

Histological Dedifferentiation in Recurrent Adamantinoma of the Tibia: A Case Report

Pavithra Ethirajan¹, Archana Lakshmanan¹

Learning Point of the Article:

Dedifferentiated adamantinoma is a rare, aggressive tumor requiring careful histopathological and immunohistochemical evaluation for accurate diagnosis and management.

Abstract

Introduction: Adamantinoma is a primary low-grade malignant bone tumor. It is most common in tibia with slight predilection in males. Dedifferentiated adamantinoma is an aggressive variant with worse prognosis.

Case Report: Patient is a 70-year-old female who presented with leg pain. Imaging showed a lytic lesion in the metaphyseal diaphyseal region. Curettings were done and were reported as adamantinoma. Two years later, the patient presented with a recurrent lesion at the same site. Histopathology showed a neoplasm with focal classical adamantinoma and many areas with aggressive morphology including sarcomatoid differentiation. The neoplastic cells in high-grade areas were positive for vimentin with variable loss of cytokeratin. Proliferative index as determined by Ki67 was 20–25% in these areas. With these given immuno-morphological findings, a diagnosis of dedifferentiated adamantinoma was rendered.

Conclusion: Dedifferentiated adamantinoma is an unusual and aggressive variant of adamantinoma. This case highlights the awareness of such a rare entity, thereby preventing misdiagnosis and improper treatment.

Keywords: Adamantinoma, tibia, malignant, osteofibrous dysplasia, sarcoma.

Introduction

Adamantinoma is a rare primary malignant bone tumor that typically occurs in individuals during their 2nd or 3rd decade of life, with a higher incidence in males. The most common location for this tumor is tibia, followed by fibula. Patients may present with swelling, which can either be painful or painless. On imaging, it appears as a well-defined cortical lesion, often extending into the medullary cavity or surrounding soft tissue. Histologically, the tumor is biphasic, containing both epithelial and bland looking osteofibrous elements. Over time, the clinicopathologic understanding of adamantinoma has

expanded, with the identification of an aggressive and rare variant, dedifferentiated adamantinoma [1, 2]. On histological examination, this subtype reveals a mixture of classic adamantinoma and areas with pleomorphic sarcomatous cells, marked by increased mitotic figures and occasional osteoid production. In addition, features such as chondroid differentiation, osteoid formation, and clear cell changes have been reported [2, 3].

Case Report

A 72-year-old female presented with leg pain and swelling.

Author's Photo Gallery



Dr. Pavithra Ethirajan



Dr. Archana Lakshmanan

Access this article online

Website:
www.jocr.co.in

DOI:
<https://doi.org/10.13107/jocr.2025.v15.i08.5902>

¹Department of Histopathology, Apollo Cancer Centre, Chennai, Tamil Nadu, India.

Address of Correspondence:

Dr. Pavithra Ethirajan,
Department of Histopathology, Apollo Cancer Centre, No. 320, Anna Salai, Teynampet, Nandanam, Chennai - 600 035, Tamil Nadu, India.
E-mail: pavithraethirajan1306@gmail.com

Submitted: 15/05/2025; Review: 05/06/2025; Accepted: July 2025; Published: August 2025

DOI: <https://doi.org/10.13107/jocr.2025.v15.i08.5902>

© The Author(s). 2025 Open Access. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted use, distribution, and non-commercial reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.



Figure 1: (a) Tibial bone with implant in situ, (b) distal portion of tibia showing a defect with surrounding gray-white area measuring $9 \times 5 \times 3.5$ cm, and (c) cut surface of lesion is gray-white and fleshy.

Imaging revealed a lytic lesion in the metaphyseal and diaphyseal regions with imaging differentials of giant cell tumor versus aneurysmal bone cyst. Curettage was performed, and the lesion was initially diagnosed as classic adamantinoma. Two years later, the patient developed a recurrence at the same site, following which right distal tibial resection was done. Distal portion of tibia showed a defect filled with bone cement surrounded by gray white lesion measuring $9 \times 5 \times 3.5$ cm (Fig. 1). Cut surface of the lesion was gray white and fleshy. Representative sections were taken, processed, paraffin embedded and 4 microns thick sections were taken and stained with hematoxylin and eosin. Histopathological examination showed a neoplasm with focal classic adamantinoma like areas

and many areas showed epithelioid looking cells with marked atypia and nuclear pleomorphism. Background showed osteofibrous stroma. Patchy sarcomatoid areas were also noted. A mitotic count of 12–14/10 high-power field was obtained in these areas (Fig. 2). Immunohistochemistry was done and the neoplastic cells in high-grade and sarcomatoid areas were positive for vimentin with patchy loss of pancytokeratin. Cells also showed p53 overexpression in both high-grade epithelioid and sarcomatoid areas. The proliferation index as determined by Ki-67 was high (20–25%) in these areas (Fig. 3). With the given immunomorphological findings, a diagnosis of dedifferentiated adamantinoma was rendered. A previous diagnosis of adamantinoma combined with the recurrence showing a foci of classic adamantinoma with a clear transition to sarcomatous areas favored this diagnosis. The patient subsequently underwent amputation but did not receive any adjuvant therapy and was lost to follow-up after 1 year.

Discussion

Adamantinoma is a biphasic tumor characterized by both epithelial component and a mesenchymal osteofibrous stroma. The epithelial component can exhibit various patterns, including basaloid, tubular, squamoid, and spindled forms [1, 2]. Adamantinoma is classified into three subtypes: Classic adamantinoma, osteofibrous dysplasia-like (OFD-like) adamantinoma, and dedifferentiated adamantinoma. The distinction between the classic and OFD-like subtypes lies in the proportion of the epithelial component. Classic adamantinoma features a predominantly epithelial component with minimal osteofibrous areas, whereas OFD-like adamantinoma is characterized by scattered nests of epithelial cells within the stroma [1, 2].

The development of adamantinoma remains a topic of intrigue, with several theories proposed to explain its origin. One theory suggests that during embryonic development, ectodermal epithelial nests become misplaced within mesenchymal tissue, particularly in the subcutaneous tibial region where adamantinoma frequently arises. Another proposed that trauma might implant epithelial cells into the bone [1]. A third hypothesis is that a possibility of a low-grade mesenchymal neoplasm undergoing transformation into an epithelial phenotype, a process that hints at OFD being a potential precursor to adamantinoma [4, 5]. While these theories provide clues, the exact pathogenesis of adamantinoma remains unclear [1, 6].

Dedifferentiation in adamantinoma is an extremely rare occurrence, with just over ten cases reported worldwide, including only two cases from India [3]. Dedifferentiation

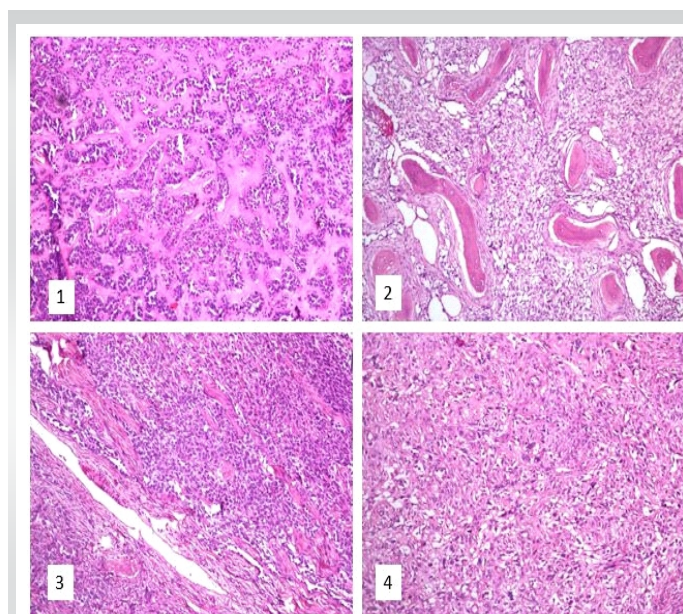


Figure 2: (a) Hematoxylin and eosin (H&E) ($\times 100$) classic adamantinoma, (b) H&E ($\times 100$) osteofibromatous areas, (c) H&E ($\times 100$) pleomorphic epithelioid areas, and (d) H&E ($\times 100$) sarcomatoid areas.

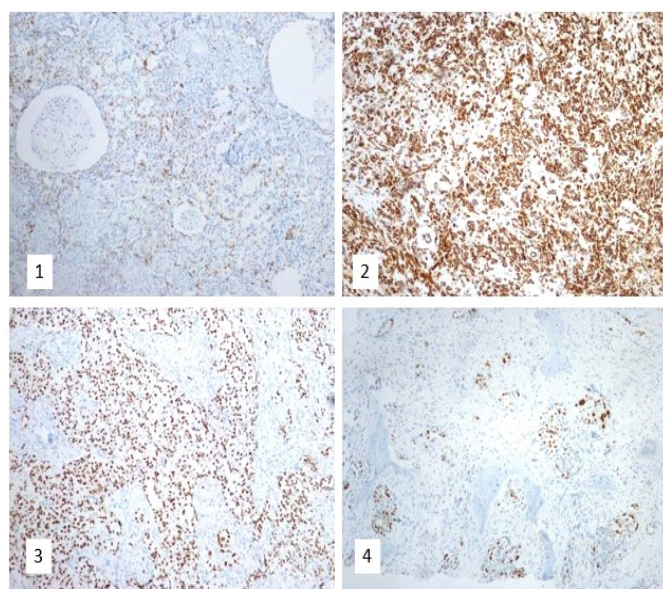


Figure 3: (a) Downregulation of CK and (b) diffuse Vimentin positive (c) p53 over expression (d) Ki67 increased.

refers to the process where the tumor's epithelial component undergoes a transformation, losing its distinct characteristics and reverting to a more primitive, mesenchymal-like state. This shift is referred to as the revertant mesenchymal phenotype by Izquierdo et al. [7].

Izquierdo et al. reported a case of adamantinoma of tibia treated with an en bloc resection. Five years later, the patient developed a recurrence consisting solely of the sarcomatous component, with no epithelial nests present. Immunohistochemical analysis was negative for cytokeratins. This case illustrates marked sarcomatous dedifferentiation with a complete loss of the epithelial phenotype [7].

Tibia is the most commonly reported site for dedifferentiated adamantinoma, which can either develop de novo or as a recurrence from a classic adamantinoma [2]. Nouri et al. and Hazelbag et al. have reported cases of dedifferentiated adamantinoma occurring in patients with fibrous dysplasia [8, 9]. It can affect individuals across a broad age range, from 21 to 83 years. Tirabosco et al. have reported two cases of dedifferentiated adamantinoma occurring in the ulna and rib [3].

The dedifferentiated component is often a high-grade sarcoma, which can include pleomorphic sarcoma, osteosarcoma with chondroblastic differentiation, and spindle cell sarcoma. Of these, osteosarcomatous dedifferentiation is most commonly reported in dedifferentiated adamantinoma [3,7,9]. A conclusive diagnosis necessitates the use of immunohistochemical staining. Epithelial marker positivity is limited to the regions of classic adamantinoma. In contrast, the sarcomatoid-appearing areas in between are negative for these

stains [7]. Rekhi et al., in his case report, demonstrated diffuse p53 expression in the sarcomatous dedifferentiated area of one case, while another case showed complete loss of expression [3]. Similarly, Hazelbag et al. reported p53 overexpression in one case [9]. In our case, diffuse p53 expression in the sarcomatous component was noted. This suggests a potential role of p53 in the dedifferentiation process [3].

Diagnostic difficulty arises when there is no definite zone of classical adamantinoma, putting forward a variety of differential diagnosis including various high-grade sarcomas and metastatic carcinoma. A panel of immunostains along with other ancillary studies would help in ruling out these differentials.

Dedifferentiated adamantinoma has a worse prognosis with local recurrence and distant metastasis. Metastasis has been reported in lymph nodes and lungs [2, 7, 8, 10].

Surgical resection remains the primary treatment approach. Adjuvant radiation therapy may be considered in instances of incomplete resection [3, 9]. Chemotherapy appears to provide limited benefit [7].

Conclusion

Dedifferentiated adamantinoma is a rare and aggressive form of adamantinoma. This case underscores the importance of recognizing this uncommon entity. A diagnosis of dedifferentiated adamantinoma should be considered when encountering a cytokeratin-positive sarcomatous lesion in the tibia. Accurate differentiation from other neoplasms is crucial for ensuring appropriate and timely therapeutic management.

Clinical Message

Dedifferentiated adamantinoma is a rare but aggressive variant of adamantinoma that poses diagnostic and therapeutic challenges. This case highlights the importance of long-term follow-up in adamantinoma patients to detect potential dedifferentiation and recurrence. A high index of suspicion, combined with histopathological and immunohistochemical evaluation, is essential for accurate diagnosis. Given its poor prognosis and potential for metastasis, early recognition and complete surgical resection remain crucial for optimal patient outcomes.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given the consent for his/ her images and other clinical information to be reported in the journal. The patient understands that his/ her names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflict of interest: Nil **Source of support:** None

References

1. Unni KK. Dahlin's Bone Tumors: General Aspects and Data On 10,165 Cases. 6th ed. Philadelphia, PA: Wollters Kluwer/Lippincott Williams and Wilkins Health; 2010. p. 402.
2. WHO Classification of Tumours Series, Soft Tissue and Bone Tumours. 5th ed., Vol. 3. Lyon, France: World Health Organization; 2020. Available from: <https://tumourclassification.iarc.who.int/chapters/33> Last accessed on 11 July 2025.
3. Rekhi B, Sahay A, Puri A. Clinicopathologic features of two rare cases of dedifferentiated adamantinomas, including diagnostic implications. *Int J Surg Pathol* 2019;27:193-202.
4. Bovée JV, Broek LJ, Boer WI, Hogendoorn PC. Expression of growth factors and their receptors in adamantinoma of long bones and the implication for its histogenesis. *J Pathol* 1998;184:24-30.
5. Hatori M, Watanabe M, Hosaka M, Sasano H, Narita M, Kokubun S. A classic adamantinoma arising from osteofibrous dysplasia-like adamantinoma in the lower leg: A case report and review of the literature. *Tohoku J Exp Med* 2006;209:53-9.
6. 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;64:2319-34.
7. Izquierdo FM, Ramos LR, Sánchez-Herráez S, Hernández T, De Álava E, Hazelbag HM. Dedifferentiated classic adamantinoma of the tibia: A report of a case with eventual complete revertant mesenchymal phenotype. *Am J Surg Pathol* 2010;34:1388-92.
8. Nouri H, Jaafoura H, Bouaziz M, Ouertatani M, Abid L, Meherzi MH, et al. Dedifferentiated adamantinoma associated with fibrous dysplasia. *Orthop Traumatol Surg Res* 2011;97:770-5.
9. Hazelbag HM, Laforga JB, Roels HJ, Hogendoorn PC. Dedifferentiated adamantinoma with revertant mesenchymal phenotype. *Am J Surg Pathol* 2003;27:1530-7.
10. Smyth SL, Siddiqi A, Athanasou N, Whitwell D, Majd HS. Adamantinoma: A review of the current literature. *J Bone Oncol* 2023;41:100489.

Conflict of Interest: Nil
Source of Support: Nil

Consent: The authors confirm that informed consent was obtained from the patient for publication of this case report

How to Cite this Article

Ethirajan P, Lakshmanan A. Histological Dedifferentiation in Recurrent Adamantinoma of the Tibia: A Case Report. *Journal of Orthopaedic Case Reports* 2025 August;15(8): 107-110.

