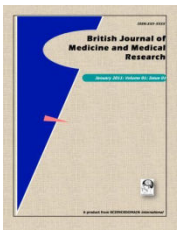

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Multidisciplinary Approach for an Initially Misdiagnosed Case of Osteosarcoma in a Medically Compromised Patient

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Case Study

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ABSTRACT

Osteosarcoma is a highly malignant bone tumour. It is derived from primitive mesenchymal bone forming cell. Osteosarcoma of the jaw is quite rare. Despite its rarity, the dentist may be the first health professional who observes tumours involving the jaws. As there is a greater variability in clinical, radiological and histopathological findings of jaw osteosarcoma, so there is greater scope for multidisciplinary approach. An early definite diagnosis is must for successful treatment which can save patient's life and esthetic. This article presents a case of osteosarcoma in medically compromised 17 years old female patient who was misdiagnosed initially and later on present as a huge size of the tumour mass with gross disfigurement than she was treated by multidisciplinary approach of oncosurgeon, medical oncologist and radiation oncologist with appropriate expertise.

Keywords: Osteosarcoma; chemotherapy; radiotherapy; radical surgery.

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1. INTRODUCTION

The term Osteosarcoma refers to a heterogeneous group of malignant neoplasia that affects the formation of bones or mesenchymal tissue, with histopathological evidence of osteogenic differentiation. It is a rare primary malignant neoplasm of jaw and accounts for approximately 7% of all osteosarcomas (Wood, 2009; Angela, 2009). The French surgeon Alexis Boyer first used the term osteosarcoma in 1805. Etiopathogenesis is unknown. Pre disposing factors being suggested are, trauma, previous radiation, preexisting benign bone disease, fibrous dysplasia, Paget's disease, genetic mutation (P-53 suppressor) and viral infection (Peltier 1993; Zarbo et al., 2008). The incidence of osteosarcoma substantially increases when the risk factors are combined. The maxilla and mandible are involved with about equal frequency. Swelling is the most common symptom which may or may not associate with pain. Loosening of teeth, paraesthesia and nasal obstruction may be associated (Angela, 2009; Warnock, 2006). Depending on progression of lesion, radiological representation of osteosarcoma described as lytic variety, mixed variety and sclerosing variety (Wood, 2009; Clark et al., 1983).

The World Health Organization's histological classification of bone tumours separates the osteosarcomas into central (medullary) and surface (peripheral) tumours and recognizes a number of subtypes within each group (Table 1). The most common pathologic subtype is conventional high grade central osteosarcoma. It accounts for 80-90% of all osteosarcomas. It's most frequent subtypes are osteoblastic, chondroblastic and fibroblastic osteosarcoma, depending on predominance component (Schajowicz, 1993).

Table 1. Osteosarcoma subtypes within central and surface tumours (The World Health Organization's histologic classification of osteosarcoma)

Central (Medullary)
a. Conventional high grade central osteosarcoma
b. Telangiectactic osteosarcoma
c. Intraosseous well-differentiated (low grade) osteosarcoma
d. Small cell osteosarcoma
Surface (Peripheral)
a. Parosteal (juxtacortical) well-differentiated (low-grade) osteosarcoma
b. Periosteal osteosarcoma-low-to intermediate-grade osteosarcoma
c. High-grade osteosarcoma

2. CASE REPORT

A female Hindu patient of 17 years old reported to G.D.C.H., Ahmedabad with chief complaint of large swelling with pain in right lower posterior region of jaw since 2 months. The patient gave past dental history of swelling in the same region with smaller size 6 months back (Fig. 1). According to her past dental records, only on the basis of clinical and radiological findings (Fig. 2: OPG shows radiolucent lesion of size approximately 3x2cm extending from right second premolar to distal aspect of right second molar. The entire periphery was scalloped with lower border completely intact), initially her lesion was diagnosed as simple benign cystic lesion and was removed surgically. After four months, there was post surgical rapid increase in swelling which was associated with pain and patient reported to our institute.

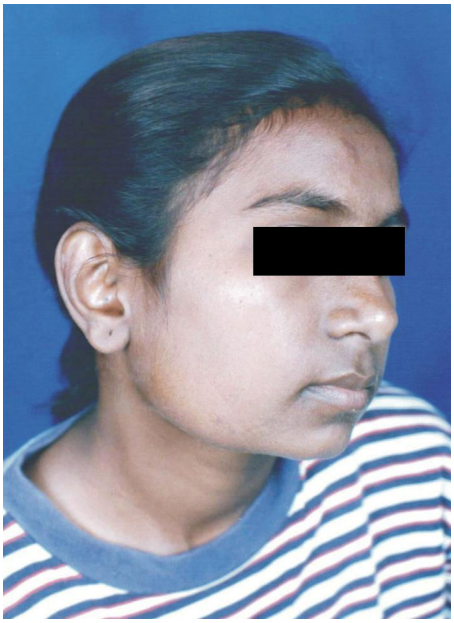

Fig.1: Swelling in right side of angle of mandible

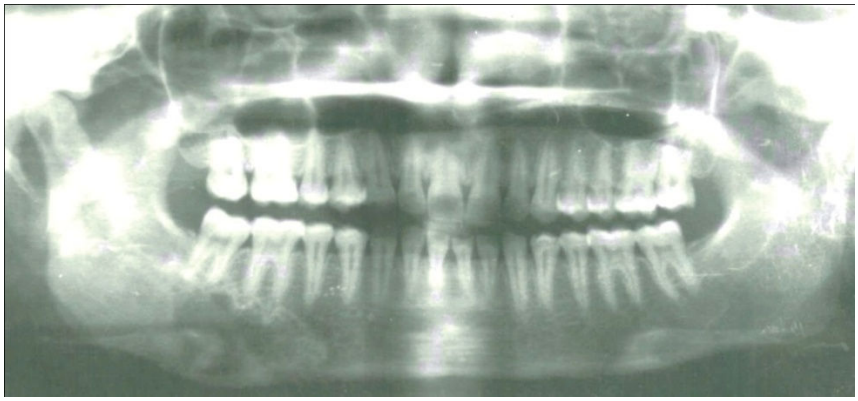

Fig.2: A clear radiolucency with entire scalloping periphery below apices of right lower molar region

Extraoral examination revealed a large well localized swelling extending posterio-anteriorly from the right side angle region to the left parasymphysis region and superior-inferiorly extending from ala tragus line to 4 to 5 cm downward from lower border of mandible (Fig. 3), approximately measuring around 9×7 cm in size with tensed and stretched overlying skin. On palpation consistency of swelling was firm to hard and marked tenderness was elicited with raised temperature. No neck lymph node was palpable. Intraorally the overlying mucosa was reddish pink in colour with uneven surface. Swelling on both buccal and lingual vestibule extending from left side of canine region to the retromolar region of right side and causing obliteration of buccal and lingual vestibule. Intraorally consistency was firm and marked tenderness was elicited (Fig. 4). Loosening of teeth was present in posterior teeth.

The patient was having difficulty in swallowing. Systemic examination revealed that she was suffering from hepatitis B and received treatment of Hepatitis B immuneglobulin 2000IU and Hepatitis B vaccine concurrently.

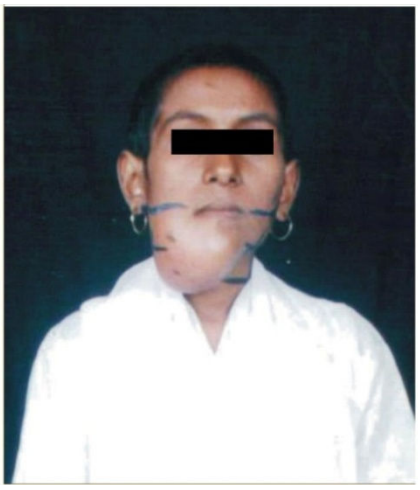

Fig. 3: Extra-orally a large expansile swelling after first surgical intervention

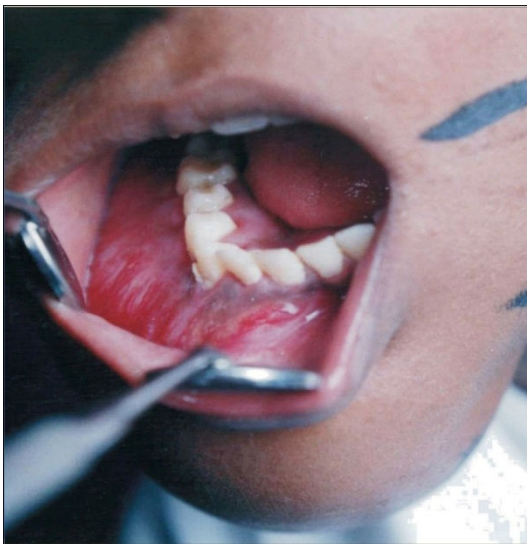

Fig. 4: Intra-orally large expansile swelling obliterating buccal and lingual vestibule of right side

CT scan showed a large expansile mass of size 65x62 mm (Axial) and 55x75 mm (Coronal) involving right side of body and angle of mandible with erosion, destruction of bone with evidence of periosteal new bone formation and also showing extra osseous mass of size 6.1x7.3 cm with outer cortical plate expansion (Figs. 5,6). On biochemical investigation normal level of alkaline phosphate was found. Incisional biopsy revealed proliferation of atypical osteoblasts showing production of osteoid tissue. Osteoblast cells arranged in a disorderly pattern and showed cellular pleomorphism & nuclear hyperchromatism. Few

areas were showing proliferation of anaplastic fibroblasts. Clinicopathological correlation suggestive of Osteoblastic variant of osteosarcoma (Fig. 7).

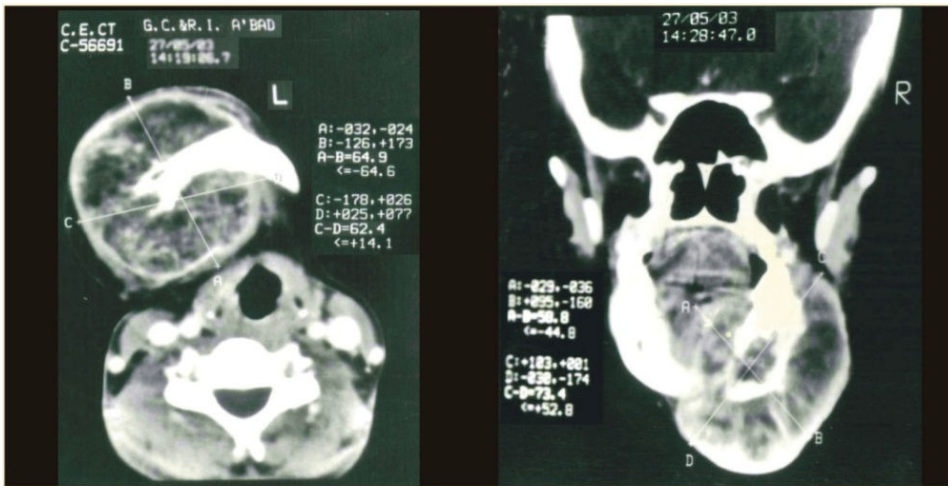

Fig. 5: CT scan axial and coronal view of mandible showing erosion, destruction and periosteal new bone formation with extraosseous mass at right side

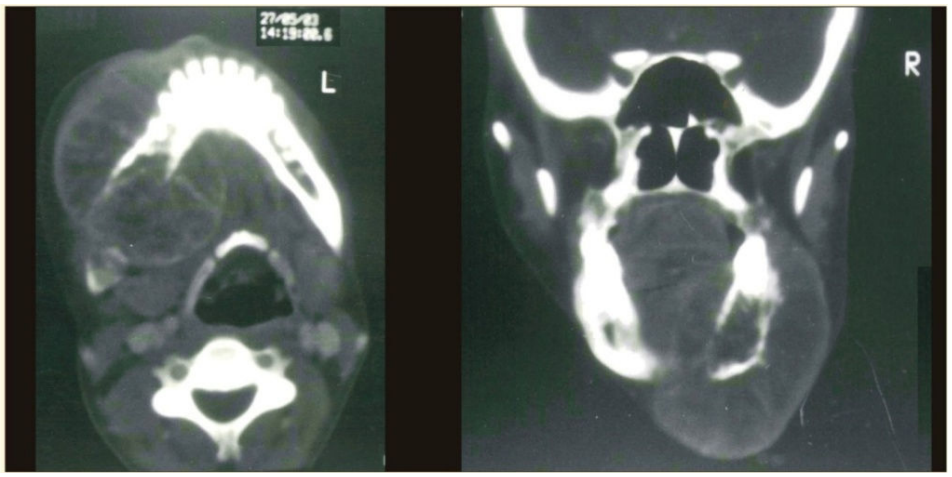

Fig. 6: CT scan (Bone window images) of axial and coronal section of mandible

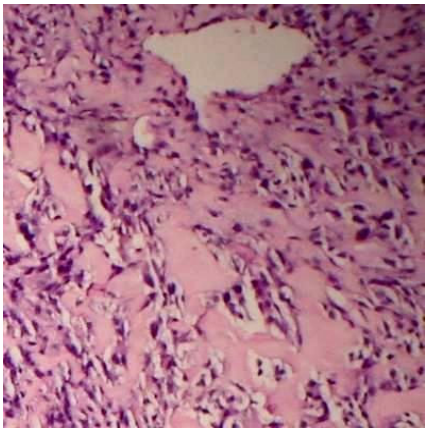

Fig. 7: H&E stained section shows Osteoblastic variant of osteosarcoma

2.1 Multidisciplinary Approach and Follow Up

The patient was referred to oncology center and was treated in multidisciplinary setting with appropriate expertise. The treatment was planned by medical oncologist in order to convert inoperable tumour to one that could be operable after chemotherapy. The chemotherapy regimen consisted of two blocks of high-dose ifosfamide (15 g/m^2), methotrexate (12 g/m^2), cisplatin (120 mg/m^2) and doxorubicin (75 mg/m^2). But chemotherapy was stopped within 1 month duration to avoid hepatic toxicity as patient was having hepatitis B at fulmating stage and size of swelling went on progressively increasing. As surgery was still inoperable, radiotherapy was planned for local control of osteosarcoma. Patient received radiotherapy for local control of osteosarcoma at a total dose of 5600cGy (56Gy) in a fraction of 200cGy (2Gy) for 4weeks.There was decrease in size of intra-oral swelling compared to pre radiotherapy status and post radiotherapy scarring was noticed on overlying skin (Fig. 8).

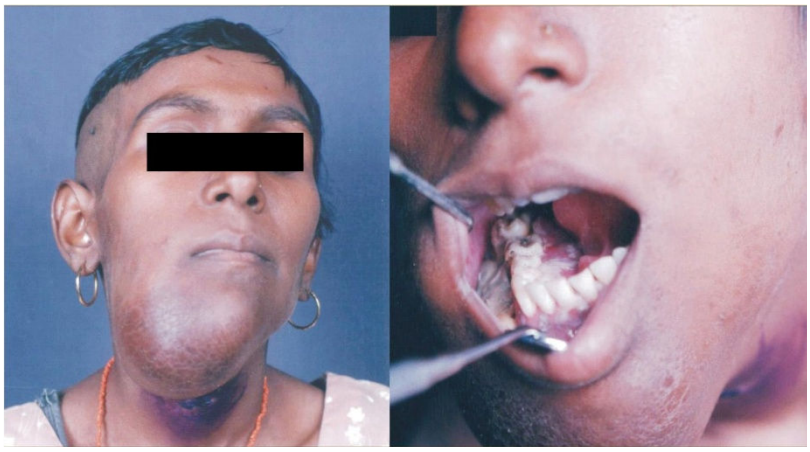

Fig. 8: Post radiotherapy decrease in size of extra oral and intra oral swelling

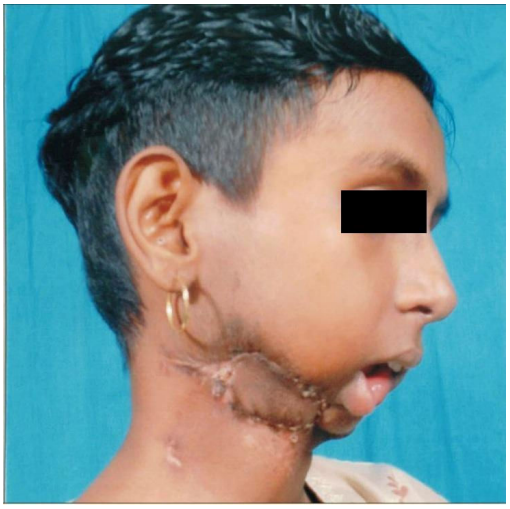

Fig. 9: Scar mark after right side hemimandibulectomy and reposition of deltopectoral flap

As liver enzymes were getting controlled, then wide excision of infiltrating mass with right side extended hemimandibulectomy and reposition of deltopectoral flap was carried out by oncosurgeon (Fig. 9). OPG radiograph showed surgically operated area extended from right side hemimandibultomy up to left first premolar region. Upper jaw appeared to be normal (Fig.10).

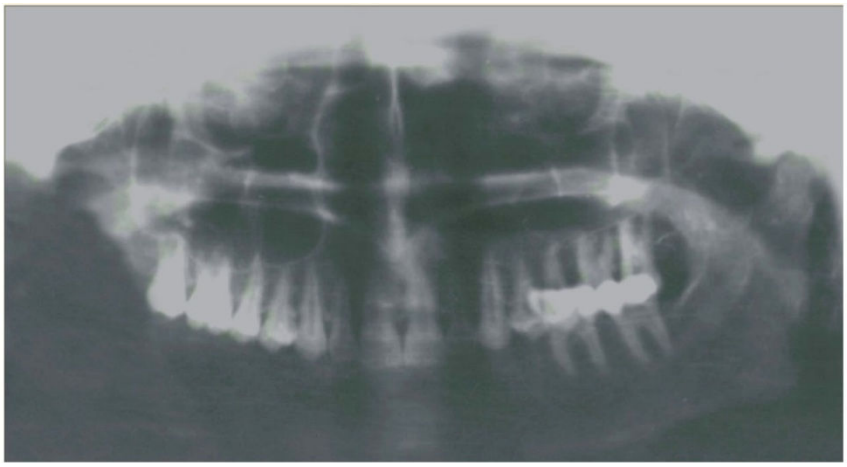

Fig. 10: OPG showing right side of hemimandibulectomy area

3. DISCUSSION

Osteosarcoma is a highly malignant tumour with extensively destructive potential (Peltie, 1993). The rarity in daily clinical practice and the lack of specific clinical and radiological findings can lead to equivocal or erroneous interpretation on many occasions. Patient generally present with an enlarging maxillofacial mass or dental problem (Wood, 2009). In

the reported case patient was initially operated for very small swelling. According to her past dental records her lesion was initially diagnosed as simple benign cystic lesion and surgically removed, only on the basis of clinical and radiological finding that leads to misdiagnosis of case because of lack of histological report. After four months of duration recurrence of the lesion occur on the same surgical site with larger size. Osteosarcoma presents various clinical, radiological and histological aspect, as well as variable disease progression. Misdiagnosed case of osteosarcoma has also been reported previously in various literatures. Rosilene et al., (2005), reported a case of osteosarcoma of mandible initially resembling of dental periapex and after initial endodontic treatment, a significant increase in the size of the lesion, resulting in visible facial asymmetry. George et al., (2010), reported a case of osteosarcoma of maxilla which was initially misdiagnosed as giant cell granuloma and after wide surgical excision it was reported as chondroblastic osteosarcoma. Ruíz-Godoy et al., (1999), reported a case which had areas suggestive of desmoplastic fibroma histopathologically but radiographic feature was helpful to reach the definitive diagnosis of osteosarcoma. Thus there is need to adopt proper correlation of clinical diagnosis, radiological diagnosis and histological diagnosis; so a preoperative conclusive diagnosis with multidisciplinary approach can give better prognosis of jaw osteosarcoma.

The reported case presented a large size of fixed tumour mass with pain, loosening of teeth and there was no lymph node palpable suggestive of sarcoma. This case reported in second decade of life in female patient with a history of swelling where as other most cases were reported in third and fourth decade of life with male predilection (Angela, 2009; Zarbo et al., 2008). The common characteristic radiological findings (typical sunray appearance, Codman triangle) were not seen in this case except destruction of bone with new periosteal bone formation in C. T. scan, which threw some light in favour of osteosarcoma (Wood, 2009; Garrington et al., 1967). According to Frankelestein, the essential radiographic criteria for a specific diagnosis of osteosarcoma is positive identification of new bone (Corbett et al., 1997), which could be best visualized when tumour extends in to soft tissue mass, that is obvious on C.T. scan findings of the present case. The presence of a destructives unicentric lesion with poorly defined margin and a predominantly sclerotic, lytic, mixed radiographic pattern should lead one to suspect an osteogenic sarcoma (Wood, 2009; Clark et al., 1983), which is in concordance with our reported case.

Production of atypical osteoblasts and osteoid production by neoplastic cells, even in small amount, is a histological diagnostic marker for Osteogenic sarcoma, which is in favour to our present reported case (Zarbo and Carlson, 2008; Rajendran, 2009). As in the reported case as surgery was not possible because of large expansile mass. First chemotherapy was planned but stopped within 1 month duration as to avoid hepatic toxicity in medically compromised patient who was under treatment for hepatitis B. Then radiotherapy was advised for local control of osteosarcoma.

Before the use of chemotherapy (which began in the 1970s), osteosarcoma was treated primarily with surgical resection along with a margin of normal surrounding tissue (Forteza, 1986). Bielack et al., (2002), in their analysis of prognostic factors in high grade osteosarcoma, concluded that incomplete surgery was the most important negative prognostic indicator, followed by poor response (Bielack et al., 2002; Bieling et al., 1996). Mandibular osteosarcomas have a better prognosis than maxillary osteosarcoma (Garrington et al., 1967). Anatomical limitations in face can sometimes cause difficulties in achievement of uninvolved margins and for this reason local recurrence of these lesions is high (Forteza et al., 1986; Bertoni et al., 1991).

The osteosarcoma of head and neck have less risk of distant metastases but a higher rate of local recurrence which may be due to difficulty in achieving wide surgical margins in head and neck surgeries due to anatomic and cosmetic reasons. Radical surgery alone results in local failure (Mark et al., 1991; deFries et al., 1971). Chemotherapy definitely reduces the risk of metastatic recurrences (Link et al., 1986). The modern treatment approach is chemotherapy followed by surgical excision aiming to achieve clear surgical margins. Hemimandibulectomy or radical maxillectomy is undertaken in preference to radiotherapy because osteosarcoma is a relatively radio-resistant tumor (Corbett et al., 1997). The optimal management of patients with osteosarcoma of head and neck is unclear. Different authors have given different treatment modalities e.g. radical surgery and/or combined therapy employing surgery, R.T. and/or chemotherapy. Improved local control and survival have been seen with adjuvant RT with or without chemotherapy. Five year survival rate have been reported in 70-75% of patients receiving pre-operative radiation followed by wide surgical excision and post-operative chemotherapy (Mark et al., 1991). deFries et al., in 1971 reported that preoperative radiotherapy can prolong the survival in osteosarcoma of long bone. Schwarz (2009), Laney et al., (2005); Machak (2003) et al., also mentioned in their study that effective local control can be done in osteosarcoma with use of radiation therapy and concluded that radiotherapy can help local control of osteosarcoma for patients in whom surgical resection with widely, negative margins is not possible. In reported patient the pre-operative radiotherapy was given to enhance the local control of tumour so that surgery could be possible to save patient's life and esthetic.

4. CONCLUSION

Osteosarcoma is not a stereotype disease, as there is a greater variability in clinical , radiological and histopathological findings of jaw osteosarcoma, there is a need to adopt a multidisciplinary approach for early definitive preoperative diagnosis rather then making individual standardization of clinical diagnosis, radiological diagnosis and histological diagnosis which were usually getting misnomer and speculative on many instances. To establish an effective treatment plan, a pre-operative conclusive diagnosis and multidisciplinary approach is must in order to increase the survival rate of patients. Patient with osteosarcoma of jaw should be treated in a multidisciplinary setting by medical oncologist, radiation oncologist and surgeons with appropriate expertise.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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