CASE REPORT

Beyond the Sun Ray of Bone: Histopathology Providing Diagnostic and Prognostic Insights into Central and High-Grade Surface Osteosarcoma of the Mandible – A Rare Case series

Lloyd Antony Ivan Joseph[1], Barath Raj. K[1], Kalaivani. P,[2] Balamurali P.D[3], Premalatha. B[4], Karthikshree V Prashad[5]

Abstract

Osteosarcoma (OS) is an aggressive, rare bone tumor that is uncommon in the jaw, where it presents unique diagnostic and prognostic challenges. Accurate histological diagnosis is crucial, as higher-grade OS subtypes are associated with worse outcomes. This case series presents two rare mandibular OS cases, each emphasizing the critical role of early diagnosis and precise grading for optimal management.

The first case describes a 52-year-old male with a painless swelling in the right mandible, displaying the classic "sunburst" radiographic pattern associated with fibroblastic central OS. The second case involves a 60-year-old female with painful swelling in the left lower jaw, initially misdiagnosed as benign. Imaging and biopsy later confirmed High-Grade Surface OS, an exceptionally rare and aggressive variant.

While the first patient responded well to surgical resection with no recurrence over three years, the second patient faced a rapid, adverse progression, succumbing shortly after her initial chemotherapy, underscoring the grave prognosis associated with high-grade subtypes.

These cases highlight the necessity of accurate histological grading and prompt treatment in mandibular OS, as timely, tailored interventions can greatly influence survival.

Key words: Osteosarcoma, mandibular tumour, High-grade surface osteosarcoma, fibroblastic osteosarcoma, histologic grading, jaw malignancy, sun ray appearance, Aggressive bone lesion.

Introduction

Osteosarcoma (OS) is the most common malignant tumor affecting the skeletal system, with recognition dating back approximately 200 years. This highly aggressive tumor originates from transformed mesenchymal cells that undergo osteoblastic differentiation and produce malignant osteoid. Although OS accounts for only about 5% of all sarcomas, it comprises around 20% of primary bone tumors[1], affecting roughly 1 in 100,000 people annually. Osteosarcoma in the jaw is relatively rare, occurring at about ten times the rate of OS in other craniofacial bones[2].

This report discusses two rare cases of osteosarcoma in the mandible. The first case involves Central Osteosarcoma of the Fibroblastic type, characterized by fibroblast-like cells and disorganized tumor bone formation. The second case presents High-Grade Surface Osteosarcoma, an exceptionally rare form of osteosarcoma that comprises <1% of all overall cases[3]. To our knowledge, this is the first documented case of High-Grade Surface Osteosarcoma in the mandible, adding to the literature on this rare and aggressive jaw tumor. Both cases highlight distinctive clinical, radiographic, and histopathologic features, emphasizing the importance of early diagnosis for effective management of such rare tumors.

Department and Institution Affiliation: Department of Oral and Maxillofacial Pathology and Microbiology, Mahatma Gandhi Postgraduate Institute of Dental Sciences, Puducherry.

Corresponding author: Dr. K. Barath Raj – Mahatma Gandhi Post-Graduate Institute of Dental Sciences, Gorimedu, Indira Nagar, Puducherry. Pin - 605006. Email address: kesavaraj1396@gmail.com

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High-Grade Surface Osteosarcoma, a particularly rare subtype, represents less than 1% of all osteosarcomas. The World Health Organization (WHO) categorizes surface osteosarcomas, or juxtacortical tumors, into three types: Parosteal, Periosteal, and High-Grade Surface, which comprise approximately 5%, 1.5%, and 0.5% of OS cases, respectively[4]. Jaw osteosarcomas display distinct clinical and biochemical characteristics, with high-grade lesions being far more common than low-grade types, making early recognition crucial for effective treatment[5]. Dental practitioners are often the first to identify these tumors, underscoring the importance of prompt and accurate diagnosis prior to histopathological confirmation[1]. In this case series, we highlight two fascinating cases of osteosarcoma, showcasing the importance of histopathological grading of osteosarcoma.

Case presentation

Case Report-1

A 52-year-old male patient with a history of smoking and smokeless tobacco use presented with a slow-growing, painless swelling in the right lower jaw. Clinical examination revealed a 6 x 6 cm firm swelling extending from the right corner of the mouth to the temple region (fig 1a), along with palpable, enlarged, mobile, and non-tender bilateral submandibular lymph nodes. Intraorally, a 5 x 7 cm swelling with bicortical expansion was noted in the lower right molar area (fig 1b). Radiographic imaging showed an osteolytic lesion with a “sunburst” appearance. (Fig 3a)

An incisional biopsy exhibited hyperchromatic mesenchymal cells which are of angular, spindle topolygonal shaped cells. These cells were seen infiltrating the dense vascular connective tissue (fig 4a). Majority of the areas were filled with atypical angular cells with hyperchromatic nucleus and surrounded in the extensive extracellular collagen (fig 4b). Based on the clinical and histological features, these findings were commonly attributed to any fibro-osseous lesions like Fibrous Dysplasia (FD), Desmoplastic fibroma (DF), and Low Grade Fibrosarcoma (LGFS) involving the bone and hence they were considered as the differential diagnosis. The appearance of the occasional immature eosinophilic bone matrix resembling “Osteoid” deposits (fig 4b) were the histological guiding pillar for adding IHC marker such as “Osteonectin”(fig 6). Cytoplasmic positivity of Osteonectin indicated the osteoblasts activity and thereby concluded the diagnosis as “Fibroblastic subtype of osteosarcoma”(fig 6a). Presence of the osteoid and osteoblastic rimming around the osteoidmaterial ruled out the FD, DF, and LGFS. The patient subsequently underwent surgical resection of the mandible from the right premolar to the right condyle, including the right submandibular lymph nodes. Osteoid deposits were seen in the lymph nodes of the excision specimen, thereby confirming the level 1b metastasis (Fig. 4c). Histopathologic evaluation of the resected specimen revealed higher pleomorphism, mitotic figures (Fig. 4d), immature bone formation, and osteoid deposits, which reconfirmed the diagnosis of “Fibroblastic subtype of Osteosarcoma” (Fig. 4a, 4b, 4c, 4d).

Case Report-2

A 60-year-old female patient presented with a gradually enlarging, painful swelling in the left lower jaw, which had been painless initially since five months, but intensified recently 20 days ago, especially while eating. An initial incisional biopsy at a private clinic suggested peripheral ossifying fibroma. On examination, facial asymmetry was observed with a 5 x 4 cm firm, tender swelling in the left lower face (fig 2a), extending intraorally from the premolar to molar region (fig 2b). Radiographic imaging showed a “sunburst” pattern with a calcified, “melon-shaped” tumor attached to the bone surface and extending into the medullary space on CBCT. Blood tests were normal, and there was no evidence of lymph node involvement. Surgical resection of the mandible segment (from 31 to 37) was performed. Microscopic analysis revealed a fibrous connective tissue with

Case-1

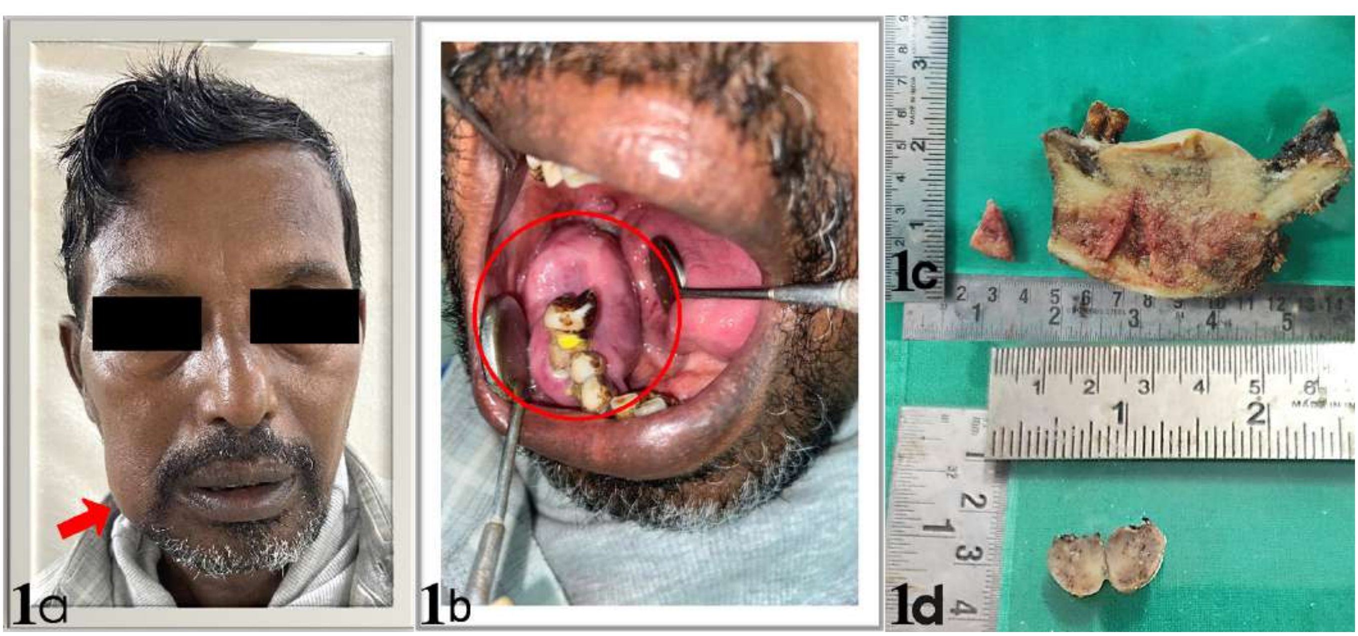

Fig. 1.a. Extra-oral clinical image of the patient indicated by arrow. Figure 1.**b.** Intra-oral image of the lesion denoted by the circle. **Fig. 1.c.** Macroscopic feature image. Figure 1d. Submandibular lymph node.

increased extracellular collagen matrix that is similar to previous case along with many osteoid trabeculae. These trabeculae were in interlacing pattern, enclosing abundant pleomorphic cells with hyperchromatism, numerous mitotic figures, disorganized tumor bone, and chondroblastic and fibroblastic areas (fig 5a,5b,5c,5d). Surprisingly there was no classic histopathological features of periosteal/parosteal osteosarcoma such as well differentiated bony trabeculae within the fibrous stroma. There were predominant areas of eosinophilic osteoid like material and immature bone formation which are suggestive of osseous malignancy. Correlating to the clinical and radiographical features surface osteosarcoma was given as a provisional diagnosis and further IHC marker such as "osteonectin" was performed. IHC positivity (fig 6b) confirmed the diagnosis of "osteoblastic osteosarcoma". Upon closer observation it revealed that the fibrous connective tissue is highly cellular with prominent atypical pleomorphic cells and high number of mitotic activity is seen. Even within the immature bone there were surplus amount of atypical cells and mitotic figures. They accounted for more than 75% of the cells, which were highly proliferating with retained heritability of undifferentiation. Considering the presence of Border's grade 4 anaplastic features like pleomorphic cells, immature cartilage, and bone formation along with marked mitotic activity within the osteosarcoma background, we favoured the "High-Grade Surface Osteosarcoma" for the final diagnosis. These Histopathological features are also supported by the medullary involvement of the lesion as visualized through the CBCT and also visible in the grossed specimen in an axial manner (fig 2d,3c,3d). Correlating clinically, radiographically and Histopathologically, final diagnosis of "High-Grade Surface Osteosarcoma" was given.

Discussion

The term "sarcoma" was coined in 1804 by a British surgeon - John Abernathy, derived from Greek, meaning "fleshy growth." A year later, in 1805, French surgeon Alexis Boyer, who was also Napoleon's personal physician, introduced the term "osteosarcoma (OS)"[1]. High-Grade Surface Osteosarcoma was first described by Francis et al. in 1964, but it wasn't until 1984 that Wold et al. published the first series of this exceedingly rare tumor[3].

Case 2

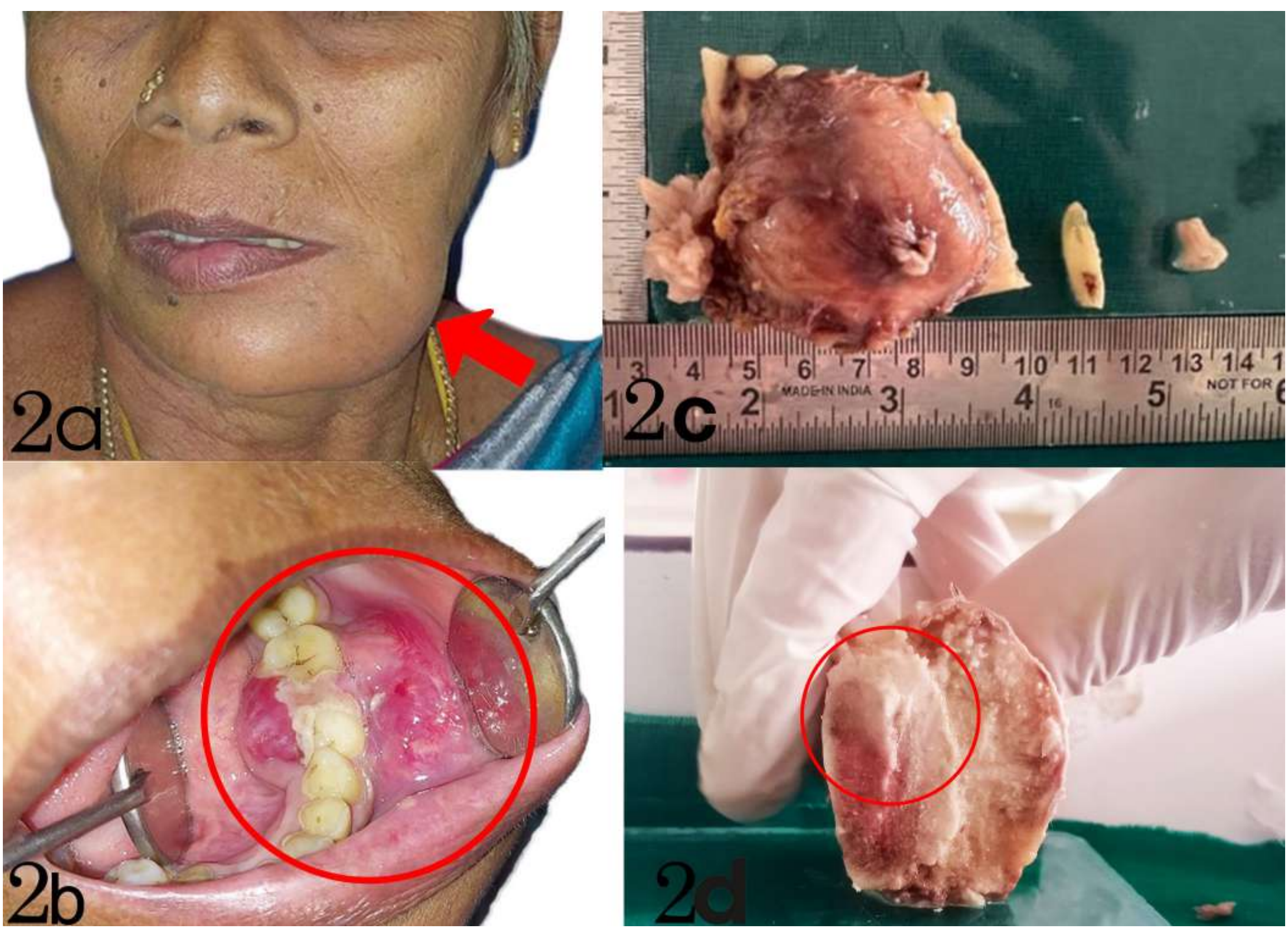

Fig. 2.a. Extra-oral swelling indicated by arrowhead. **Fig. 2.b.** Intra-oral swelling denoted by a circle. **Fig. 2.c.** Macroscopic image. **Fig. 2.d.** Cut surface of the lesion showing the mild intramedullary extension of the lesion denoted by a circle.

These tumors are uncommon in the jaws especially mandibular osteosarcomas (MOS), accounting for 1.6% of all bone malignancies and up to 5% of all osteosarcomas[6]. Mandibular osteosarcoma (MOS) typically occurs in the third and fourth decades of life, contrasting with long-bone osteosarcomas that primarily affect younger individuals. Some studies indicate a mild male predominance, and its incidence remains consistent worldwide, suggesting minimal influence from regional or ethnic factors. The exact cause is unclear, but risk factors for osteosarcoma include genetic predispositions (e.g., Li-Fraumeni syndrome), prior radiation, and Paget's disease. Survival has improved with advanced surgical techniques and adjuvant therapies, though MOS remains difficult to treat due to the complex mandible anatomy. Clinically, patients often present with painless swelling that may progress to pain, facial asymmetry, numbness, and trismus. Diagnosis requires radiographic imaging and biopsy for early intervention. In both cases, the radiographic characteristics were instrumental in distinguishing the lesion as of osseous origin. In the initial stages, radiographic results may reveal a combination of opaque and radiolucent regions, which frequently causes an X-ray "sunburst appearance". However, a biopsy is necessary to establish the grading of osteosarcoma conclusively, as radiography alone is not adequate for confirmation[7].

Proposed diagnostic workflow for the subtypes of Osteosarcoma are given in Table 1. Since the present case series deals with two cases of both conventional central OS (COS) and High Grade surface Osteosarcoma, it is crucial to differentiate the respective categories because they both have different prognosis. Differentiating Intramedullary/central and Juxtacortical types of OS [7–10] is necessary for the estimating the prognosis (Table 2). Because the High grade Osteosarcoma has high rate of metastatic progression to distant sites thereby having lesser survival rate of the affected patients.

In this series, Case 1 presented Conventional Central Osteosarcoma (COS), radiologically displaying "Codman's triangle" is a triangular periosteal reaction indicative of aggressive bone erosion[11] (fig 3b). Case 2 exhibited High-Grade Surface Osteosarcoma (HGSO), radiologically characterized by the "string sign," a thin radiolucent line separating the tumor from the

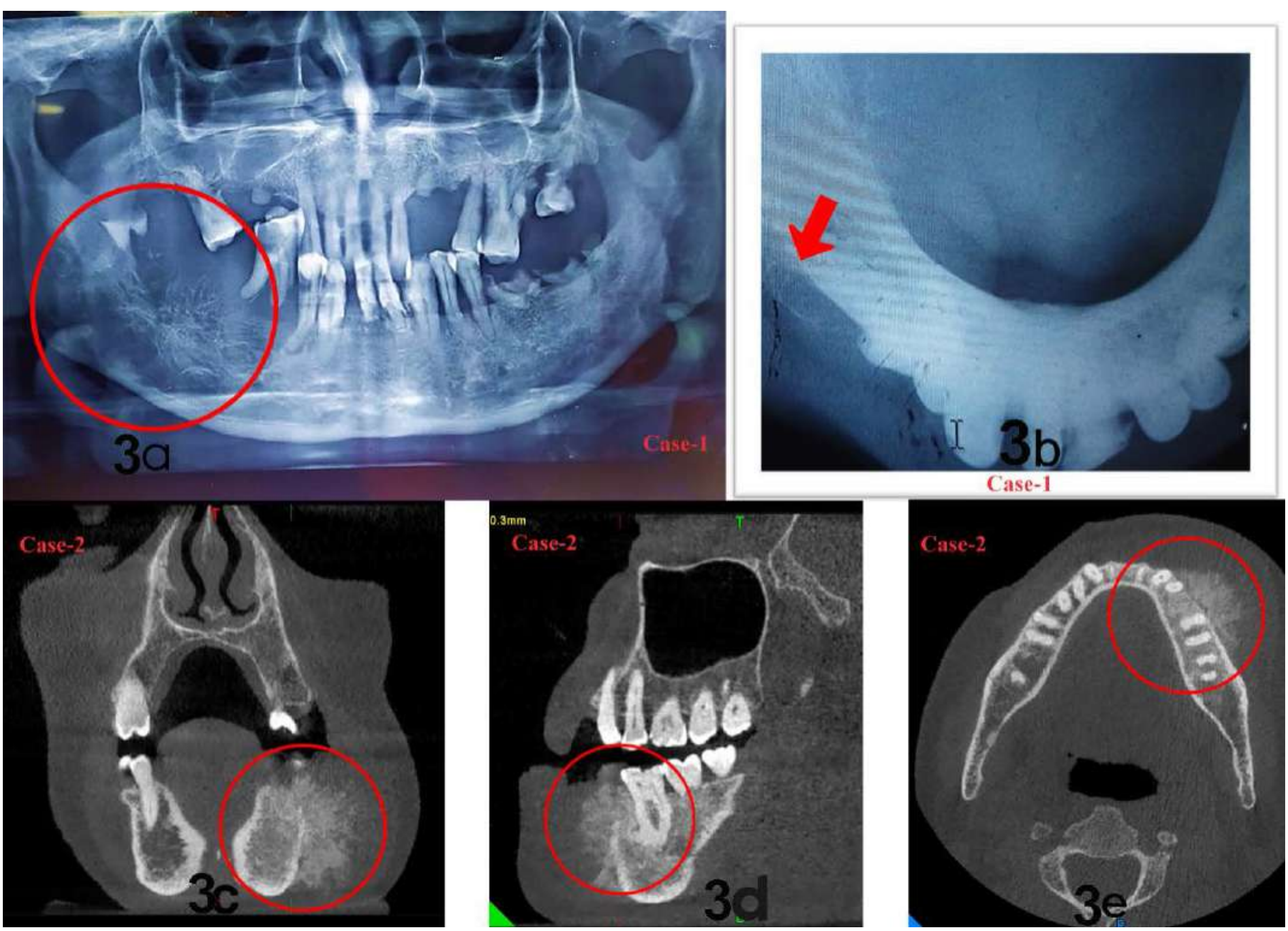

Fig. 3.a. OPG image of case-1, indicating sun burst appearance by circle. **Fig. 3.b.** Mandibular occlusal image radiograph of case-1, showing codman triangle. **Fig. 3.c.** CBCT images of case-2, exhibiting sunburst pattern with a calcified melon-shaped tumor attached to the bone surface and extending to medullary space (indicated by arrows)

cortex, except in areas of medullary invasion[12] (fig 3e). This series not only emphasizes distinct radiographic features but also highlights histological variations between osteosarcoma subtypes (Table 2).

Histologically, osteosarcoma (OS) encompasses several subtypes: osteoblastic (50%), chondroblastic (25%), fibroblastic (25%), small cell, telangiectatic, and rare types like osteosarcoma resembling osteoblastoma, HGSO, and epithelioid OS[13]. By convention, COS, including the Osteoblastic, chondroblastic, and Fibroblastic subtypes, is classified as high-grade, whereas juxtacortical types, such as Periosteal and Parosteal osteosarcoma, are as considered low-grade[11]. In this series, both cases displayed high-grade histological features with higher rate of pleomorphism, mitotic figures in both the cases and even metastasis to right submandibular node in the case 1. Case 2, representing the rare subtype High-Grade Surface Osteosarcoma (HGSO), clinically resembles parosteal osteosarcoma but histologically aligns with conventional central osteosarcoma (COS). HGSO, accounting for less than 0.5% of all osteosarcoma cases, showed malignant spindle cells with Broder's atypia grades of 3 or 4, highlighting its aggressive pathology. Notably, HGSO has the poorest prognosis among osteosarcoma subtypes, with a 5-year survival rate as low as 37.6% due to its high metastatic potential[3]. Even in the present case 2, the patient subsequently succumbed to the disease even after the successful surgery and completion first chemotherapeutic cycle, thereby re-affirming the necessity for histological grading of high and low-grade OS[14] (Table 3) for the future treatment.

The histopathological differential diagnosis of osteosarcoma of the jaws includes osteoblastomas, Nora's lesion (bizarre parosteal osteochondrosarcoma), benign fibro-osseous lesions like fibrous dysplasia and ossifying fibroma, and osteomas. Nora's lesion is distinguished by its characteristic cartilage cap and discrete zones. Osteomas and ossifying fibroma, composed of mature and immature bone, lack cellular polymorphism, anaplasia, mitotic activity, and the spindle cell proliferation seen in osteosarcoma. Immunohistochemistry can differentiate osteoblastoma from osteosarcoma using beta-catenin staining. Nuclear beta-catenin staining is characteristic of osteoblastoma, whereas cytoplasmic or membranous beta-catenin staining is indicative of osteosarcoma[15,16]. Histologically Low-grade osteosarcomas can be challenging to differentiate from fibrous

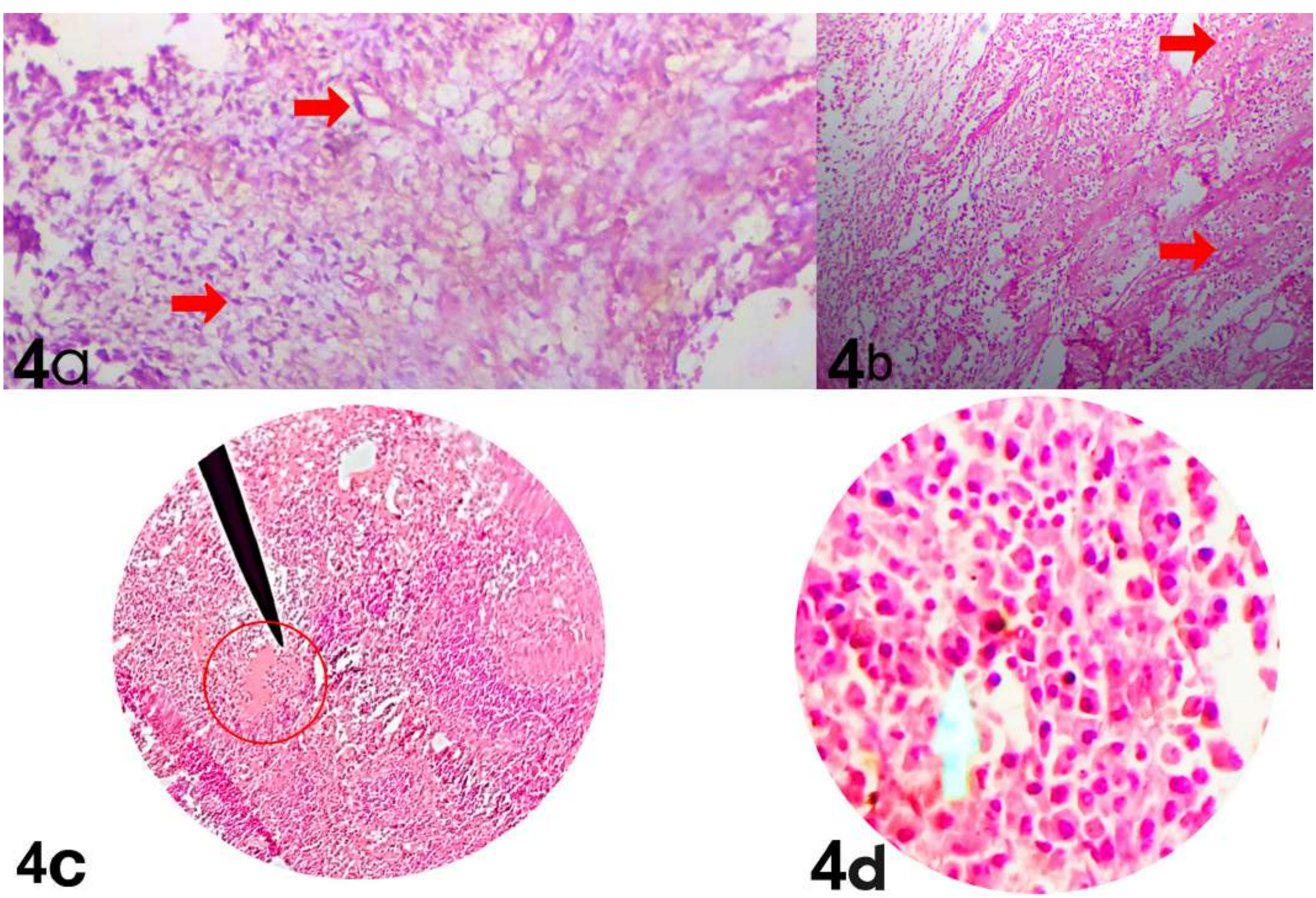

Fig. 4. Histopathologic pictures of case-1 showing pleomorphic mesenchymal cells with a highly fibrous nature. **Fig. 4.b** shows osteoid like materials. **Fig..4.c.** osteoid elements in the submandibular lymph node. **Fig. 4.d.** Anaphase of mitoses under high power

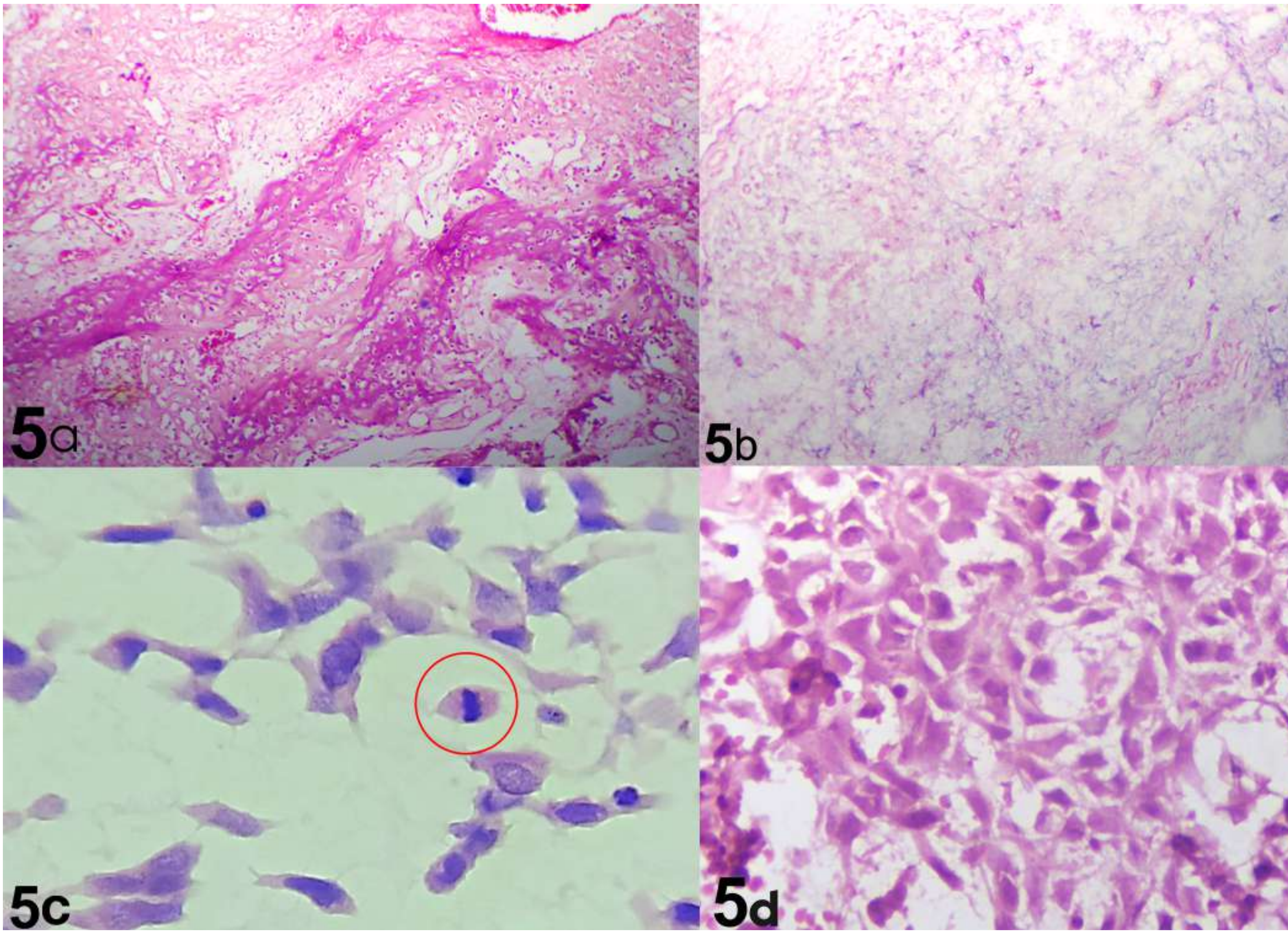

Fig. 5. Histopathologic pictures of case 2, Under low power view showing hyperchromatic spindle shaped malignant mesenchymal cells with pleomorphic osteoblasts. **Fig 5.b.** Under low power view myxoid like stroma present surrounding pleomorphic osteoblast cells **Fig 5 c.** Shows Metaphase of mitosis under high power. **Fig5.d.** Under high powerview- pleomorphic osteoid cells.

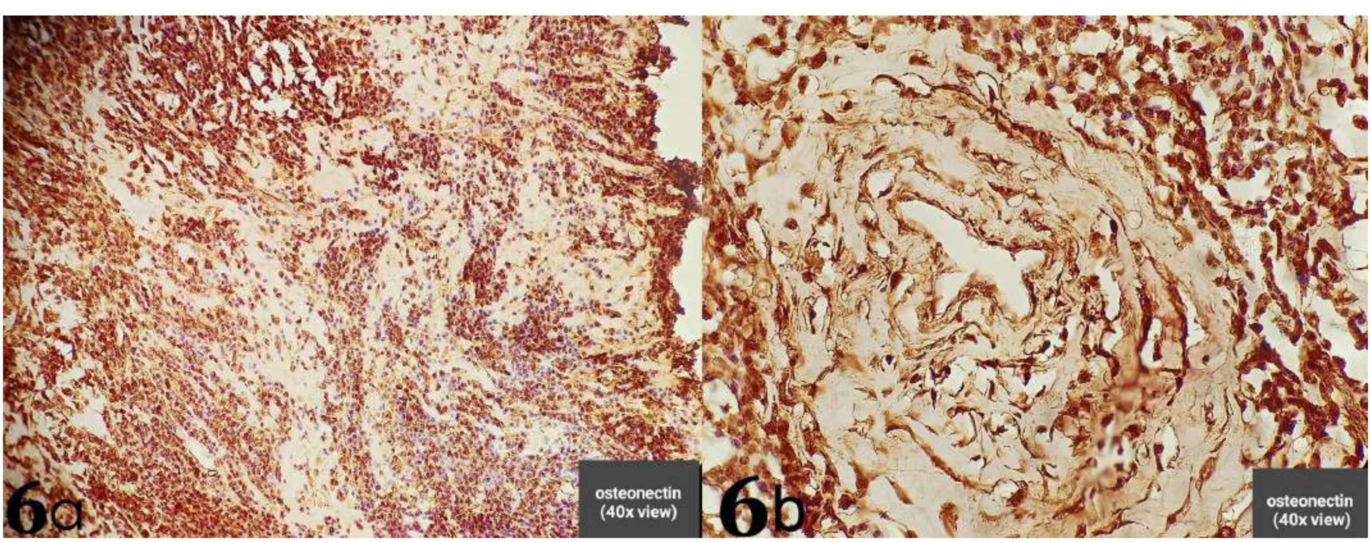

Fig. 6.a IHC expression of Osteonectin for case-1. **Fig. 6.b.** IHC expression of Osteonectin for case-2

dysplasia due to similar features like well-formed osteoid and minimal mitosis. Using MDM2 and CDK4 markers helps distinguish malignancies, as they are expressed in osteosarcomas but not in benign fibrous lesions[17].

Bone matrix proteins, such as osteocalcin, alkaline phosphatase, and osteonectin, are expressed in OSs. Both the cases exhibited strong positivity for osteonectin thereby confirming the presence of osteoblast, pathognomic of OS[18].

Cancer treatments are tailored to the tumor stage, patient age, overall health, quality of life, and life expectancy. For OS, the primary therapies remain surgical management, chemotherapy, and radiotherapy. In order to eradicate any remaining tumor cells and target any possible micro-metastases, adjuvant chemotherapy or radiation treatment is usually used after surgery in the current care of OS[11].

Following surgery, Case 1 (fibroblastic COS) has shown no recurrence over a three-year follow-up, while Case 2 (HGSO) had a rapid deceased even after the first chemotherapy dose. This outcome emphasizes the aggressive nature of HGSO and the importance of accurate identification, which can often be misdiagnosed as the less aggressive parosteal OS.

Conclusion

In conclusion, this report highlights the clinical, radiographic, and histopathologic characteristics of two rare mandibular osteosarcomas, underscoring the importance of prompt diagnosis and accurate subtype differentiation for effective management.

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