Diagnostic pitfalls in tibial adamantinoma: two cases with a clinicopathological review

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Abstract

Adamantinoma is a rare primary bone tumor that commonly arises in the jaw and has also been described in the appendicular skeleton such as the tibia. We report 2 cases of tibial adamantinomas that were originally misdiagnosed; one as fibrous dysplasia of the tibia and the other as a cutaneous eccrine carcinoma in a groin mass, which was metastatic adamantinoma to the inguinal lymph nodes. Such metastatic adamantinoma to the groin lymph nodes is extremely rare. The clinical and pathological data with a review of the available literature on inguinal lymph node metastases from primary tibial adamantinoma are reported. Increased clinical awareness and accurate recognition of such uncommon patterns of inguinal nodal metastases are imperative for appropriate planning of therapeutic strategies and risk management in these patients.

Introduction

Adamantinoma of the tibia is a rare slow-growing primary tumor of the bone. There has been much controversy on the origins of this tumor with one major focus being the relationship between osteofibrous/fibrous dysplasia and adamantinoma.[1-6] There have been approximately 300 cases of tibial adamantinoma reported in the published English language literature.[6-8] Of these cases, 15-20% have been reported to metastasize.[7-9] The most common site of metastasis is to the lungs.[7-9] As metastases to the regional lymph nodes are rare, there is limited information regarding the best practice plan for their management in the literature.

We report 2 cases of tibial adamantinoma, which were problematic from a diagnostic point of view. Case 1 is of a tibial adamantinoma that was initially diagnosed as fibrous dysplasia. Case 2 is of a tibial adamantinoma that presented with groin metastases which was initially diagnosed as a cutaneous adnexal carcinoma. A review of inguinal nodal metastatic adamantinoma is outlined in addition to the clinic-pathological data on these cases.

Case Reports

Case #1

In 2007, a 29-year-old female presented with a swelling in her left inguinal area. The rest of her physical examination was unremarkable. Investigations including a computed tomography (CT) scan showed an extremely large heterogeneous, hyperdense, lobular lymph node centered in the left inguinal region measuring 6.5×4.6 cm. A biopsy was obtained under radiological guidance for a suspected diagnosis of *lymphoma*.

Histopathological examination revealed the presence of a malignant neoplasm that was composed of sheets of basaloid cells with round vesicular nuclei and minimal cytoplasm. This lesion was interpreted as a cutaneous eccrine carcinoma (Figure 1A-C). Due to the unusual diagnosis, an external consultation and a request for additional clinical history were obtained. On detailed review, the pathological report was reinterpreted as metastatic adamantinoma in conjunction with a confirmed past clinical history of surgical excision of a left tibial adamantinoma three years previously in 2004.

The patient underwent a formal inguinal lymphadenectomy for metastatic adamantinoma. The specimen consisted of a firm rubbery mass of fibro-fatty tissue that measured 18.5×11.3×7.2 cm with an ellipse of skin measuring 8×2×0.3 cm. The cut surface revealed a multi-lobulated light brown well-circumscribed mass that measured 10.4×7×5.5 cm. On microscopic examination, the neoplastic cells were composed of predominantly basaloid and tubular nests of malignant cells with some peripheral palisading (Figure 1D-F). The histomorphological appearance of these cells was identical to the previous histology in this case (Figure 1A-C) confirming the presence of inguinal lymph nodal metastases from adamantinoma of the tibia.

In April 2009, a new node along the left external iliac in the retroperitoneum was detected and biopsied under radiological guidance. Histopathological examination showed similar findings confirming the presence of metastatic adamantinoma (Figure 2A and B). CT scans of the chest showed the presence of two nodules in the right lung, which remained stable on follow up over the following year. The patient refused any active intervention in relation to the pulmonary nodules. Follow up in early 2011 shows stable residual disease with no additional findings of note.

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Case #2

In 1999, a 58-year-old female presented with a painful swelling on the mid shaft of her left tibia. The lesion was treated with curettage and bone grafting. Histopathological examination showed the presence of islands of woven bone in a background of bland spindled fibrous tissue, which was interpreted as fibrous dysplasia (Figure 3A and B).

Nine years later, in 2008, she was seen for a painful swelling in the same region, which had been increasing in size since her previous operation. A biopsy was undertaken that was interpreted as adamantinoma. A wide excision of the lesion with a tibial allograft and intramedullary nail fixation was performed in October 2009. The histopathology of this specimen was compared with the previous one. In both specimens there was a predominant *fibrous dysplasia like pattern* consisting of cellular bland, spindled fibroblastic proliferation with scattered islands of woven bone. Embedded within the spindle cells were occasional clusters of plump epitheliod appearing cells that had a corded arrangement in focal regions (Figure 3C). Immunohistochemistry confirmed the epithelial nature of these cells with strong positive staining to pankeratin antibodies (Figure 3D). Such areas were not identified even on retrospective detailed examination of the previous biopsy from 1999.

The patient underwent revision surgery for non-union of the left tibia in 2010. Her postop-

erative course was uneventful. Follow up in January 2011 showed no evidence of local recurrence or distant metastases.

Review and Discussion

A literature search limited to the English language using the search terms *adamantinoma of tibia* AND *tibial adamantinoma* AND *metastases* AND *inguinal lymph node metastases* was conducted. Research engines used included Pubmed, Medline, Scopus, Embase, and Google/Google scholar. Table 1 provides a comprehensive chronological review of 10 cases with inguinal lymph node metastases with details of reference number, year reported, author, sex, age at diagnosis, bone involved, location in bone, character and duration of symptoms +/- history of trauma, latent period, treatment, and outcome.[6,10-16] Six cases with lymph node metastases as described in Keeney's study are not included in this table due to the lack of supporting clinical information.[9] Similarly, cases with inguinal lymph node metastases as described in Moon's review have been excluded from this table as the original reports are not in English.[5,8,17]

Adamantinoma of the tibia is an uncommon primary bone tumor. The name *adamantinoma* comes from the Greek word *adamantinos* which means *very hard*. It was first described by Maier in 1900 as a primary bone tumor with epithelial characteristics. Later in 1913, Fischer named the tumor *primary adamantinoma* of the tibia because of its resemblance to adamantinoma (also known as ameloblastoma) of the jaw and the pituitary gland.[8] Although, adamantinoma of the tibia histologically resembles adamantinomas of the jaw and pituitary, there has been no evidence to suggest that these tumors are of similar origin.[1,5]

The precise cellular origin for adamantinoma of the tibia remains controversial. Various theories of origin including epithelial, synovial, and endothelial have been proposed.[9,13,18] Adamantinoma has also been associated with osteofibrous/fibrous dysplasia and in this regard is considered by some authors to represent a spectrum of disease with evidence of progression from osteofibrous/fibrous dysplasia to adamantinoma in some cases.[1] Due to the rarity of this lesion and the varied histological phenotypes, adamantinoma of the tibia can be a diagnostic dilemma leading to misdiagnosis, delay, and suboptimal treatment, as seen in our cases.

Adamantinoma represents approximately 0.3-0.5% of primary bone tumors.[7] It can present at any age but mostly occurs in the second to fourth decade.[19] A slight male predominance with a ratio of 5:4 is reported.[7] They are most commonly (85-90%) localized in the tibial diaphysis[7,16] Rarely, it has been described in other bones of the appendicular skeleton including the fibula, ulna, femur, humerus, radius, and short bones of the feet.[9,12,16,17,18,20]

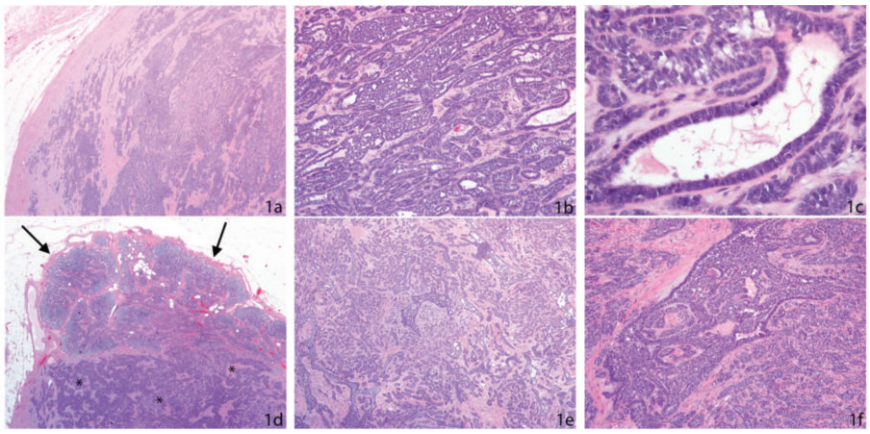

Figure 1. Case 1 Classical adamantinoma. Biopsy of Left Inguinal Mass (A,B,C) and Left Inguinal Lymphadenopathy (D,E,F). Photomicrographs of hematoxylin and eosin stained slides at low power (lens objective x2) shows the presence of a malignant neoplasm in the subcutaneous fat (A). Lesional cells are composed predominantly of basaloid cells with round vesicular nuclei and minimal cytoplasm as seen at medium power (B) (lens objective x4) and at high power (C) (lens objective x10). Photomicrographs of hematoxylin and eosin stained slides at low power (lens objective x2) shows the presence of a metastatic malignant neoplasm in the lymph node (↓) (D). The neoplastics cells were composed of basaloid and tubular nests of malignant cells with some peripheral palisading as seen at medium power (E) (lens objective x4) and at high power (F) (lens objective x10).

Adamantinoma of the tibia can be divided into two main groups based on their histology and biological behavior. Classical adamantinoma refers to the prototype cases with a predominance of epithelial tumor cells and are associated with a destructive growth pattern on radiology. Patients with classical adamantinoma are usually of an older age group with a reported range of 15-65 years. This variant of classical adamantinoma has a stronger predisposition to local recurrences and a higher potential for distant metastases.[1]

In contrast, differentiated adamantinoma of the tibia has a predominance of a osteofibrous/fibrous dysplasia like pattern with scant epithelial tumor elements and is commonly seen in an intracortical location. Patients in this group are usually under 20 years of age.[1] Many authors suggest that osteofibrous/fibrous dysplasia, a benign lesion occurring commonly in the tibia of children under 10 years of age, is related to adamantinomas and may even be a precursor lesion for adamantinomas.[2] This possible relationship has been supported by immunohistochemical and cytogenetic studies.[1,2,6,13,19] In such scenarios, tibial adamantinomas have often been misdiagnosed as fibrous dysplasia, as seen in our case.[7] The association of fibrous dysplasia with adamantinoma was first described by Cohen *et al.* in 1962 who proposed that the fibrous pattern seen in such cases was different from that seen in classical fibrous dysplasia.[1,4] This variant of differentiated adamantinoma is considered by some authors as a secondary reparative process that is associated with a more benign behavior and better prognosis.[1,2]

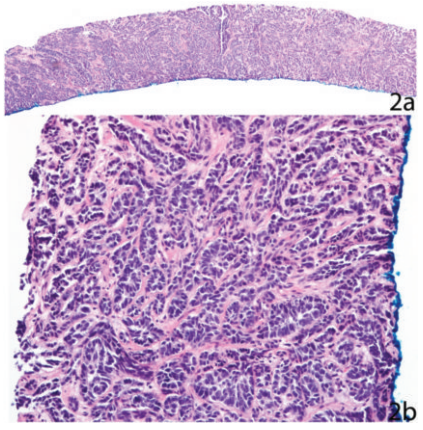

Figure 2. Case 1 Classical Adamantinoma. Core biopsy of Left Retroperitoneal Mass. Photomicrographs of hematoxylin and eosin stained slide at low power (A) (lens objective x2) shows the presence of a malignant neoplasm. The neoplastic cells (B) at high power (lens objective x10) shows a similar morphology of basaloid cells as seen in Figure 1.

Distant metastases have been reported in adamantinoma of the long bones in about 15-20% of cases[7-9] This may be falsely low due to the slow growing nature of the tumor as long

Table 1. Inguinal lymph node metastases from *adamantinoma of the tibia* as reported in the English literature (Pub Med, Medline, Scopus, Embase, Google/Google Scholar) since 1930-search terms included adamantinoma of the tibia, AND *tibial adamantinoma* AND *metastases*, AND *inguinal lymph node metastases*.

Reference number	Year reported	Author	Sex	Age at diagnosis	Bone involved	Location in bone	Character and duration of symptoms +/-history of trauma	Latent period	Treatment	Outcome
#10	1938	Dunne	M	32	Left tibia	Upper and middle thirds	Swelling, 4yr; pain later months Severe Contusion	Nine months	High voltage roentgen, AK amputation 9 months later	Died, 8 years Inguinal lymph nodes*
#11	1942	Dockerty, Meyerding	F	24	Left tibia	Middle	Recurrent pain, 8 yr., swelling, 4yr. No history of trauma	None	Local excision, AK amputation 15 months later	Died, 1 year, inguinal lymph node metastases
#12	1952	Mangalik, Lal Mehrotra	M	40	Femur, tibia, fibula	Distal Proximal Middle	Duration of symptoms for 12 months. Previous injury to leg	1 year	AK amputation, irradiation of metastatic nodes	
#13	1962	Knapp	F	14	Left tibia	Middle	Mass for 4 years No history of trauma		AK amputation	Total survival 16 years. pulmonary and inguinal lymph node metastasis
#14	1976	Winter WG	M	30	Left tibia	Distal	None		Resection, disarticulation of LK, inguinal node dissection, pleurectomy	Died with inguinal nodes, pulmonary, brain-right occipital mets
			M	37	Tibia	Middle	None		Resection and bone grafting very late knee disarticulation	Died, 8 years after initial surgery Inguinal lymph nodes and pulmonary metastasis
#15	1990	De Keyser	F	13	Tibia		Pathological fracture		Intramedullary nailing several curettages, en bloc resection BK amputation, AK amputation	Died 4 years after AK amputation had pulmonary and lymph node metastasis
#6	1994	Hazelbag	M	26	Left tibia	Distal	None		Amputation Metastasis to groin lymph node, pelvis	Died of disease
			M	15	Left tibia	Distal	None		Chemotherapy, amputation	Died of disease. lung/lymph metastases
#16	2008	Frey	M	20	tibia		NAD	NAD	Total tibia allograft knee disarticulation Polychemotherapy	Pulmonary and inguinal lymph node metastases Amputation
	2011	*Tharmabala et al.*	*F*	*24*	*Left tibia*		*Swelling Left tibia* *Swelling in left groin*	*4 years*	*Surgical excision in Left Tibia 2004.* *Groin mass excision in 2007.* *Left retroperitoneal mass excision 2009*	*Left inguinal nodal metastasis, stable pulmonary nodules with routine follow up in 2011*

*This is reported in reference #17 by Moon in 1965.

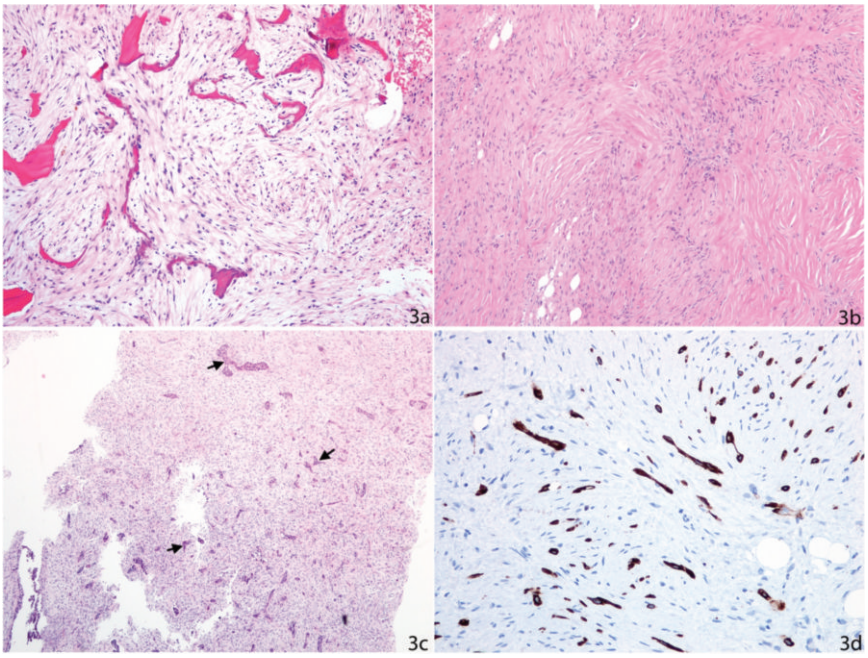

Figure 3. Case 2 differentiated adamantinoma. (A and B) 1999 Histopathological examination of the tibial lesion. Photomicrographs of hematoxylin and eosin stained slides at low power (lens objective x2) shows the presence of islands of woven bone amidst a background of bland fibrous spindle cells (A). Medium power examination (B) (lens objective x4) shows the presence of a rich fibro-collagenous stroma. (C and D) 2009 Histopathological examination of the tibial lesion Photomicrographs of hematoxylin and eosin stained slides at low power (lens objective x2) shows the presence of occasional clusters of plump epitheliod appearing cells with a corded arrangement in focal regions amidst a fibrous spindle background as seen (C) which are strongly positive to pankeratin antibodies on immunohistochemical examination (D).

term follow up is required to evaluate its true metastatic potential.[3] Pulmonary metastases are more common than regional nodal metastases. An approximate 5-year survival in disseminated adamantinoma is reported to be 50-60%. Regional or other distant metastases as seen in the lung are found more frequently in patients who have a history of repeated local recurrences linked to inadequate primary excision of this lesion.[7] However, in our case (Case 1) inguinal nodal metastases occurred with no evidence of local recurrence. Risk factors for metastases include male sex, persistent pain, symptoms of less than five years duration, and inadequate initial treatment by biopsy curettage/excision, or resection. The only histological feature associated with an increased recurrence rate was lack of squamous differentiation.[9] In view of the relationship between adamantinoma and osteofibrous dysplasia, Czerniak et al. proposed two biological courses that a tibial adamantinoma may follow. One is by the differentiated adamantinomas, which are predominantly intracortical and behave as a reparative process with a low potential to metastasize. The second, such as that seen in our case (Case #2) of classical adamantinoma, is one of progressive tumor growth with a higher potential to metastasize.[1]

Early metastases within the first two years of initial diagnosis is commonly seen to occur to the regional lymph nodes, whereas delayed metastases is almost always pulmonary or osseous.[3] Given that lymph node metastasis usually occurs within the first two years, this is suggestive that these were present at the time of initial diagnosis. In this context, we recommend ultrasound imaging of regional lymph nodes as an essential component in the follow-up examinations of these cases. The current practice recommends surgical extirpation as the primary mode of treatment for localized regional lymph node metastases with radiotherapy and chemotherapy as suggested alternatives. The exact role for sentinel node biopsy and its cost/benefit ratio is unknown due to limited clinical experience in these rare lesions.

In conclusion, tibial adamantinoma is a rare primary bone tumor that can cause diagnostic dilemmas especially with clinical presentations of the uncommon pattern of regional nodal metastases. Increased clinical awareness of such rare neoplasms with recognition of uncommon patterns of metastases is essential for accurate diagnosis and optimal patient management. Additionally, due to the slow-growing nature of tibial adamantinomas we recommend continuous long-term follow up for these patients.

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