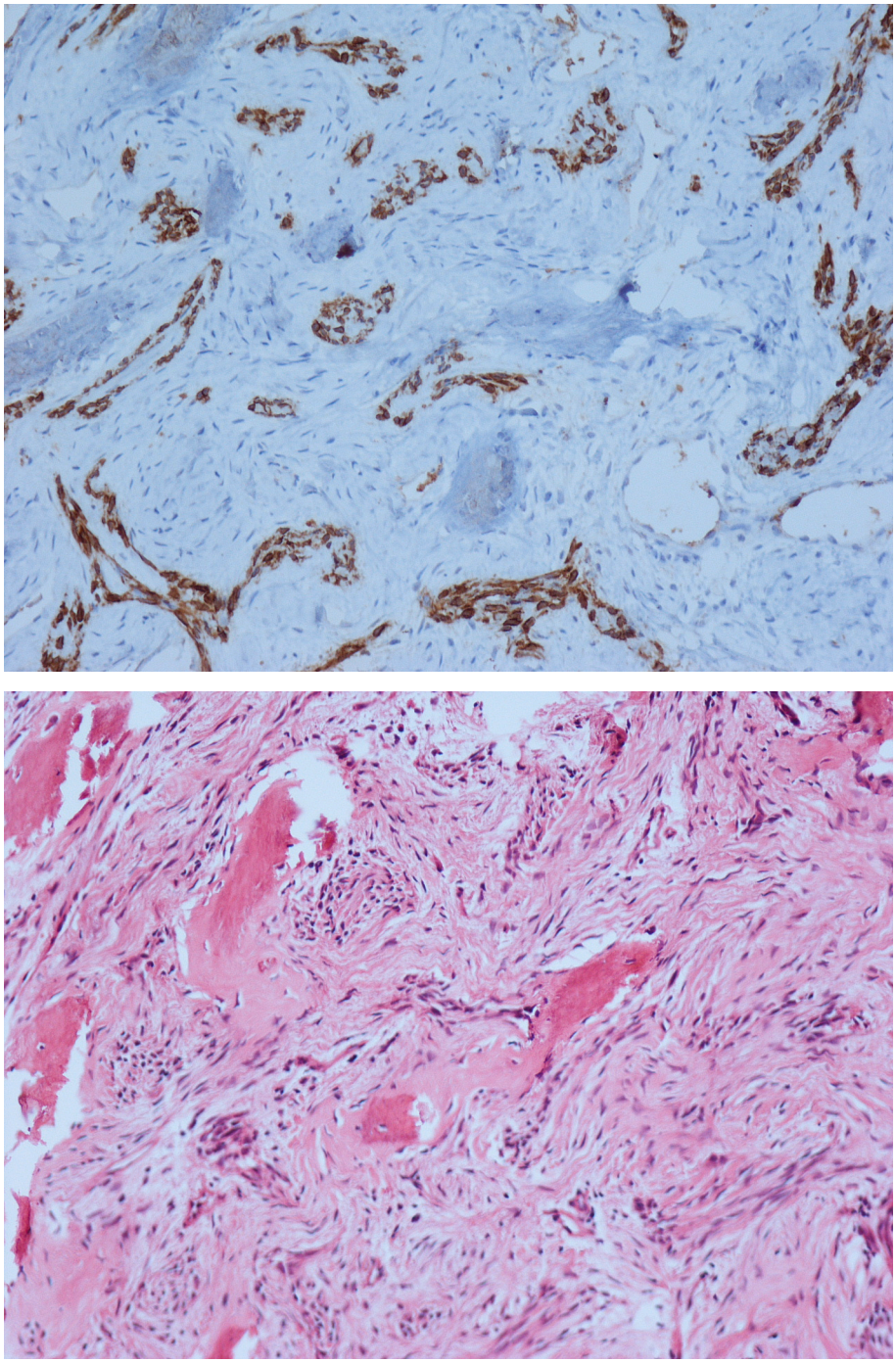

Fig. 5. *(Left)* Osteofibrous dysplasia-like (differentiated) adamantinoma with haematoxylin-eosin staining. *(Right)* Osteofibrous dysplasia-like (differentiated) adamantinoma with cytokeratin staining.

to palliative radiation, resulting in a protracted duration of metastatic disease over three years [47].

2.3. Prognosis

Links between a less favourable clinical outcome have been demonstrated based on male gender, short duration of symptoms particularly with predominating pain, younger age at presentation, histological lack of squamous differentiation and intraregional treatment modalities [11,39]. Further to this, EMSOS reported that resection margins, incidence of pathological fracture and patient gender significantly attributed to local recurrence risk [26]. No statistically significant difference has been reported between local recurrence rate and tumour stage, type of biopsy or method of graft reconstruction used. In a series of 92 patients by Aytekin et al, this also applied to survival times and additionally included patient race, year of diagnosis and primary tumour location. Another reported case of adamantinoma with aggressive liver and pulmonary metastases further postulated on possible improvement in overall outcome based on cellular malignant potential at biopsy. The author found very dense cell proliferation without interstitial tissue and dominant epithelial parts. They suggested that if recurrences and metastases were under good control, resection should be curtailed to include only newly appearing high grade lesions [3,41,42,48]. Adamantinoma has been reported to be fatal in up to 11%

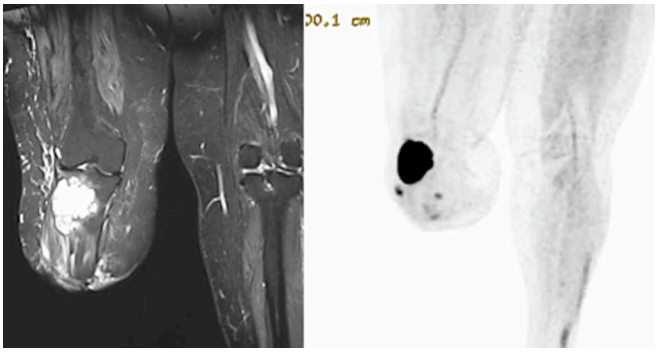

Fig. 6. *(Left)* MRI and *(right)* PET scans demonstrating recurrence affecting the right leg stump site following previous *trans*-tibial amputation for recurrence despite 7 cm surgical margin.

of cases [26]. Recent data has demonstrated a five and ten year overall survival rate of 98.8% and 91.5%. This author concluded that patients generally have an excellent prognosis [48].

2.4. Follow up

In view of late recurrences and metastases, all patients require long-term follow up, with some authors suggesting this should be life-long. There has, however, been a noted paucity of evidence regarding the best modality of follow up imaging and surveillance intervals [4,11,25]. In the Houdek et al case series, 42% of patients with distant metastatic disease focused on abdominal recurrences or pelvic lymphadenopathy, indicating consideration for abdominopelvic CT or PET scans. However, the same authors reported their current practice to include only MRI of the involved extremity and chest CT for 10 years [9]. Most authors suggest regular clinical and radiograph follow up focusing on MRI or radiograph of the extremity with some going on to suggest surveillance chest radiograph, chest CT or whole body MRI. EMSOS also emphasized the need for long-term follow up of twenty years or more using chest and local radiographs or MRI of the surgical site as 11% of their cases of local recurrence were diagnosed more than ten years following initial treatment [26]. Another consideration may be to highlight the need for a more or less intensive individualized action plan given each patient's disease course to date [3,23,24,39].

3. Conclusions

Adamantinoma is a rare long bone tumour of uncertain origin with late recurrences and metastases. Complex unspecific presentations warrant careful consideration and planning with a full complement of specialist knowledge and expertise. The heterogeneous nature of this tumour presents challenges regarding diagnosis and treatment from both radiology and histology perspectives. The MDT approach is required to direct and achieve appropriate management. Such cases require the application of advanced surgical skills and experience. Complete resection and reconstruction should be completed with wide surgical margins where possible, resulting in reported good prognostic outcomes. There remains a lack of structured guidance regarding appropriate follow up and surveillance. This should perhaps warrant an individualized approach taking into consideration the patient's disease course so far; and generally encompasses both clinical and radiological investigations on a long-term basis.

4. Studies in humans and animals

Not applicable.

5. Informed patient consent

Obtained.

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7. Contributions

SLS proposed the literature search and composed the manuscript, AS edited the manuscript, NA/SLS/AS provided illustrative figures, DW/HSM/NA senior reviewed the manuscript. HSM proposed the concept of the manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] P. Kitsoulis, A. Charchanti, G. Paraskevas, A. Marini, G. Karatzias, Adamantinoma, Acta Orthop. Belg. 73 (4) (2007) 425–431.
[2] N.F. Moon, H. Mori, Adamantinoma of the appendicular skeleton–updated, Clin. Orthop. 204 (1986) 215–237.
[3] P.J. Papagelopoulos, A.F. Mavrogenis, E.C. Galanis, O.D. Savvidou, C.Y. Inwards, F. H. Sim, Clinicopathological features, diagnosis, and treatment of adamantinoma of the long bones, Orthopedics 30 (3) (2007) 211–215.
[4] D. Jain, V.K. Jain, R.K. Vasishta, P. Ranjan, Y. Kumar, Adamantinoma: A clinicopathological review and update, Diagn. Pathol. 15 (3) (2008) 8.
[5] Gulia and Panda, Adamantinoma; An update, J Bone Soft Tissue Tumors. 3 (2) (2017) 16–19.
[6] B. Fischer, Uber ein primares Adamantinoma der Tibia, Frankf. Z. Pathol. 12 (1913) 422–441.
[7] A. Llombart-Bosch, G. Ortuño-Pacheco, Ultrastructural findings supporting the angioblastic nature of the so-called adamantinoma of the tibia, Histopathology 2 (3) (1978) 189–200.
[8] G.W. Changus, J.S. Speed, F.W. Stewart, Malignant angioblastoma of bone; a reappraisal of adamantinoma of long bone, Cancer 10 (3) (1957) 540–559.
[9] M.T. Houdek, C.E. Sherman, C.Y. Inwards, D.E. Wenger, P.S. Rose, F.H. Sim, Adamantinoma of bone: Long-term follow-up of 46 consecutive patients, J. Surg. Oncol. 118 (7) (2018) 1150–1154.
[10] A.G. Huvos, R.C. Marcove, Adamantinoma of long bones. A clinicopathological study of fourteen cases with vascular origin suggested, J. Bone Joint Surg. Am. 57 (2) (1975) 148–154.
[11] G.L. Keeney, K.K. Unni, J.W. Beabout, D.J. Pritchard, Adamantinoma of long bones. A clinicopathologic study of 85 cases, Cancer 64 (3) (1989) 730–737.
[12] D.N. Varvarousis, G.P. Skandalakis, A. Barbouti, G. Papathanakos, P. Filis, K. Tepelenis, A. Kitsouli, P. Kanavaros, P. Kitsoulis, Adamantinoma: an updated review, In Vivo 35 (6) (2021) 3045–3052.
[13] D. Plump, E.F. Haponik, R.S. Katz, A. Tipton-Donovan, Primary adamantinoma of rib: thoracic manifestations of a rare bone tumor, South. Med. J. 79 (3) (1986) 352–355.
[14] H. Beppu, H. Yamaguchi, N. Yoshimura, K. Atarashi, K. Tsukimoto, Y. Nagashima, Adamantinoma of the Rib Metastasizing to the Liver, Intern. Med. 33 (7) (1994) 441–445.
[15] L.I. Dini, R. Mendonça, C.A. Adamy, G.A. Saraiva, Adamantinoma of the spine: case report, Neurosurgery 59 (2) (2006) E426.
[16] W.F. Mosher, Adamantinoma of the maxillary sinus, Arch Otolaryngol - Head Neck Surg. 40 (1) (1944) 61–62.
[17] S.E. Mills, J. Rosai, Adamantinoma of the prétibial soft tissue: clinicopathologic features, differential diagnosis, and possible relationship to intraosseous disease, Am. J. Clin. Pathol. 83 (1) (1985) 108–114.
[18] E.A. Bambirra, A.M. Nogueira, D. Miranda, Adamantinoma of the soft tissue of the leg, Arch. Pathol. Lab. Med. 107 (9) (1983) 500–501.
[19] F. Bertoni, V. Zucchi, S. Mapelli, P. Bacchini, Case report 506: Adamantinoma of the soft tissues of the leg, Skeletal Radiol. 17 (7) (1988) 522–526.
[20] K.H. Thoma, Clinical pathology of the jaws: with histologic and roentgen study of practical cases, C. C. Thomas (1934) 676.
[21] H.B.G. Robinson, Ameloblastoma: survey of 379 cases from the literature, Arch Path. 23 (1937) 831–843.
[22] S. Smyth, S. Addley, M. Alazzam, H.S. Majd, Adamantinoma: metastatic disease masquerading as a gynaecological malignancy, BMJ Case Rep CP 14 (6) (2021) e241615.
[23] B.R. Southam, A.H. Crawford, D.A. Billmire, J. Geller, D. Von Allmen, A. P. Schumaier, S. Szabo, Long-term follow-up of adamantinoma of the tibia

complicated by metastases and a second unrelated primary cancer. A case report and literature review, Case Rep Orthop 2018 (2018) 1–9.
[24] J.S. Virk, M. Pruthi, B. Rekhi, S. Pasricha, Adamantinoma of pelvis: A rare tumor at an uncommon site, with diagnostic implications, Indian J. Orthop. (2020), https://doi.org/10.1007/s43465-020-00196-2.
[25] F. Binesh, J. Abrisham, M. Sobhan, H. Navabii, M.R. Vahidfar, K. Ashrafi, Adamantinoma of the pelvic bone, a difficult diagnosis with fatal outcome, Chin.-Ger. J. Clin. Oncol. 11 (7) (2012) 425–428.
[26] E.M. Schutgens, P. Picci, D. Baumhoer, R. Pollock, J.V.M.G. Bovée, P.C. W. Hogendoorn, et al., Surgical outcome and oncological survival of osteofibrous dysplasia-like and classic adamantinomas: an international multicenter study of 318 cases, J. Bone Joint Surg. Am. 102 (19) (2020) 1703–1713.
[27] S.S. Desai, N. Jambhekar, M. Agarwal, A. Puri, N. Merchant, Adamantinoma of tibia: a study of 12 cases, J. Surg. Oncol. 93 (5) (2006) 429–433.
[28] G. Jundt, K. Remberger, A. Roessner, A. Schulz, K. Bohndorf, Adamantinoma of Long Bones: a histopathological and Immunohistochemical study of 23 cases, Pathol - Res Pract. 191 (2) (1995) 112–120.
[29] M. Maki, K. Saitoh, Y. Kaneko, M. Fukayama, T. Morohoshi, Expression of cytokeratin 1, 5, 14, 19 and transforming growth factors-beta1, beta2, beta3 in osteofibrous dysplasia and adamantinoma: A possible association of transforming growth factor-beta with basal cell phenotype promotion, Pathol. Int. 50 (10) (2000) 801–807.
[30] J.L. Bloem, R.O. van der Heul, H.M. Schuttevaer, D. Kuipers, Fibrous dysplasia vs adamantinoma of the tibia: differentiation based on discriminant analysis of clinical and plain film findings, AJR Am. J. Roentgenol. 156 (5) (1991) 1017–1023.
[31] N.K. Dashti, B.M. Howe, C.Y. Inwards, K.J. Fritchie, J.M. Carter, High-grade squamous cell carcinoma arising in a tibial adamantinoma, Hum. Pathol. 91 (2019) 123–128.
[32] H.M. Hazelbag, G.J. Fleuren, L.J.C.M. vd Broek, P.C.W. Hogendoorn, A.H. M. Taminiau, Adamantinoma of the long bones: keratin subclass immunoreactivity pattern with reference to its histogenesis, Am. J. Surg. Pathol. 17 (12) (1993) 1225–1233.
[33] H.M. Hazelbag, P.C.W. Hogendoorn, Bone: Adamantinoma, Atlas Genet. Cytogenet. Oncol. Haematol. 7 (2) (2003) 122–124.
[34] A. Horvai, N.K. Dashti, B.P. Rubin, S.E. Kilpatrick, E.R. Rudzinski, D. Lopez-Terrada, M.B. Hubley, J.L. Davis, K. Fritchie, Genetic and molecular reappraisal of spindle cell adamantinoma of bone reveals a small subset of misclassified intraosseous synovial sarcoma, Mod. Pathol. 32 (2) (2019) 231–241.
[35] K. Bohndorf, A. Nidecker, K. Mathias, H. Zidkova, H. Kaufmann, G. Jundt, Radiologische Befunde beim Adamantinom der langen Röhrenknochen, RöFo - Fortschritte Auf Dem Geb Röntgenstrahlen Bildgeb Verfahr. 157 (09) (1992) 239–244.
[36] R.M. Taylor, T.G. Kashima, D.J. Ferguson, K. Szuhai, P.C. Hogendoorn, N. A. Athanasou, Analysis of stromal cells in osteofibrous dysplasia and adamantinoma of long bones, Mod. Pathol. 25 (1) (2012) 56–64.
[37] M. Kanamori, C.R. Antonescu, M. Scott, R.S. Bridge, J.R. Neff, S.S. Spanier, M. T. Scarborough, G. Vergara, H.G. Rosenthal, J.A. Bridge, Extra copies of chromosomes 7, 8, 12, 19, and 21 are recurrent in adamantinoma, J Mol Diagn JMD. 3 (1) (2001) 16–21.
[38] E. Hauben, L.C.J.M. van den Broek, E. Van Marck, P.C.W. Hogendoorn, Adamantinoma-like Ewing's sarcoma and Ewing's-like adamantinoma. The t(11; 22), t(21; 22) status, J. Pathol. 195 (2) (2001) 218–221.
[39] J.T. Schowinsky, D.R. Ormond, B.K. Kleinschmidt-DeMasters, Tibial adamantinoma: late metastasis to the brain, J. Neuropathol. Exp. Neurol. 74 (1) (2015) 95–97.
[40] D.K. Giannoulis, A. Gantsos, D. Giotis, N.K. Paschos, A. Vagionas, C. M. Arnaoutoglou, G. Pentheroudakis, T.A. Xenakis, Multiple recurrences and late metastasis of adamantinoma in the tibia: a case report, J. Orthop. Surg. Hong Kong. 22 (3) (2014) 420–422.
[41] T. Kurata, H. Tajima, Y. Obatake, S. Nakanuma, I. Makino, H. Hayashi, et al., A case of liver and pulmonary metastases from adamantinoma, a bone tumor, Gan To Kagaku Ryoho 42 (12) (2015) 1677–1679.
[42] A.A. Qureshi, S. Shott, B.A. Mallin, S. Gitelis, Current trends in the management of adamantinoma of long bones. An international study, J. Bone Joint Surg. Am. 82 (8) (2000) 1122–1131.
[43] H.M. Hazelbag, A.H. Taminiau, G.J. Fleuren, P.C. Hogendoorn, Adamantinoma of the long bones. A clinicopathological study of thirty-two patients with emphasis on histological subtype, precursor lesion, and biological behavior, J. Bone Joint Surg. Am. 76 (10) (1994) 1482–1499.
[44] Y. Cohen, J.E. Cohen, A. Zick, M. Orevi, V. Doviner, R. Rubinstein, H. Goldshmidt, N. Peylan-Ramu, D. Katz, A case of metastatic adamantinoma responding to treatment with pazopanib, Acta Oncol Stockh Swed. 52 (6) (2013) 1229–1230.
[45] U.J. van Haelst, A.H. de Haas van Dorsser, A perplexing malignant bone tumor. Highly malignant so-called adamantinoma or non-typical Ewing's sarcoma, Virchows Arch. A Pathol. Anat. Histol. 365 (1) (1975) 63–74.
[46] A.D. Liman, A.K. Liman, J. Shields, B. Englert, R. Shah, A case of metastatic adamantinoma that responded well to sunitinib, Case Rep. Oncol. Med. 2016 (2016) 1–5.
[47] J. Lokich, Metastatic adamantinoma of bone to lung: A case report of the natural history and the use of chemotherapy and radiation therapy, Am. J. Clin. Oncol. 17 (2) (1994) 157–159.
[48] M.N. Aytekin, R. Öztürk, K. Amer, Epidemiological study of adamantinoma from US surveillance, epidemiology, and end results program: III retrospective analysis, J. Oncol. 2020 (2020) 1–8.
[49] Eurorad.org [Internet]. Eurorad - Brought to you by the ESR. [cited 2023 May 31]. Available from: https://www.eurorad.org/case/2824.