CASE REPORT

Ewing-like adamantinoma

M.M. Hamdane a, *, L. Charfi a, M. Driss a, H. Nouri b, R. Sellami-Dhouib a, K. Mrad a, M. Mestiri b, K. Ben Romdhane a

a Histopathology Department, Salah Azaiez Institute, Bab Saadoun, 1006 Tunis, Tunisia
b Adult Orthopaedics Department, Mohamed-Kassab Orthopaedics Institute, Ksar Said, 2010 Mannouba, Tunisia

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Summary  The Ewing-like variation of adamantinoma is a rare entity, leading to challenge its differential diagnosis, notably with Ewing’s sarcoma. We are reporting a case of a 20-year-old male who presented with swelling in the left leg that had progressed over a 2-year period. X-rays revealed a tumour in the tibia that was intracortical, osteolytic, multilocular and invaded the soft tissues. A surgical biopsy was performed. Histopathology examination showed a tumour growth with small round cells expressing CD99. A diagnosis of Ewing’s sarcoma was made. Since the patient declined surgical treatment, chemotherapy was administered. Two years later, the patient returned because the tumour had grown in size. A second biopsy was performed. Microscopic evaluation showed a tumour growth with osteofibrous and epithelial components, which expressed pankeratin and vimentin, but was negative for CD99. A diagnosis of Ewing-like adamantinoma was made.

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Introduction

Adamantinoma is a rare bone tumour in young adults that usually affects the diaphysis of the tibia. This is a low-grade, malignant tumour, which histologically appears as a biphasic tumour with intermingled epithelial and osteofibrous components. A differential diagnosis with other lesions (both benign and malignant) can be challenging to make based on the histopathology. The diagnosis is even more challenging when this growth looks like a round cell tumour.

We are reporting here on a rare case of Ewing-like adamantinoma.

Observation

This is the case of a 20-year-old male who presented with swelling on the anterior aspect of the left leg, which had become more evident over a 2-year period. Clinical examination revealed a soft, painless swollen area, 5 cm in diameter, on the anterior aspect of the left leg, without signs of inflammation or satellite lymphadenopathy. Standard X-rays showed an intracortical, osteolytic, multilocular lesion with peripheral sclerosis on the anterior tibia that extended forward into the soft tissues and had a vacuolar, “soap-bubble” like appearance. MRI showed an aggressive tumour...
starting from the anteromedial cortex of the tibia, invading most of the soft tissues, but not affecting the medullary canal (Fig. 1).

A surgical biopsy was performed. Histopathology showed a tumour growth with diffuse layers of small, round, monomorphic cells, with little cytoplasm, a round nucleus and thin chromatin. The stroma was fibrous and highly vascularized. Immunohistochemistry showed that the tumour cells were intensely and diffusely stained for CD99 and vimentin, and to a lesser degree for S100 proteins. Based on these morphological and immunohistochemical features, a diagnosis of Ewing’s sarcoma was made. The patient underwent four rounds of chemotherapy. Amputation of the leg was then proposed to the patient, who refused.

Two years later, the patient returned because the tumour had increased in size. Physical examination showed a swollen area, 17 cm in diameter, on the anterior aspect of the left leg that was soft and slightly painful (Fig. 2). Standard X-rays showed intracortical osteolysis with cortex rupture and extension to the soft tissues (Fig. 3). MRI showed a large superficial lesion starting at the cortex with significant involvement of the soft tissues, having cavities separated by T1 and T2 hyposignal partitions. These cavities had fluid-fluid levels suggestive of associated aneurysmal cysts (Fig. 4).

Based on the lengthy progression and radiological appearance of the lesion, the diagnosis of Ewing’s sarcoma was disputed. A second surgical biopsy was performed. Microscopic evaluation showed a tumour growth organized in layers and streaks, within abundant fibrous and collagenous stroma (Fig. 5). The tumour cells were basophilic, cohesive, rounded, polygonal or fusiform. In some areas, clear epithelial differentiation was noted. There was moderate atypism and many mitotic cells. Immunohistochemistry showed that the tumour cells expressed both keratin and vimentin (Figs. 6 and 7) and were negative for CD99. A diagnosis of Ewing-like adamantinoma was then made.

No distant metastasis was found. The tumour was excised surgically as a whole block. Reconstruction was performed with a translated ipsilateral vascularized fibula; an external fixator was used for stabilisation. The fixator was removed after 1 year and a walking boot was used for the next 6 months. Three years after the surgery, the patient was doing well.
Ewing-like adamantinoma

Figure 4  MRI: frontal reconstruction without (a) and with (b) gadolinium injection and axial slice (c): polycystic cortical lesion with changes to the medullary canal signal. Note the appearance of the fluid-fluid level (c).

Figure 5  Tumour growth, epithelial in nature, organized in layers and streaks, within abundant fibrous and collagenous stroma (HE, 100×).

Figure 6  Tumour cells expressing keratin (IHC, 400×).

Figure 7  Tumour cells expressing vimentin (IHC, 200×).
Discussion

Adamantinoma is a rare, low-grade, malignant tumour that consists 0.4% of all primary bone tumours and affects the diaphysis of the tibia in 85 to 90% of cases [1]. It can occur at any age, but mostly affects young adults (average age of 25 to 35 years), with men being affected slightly more often than women [1]. Clinically, adamantinoma presents as swelling of the leg that has slowly increased in size over time and may or may not be painful [1]. X-rays usually show an osteolytic, intracortical lesion, often having multiple partitions giving it a "soap-bubble" like appearance; the lesion is surrounded by peripheral sclerosis [1]. Histopathology is required for a positive diagnosis. Adamantinoma is characterised histologically by a biphasic growth with various amounts of intermingled epithelial and osteofibrous components. In classic adamantinoma, the epithelial component has four potential morphological variations: basaloid, tubular, squamoid and spindle cell. A fifth histological subtype can be distinguished from classic adamantinoma and is characterised by a large amount of osteofibrous tissue.

The Ewing-like form is a rare variant of adamantinoma, with only five cases described in the published literature [2–5]. It is characterised by a growth of small, round, uniform cells that express both epithelial and neural cell immunohistochemical markers, including those typical of Ewing’s sarcoma (CD99+). These cells also have ultrastructural characteristics of both epithelial and neuroendocrine cells [2,3,6,7].

The histogenesis of this tumour is not clear, but the most likely hypothesis is that this adamantinoma variation is issued from the same multipotent cell line that is at the source of Ewing’s sarcoma. In fact, the latter is known to have the ability to differentiate into either mesenchymal, epithelial or neural cell lines [8–10]. This would explain the double phenotype (epithelial and neuro-ectodermal) of this tumour.

As would be expected from its name, Ewing-like adamantinoma results in diagnostic challenges relative to classic Ewing’s sarcoma. In our case, this led to a delayed diagnosis and inadequate treatment. However, the patient’s age, tibial placement of the tumour and intracortical location should guide the pathologist to look for the expression of epithelial immunohistochemical markers.

A differential diagnosis is even harder to make with adamantinoma-like Ewing’s sarcoma. This is a rare type of Ewing’s sarcoma that, other than showing neuro-ectodermal differentiation, shows morphological, ultrastructural and/or immunohistochemical characteristics of epithelial tumours. It is essential for these two entities to be distinguished as the prognosis and treatment are different. In the most difficult cases, the differential diagnosis is based on cytogenetic studies to identify the genetic abnormalities typical of Ewing’s sarcoma, notably (11;22) translocation and/or EWS/FLI1 or EWS/ERG fusion genes [1,11–13]. These genetic abnormalities are not present in adamantinoma [1,14].

We did not perform a cytogenetic study for our case. However, the clinical, radiological and especially progression data provided sufficient information for this tumour to be labeled as Ewing-like adamantinoma. Histological assessment of the tumour after 2 years of progression revealed a different morphological appearance than that of the initial tumour: there was a predominant epithelial component, the round cells had disappeared and there was no CD99 expression.

Treatment approaches for Ewing-like adamantinoma have not yet been standardized, given how rare this entity is. In our reported case, the treatment approach was similar to treatment of a classic adamantinoma; a wide resection of the tumour was performed.

Conclusion

The Ewing-like form of adamantinoma is a rare variant. The aetiology of this pathology is not yet known. The histopathology diagnosis is difficult. However, when a tumour appears in the tibia of a young adult and has an intracortical location, a diagnosis of adamantinoma must be considered and further immunohistochemistry work must be done to look for expression of epithelial markers. In the most challenging cases, molecular biology studies can now be done on depaffinised tissues, which would help to differentiate between adamantinoma and Ewing’s sarcoma.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References

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