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Osteosarcoma -An Osteolytic Lesion inthe Posterior Mandible –A Case Report With Review of Literature

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Abstract:*Osteosarcoma is a malignancy of mesenchymal cells able to produce osteoid or immature bone. Osteosarcoma of the jaw is uncommon and represents 6-8% of all osteosarcomas. There are 3 conventional types of osteosarcoma of the jaw i.e. osteogenic, chondroblastic and fibroblastic. Fibroblastic variant scarcely discussed in dental literature as it is extremely rare in the oral cavity and exhibits diverse clinical, radiological and histopathological manifestations resulting in misdiagnosis and diagnostic delay.*
This article reports a case of fibroblastic variant of osteosarcoma in the mandible of a 30 years old female with changing radiographic patterns which resulted in recurrence due to misdiagnosis.
Key Words:*osteosarcoma, , fibroblastic type, osteolytic, herring bone pattern, special stains ,IHC*

I. Introduction

Osteosarcoma has been recognized for almost two centuries and is the most commonmalignancy of the skeletal system. [1]
It is an aggressive cancerous neoplasm arising from primitive transformed cells ofmesenchymal origin that exhibit osteoblasticdifferentiation andproduce malignant osteoid . It accounts for approximately 20% of sarcomas but only 5% occur in jaws. Osteosarcomas of jaw are uncommon and despite its histopathologic similarities with long bonesit is biologically different. They are locally aggressive and tend to recur. [2, 3]There are 3 traditional subdivisions of osteosarcoma i.e., osteoblastic, chondroblastic, and fibroblastic osteosarcoma.[4]
Fibroblastic osteosarcoma isvery rare and is characterized by the presence of spindle cells with minimal amounts of osteoid matrix.[5]
Osteosarcoma may arisede novoor subsequent to previous irradiation and pre-existing disease of bone. The reported case appears to have developed de novo; as no history of any pre-existing diseasecould be elicited.[5]
Dental professionals may be the first to detect jaw osteosarcomas in their initial stages but it often goes unnoticed, thus stressing on the need for an early diagnosis before its confirmation by histopathology [6, 7, 8]
We present here a unique case of fibroblasic variant of osteosarcoma arising de novo in posterior mandible in 30 year old female which is a rare entityin jaws showing diversehistopathologic and radiographic findings.

II. Case report

A 30 -year-old, female patient referred at our institute with a chief complaint of a swelling on the right side of the mandible that had recurred after two months of conservative excision.

According to the referral she initially noticed the swelling at the site of extraction of lower right second molar which was removed one year back. Medical as well as systemic examinations did not reveal abnormal clinical findings.

On extra oral examination,recurrent lesionwas diffuse, bony hard and roughly about 6 × 5 cm in size at the angle of the mandible. The skin overlying the swelling was of normal colour but had a glossy appearance, probably due to tautness of the skin over the swelling.(Fig 1, 2)

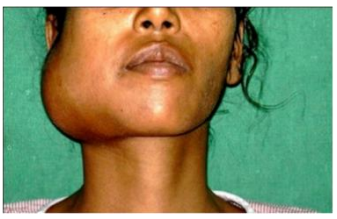
Fig1- Extra oral photograph shows swelling in the right side of mandible

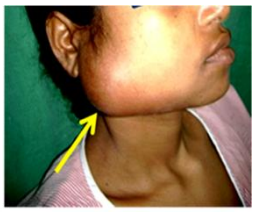
Fig2- Extra oral photograph shows swelling in the right side of mandible (lateral view).

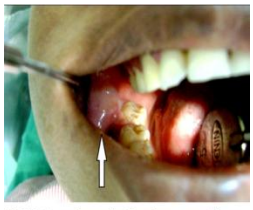
Fig3-Intraoral examination shows growth near the extracted lower right second molar.

Intraorally, the swelling was evident on the mandibular buccal vestibule extending from 46 region to the ascending ramus. Bidigital palpation did not reveal any lymph node enlargement anywhere in the cervicofacial chain. (Fig.3)

The recurrent swelling was completely radiolucent(fig.4), but according to referral the firstlesion mimicked fibrous dysplasia with mixed radiolucency and radiopacity. A CT scan (fig.5) and 3D reconstruction (fig.6) of the lesion showed lytic area. However MRI could not be done due to financial limitations, as the patient belonged to a lower socio-economic group.

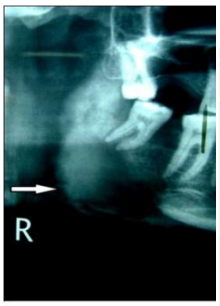

Fig 4-Lateral oblique radiograph shows radiolucent lesion.

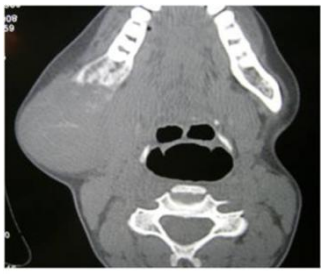

Fig5 –CT SCAN of the swelling .

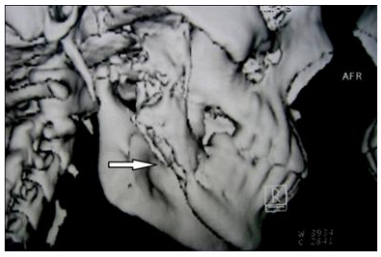

Fig6-3D reconstruction of CT scan .

Clinical findings were dissonant with the previous diagnosis of fibrous dysplasia. An immediate hemi mandibulectomy was performed (fig.7) based on the clinical features, computed tomography, to avoid encroachment of the adjacent structures .Subsequent microscopic examination revealed primarily of spindle-shaped highly polymorphic cells showing "herring bone pattern", proliferating in an intertwining fascicular fashion with multinucleated giant cells. In addition, scanty hyalinised material resembling neoplastic osteoid was observed. The findings were most consistent with a fibroblastic osteosarcoma. (fig.8)

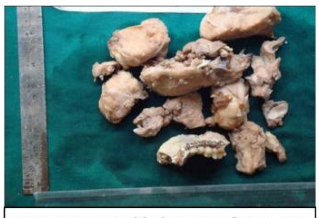

Fig7- Hemi mandibulectomy of recurrent lesion

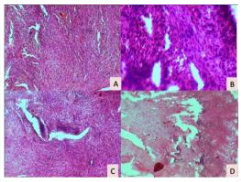

Fig 8-H&E STAIN of tissue showing (A) herring bone arrangement of lesional tissue(B)higher magnification of lesional tissue showing malignant features.(C) scanty osteoid tissue (D)areas of necrosis

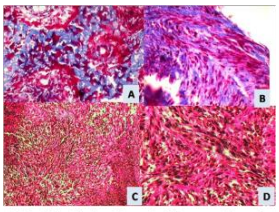

Fig9-A&B- showing Masson's trichrome staining of lesional tissue showing malignant osteoblasts. C&D - Van Giessen's stain showing malignant osteoblasts .

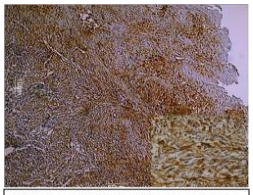

Fig10-Immunohistochemistry shows strongly vimentin positive lesional tissue. Inset shows higher magnification. Fig10- Immunohistochemistry shows strongly vimentin positive lesional tissue. Inset shows higher magnification.

Masson's trichrome and van Giessen stains were also performed which showed prominently malignant fibroblast, osteocytes and osteoblasts (fig.9). IHC was positive for vimentin (fig10). Features confirmed the diagnosis of fibroblastic variant of osteosarcoma. Radicle resection of the tumour under general anaesthesia followed by chemotherapy was planned but the patient refused surgery. The Patient was motivated to undergo surgery, but she was reluctant and did not turn up for follow-up and she died within few months at her native place.

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III. Discussion

The term "osteosarcoma" as opposed to "osteogenic sarcoma" is preferred by the World Health Organization (WHO).The term "sarcoma" was introduced by the English surgeon John Abernathy in 1804 and was derived from Greek roots meaning "fleshy excrescence". In 1805, the French surgeon Alexis Boyer (personal surgeon to Napoleon) first used the term "Osteosarcoma [7, 9, 10, 11]

Although the number of craniofacial osteosarcomas is very low, the prevalence of jaw osteosarcoma is in fact 10 times greater than that of osteosarcoma in the total body skeleton, considering that jaws represent only 0.86% of total body volume. Jaw osteosarcoma have been reviewed by various authors with rarely reported fibroblastic variant in the literature [12-20,] (Table 1).

They commonly present in the third or fourth decades. Males slightly out number females but the present case occurred in female [21]. The mandible is involved more frequently than the maxilla with posterior body, horizontal ramus and the ascending ramus being the most commonly affected site as seen in our case.

TABLE 1. MAJOR MANUSCRIPTS OF GNATHIC OSTEOSARCOMAS IN THE LITERATURE			
S.NO	**AUTHORS**	**PERIOD**	**TOTAL .NO OF PATIENTS**
1.	Schwatz and Apert 1963	1940-1961	66
2.	Potdar 1970	1970	14
3.	Roca et al 1970	1970	20
4.	Caron et al 1971	1930- 1966	43
5.	Russ and Jesse 1980	1948- 1977	30
6.	Raymond et al 1989	- 1989	55
7.	Colmenero et al 1990	1968- 1988	15
8.	Goepfert et al 1990	1953- 1987	70
9.	Doval et al, 1997	1986- 1992	8
10.	Oda et al. 1997	1981 -1996.	17
11.	Vege et al. 1991	1963-1981	34
12.	van Es et al. 1997	1964 to 1992	46
13.	Delgado et al 1994 23	1972- 1990	28
14.	Caron et al.1971	1930- 1966	43
15.	Mark et al.1991	1955 - 1987.	18
16.	Junior et al. 2003	-	24
17.	Lewis et al.1997	6 years	12
18.	Clark et al1983	1916-1976	66
19.	Forteza et al.1986	1967- 1985	9
20.	Lindqvist et al 1986	1953- 1983	9
21.	Ajagbe et al 1986	1960- 1984	21
22.	Bertoni et al. 1991	1950-1987	28
23.	Doval et al. 1997	1986–1992.	8
24.	Tanzawa et al. 1991	1930-1989	114
25.	Slootweg and Muller1985	1950- 1983	18
26.	Ryan et al 1986	1973- 1983	24
27.	Daw et al.2000	1962 - January 1998	28
28.	Can Soc OLHNSOSG	-	35
29.	August et al1997	1967-1991	30
30.	Smith et al.2003	1985 to 1996.	496
31.	MardingerOet al 2001	1989 to 1998	14
32.	Nissanka et al. 2007	1993 to 2003	19
33.	Bennett et al. 2000	30 years from 1968 to 1998	25
34.	McHugh et al.2006	-	21
35.	Fernandes et al2007	1993 to 2003..	16
36.	Jasnau et al.2008	1977 to 2004	49
37.	Guadagnolo et al.2009	1960 - 2007	119
38.	Ogunlewe et al 2006	1983- 2003	17
39.	Huber et al.2008	1974 - 1999	14
40.	Oliveira et al 1997	-	17
41.	Smeele et al 1994	1969- 1993	14
42.	Wanebo et al 1992	1982- 1990	29
43.	Garrington et al. 1967	1967	56
44.	Ha et al.1999	1946 - 1998	17
45.	Thiele et al.2008	1990-2004	12
46.	Mark et al.,1991	1955–1987	18
47.	Snehal G. Patel et al2002	1981 and 1998	44
48.	Shyam R. Gadwal2000	1970 and 1997	22
49.	Panizzoni et al 1992	1980- 1990	11
50.	Takahama Junior et al 2003	1958- 2001	23
51.	Padilla and Murrah2011	-	7
52.	Huh et al.2011	1983 to 2008	12
53.	Chaudhary M, Chaudhary SD.et al2012 .	1967 to 2010	300
54.	Peter M Nthumba2012	1992 and May 2011	235
55.	PrabhuS,et al2013	1990 -2010	13

Osteosarcoma may develop in pre-existing conditions. But the present case appears to have developed de novo as no history of pre-existing disease was associated which makes this report unusual.[9, 22,23]History of extraction of second molar ,one year back, could be considered as predisposing factor as extraction wound

didnot heal and the swelling appeared at the same site.Similar findings were reported by Prabhu. S .et al [21,] as well as Daffer[24]in their studyin which many patients had a history of extraction before the onset of the lesion.[2] Nissanka et al also showed history of previous dental treatments mostly dental extractions.The reason for this is most likely to be the rapid growth of tumour immediately after extraction, a phenomenon often showed by bone tumours. [25]

As this case occurred in female, possibility of hyperthyroidism could be considered. Although this aetiology was not thought butCamilo Jimenez et al reported many patients in their case series of 1234 patients who had hyperthyroidism [26]

Oxygen or nutrient gradient may have a role on cell differentiation of undifferentiated mesenchymal precursors to osteoblastic,chondroblasticorfibroblastic pathway. Furthermore factors such as angiogenesis or local biological mediators may have effects on localized area differentiation.[27]

The fibroblastic type is very rare, especially in the jaws. [8, 12]

Variousother aetiologies have been mentioned in the literature such as genetic predisposition[4], bone dysplasias[3], Li-Fraumeni Syndrome, Rothmund-Thomson syndrome [4, 6] fluorides[28],Radiotherapy[29], cancer stem cell hypothesis.[30], hyperparathyroidism[26], viral[31], osteitisfibrocystica, Hereditary Retinoblastoma[1],Trauma[2], chemical factors, which include beryllium compounds and methylcholanthrene,and Rapid bone growth .[32]

Unique feature of the disease was changing radiographic pattern form mixed to completely radiolucent in between two surgeries whichcaused much diagnostic predicament as jaw osteosarcomas does not necessarily show classic radiographic signs such as Codman's triangle and Garrington'ssign as seen in osteosarcoma of the long bones. Since swelling showed mixed radiolucency and radio opacity before the first surgery, a provisional diagnosis of fibrous dysplasia was consideredalthough it is rare in mandible. Malignancy was not considered initially as there was no historyof underlying pre-existing disease. Lesion recurred extensivelyandsubsequently became completely radiolucent suggesting mesenchymal malignancy or fibrous dysplasia turning into fibroblastic variant of osteosarcoma. [10,19] The differential diagnosis of fibroblastic osteosarcoma should include, Ewing's sarcoma, bone metastasis, fibrous dysplasia in early stage , osteomyelitis, and even lesions that do not usually affect the jaw bones, such as fibrosarcoma, leiomyosarcomas, or rhabdomyosarcomas.[33]

Misdiagnosed cases of osteosarcoma frequently reported in various literatures.Rosilene et al., reported a case of osteosarcoma of mandible initially resembling of periapical lesion and after initial endodontic treatment, a significant increase in the size of the lesion occurred[34]PriyankaDebta[35et] al also misdiagnosed a case of osteosarcoma as benign cystic lesion which recurred aggressively to cause extensive destruction. CD Mounesh at el misdiagnosed asneurofibroma[23].

It could be hypothesized that the first lesion presented by the patient was a low-grade central osteosarcoma, since this neoplasia is often misdiagnosed radiographically, clinically and microscopically as fibrous dysplasia. Furthermore, low-grade central osteosarcomas characterized by high incidence of local recurrence after inadequate surgical removal and can transform into higher-grade osteosarcoma .Another hypothesis is the malignant transformation of fibrous dysplasia, a rare but possible event.[37]although fibrous dysplasiais comparatively rare in mandible.[35]

Recurrence after inadequate surgical removal is a frequent phenomenon as reported by siew[38] and abbas[3];ourcase also recurred within 2 months.

Shah et al, Bennet et al, Hauben et al and Cavalcanti found high numbers of craniofacial osteosarcomas with fibroblastic variant behaved more aggressively. [39,40,41,42]

As per literature various histochemical stains have been used to study thehistopathological features of osteosarcoma for e.g. picrosirius red, improved Ponceautrichrome and Masson trichrome staining .Similar findings were noted in our study using MassonsTrichrome and Van Giessen's Staining.[43]

The growth in this case was so rapid that in contrast to the literature, the time span between diagnosis and death was only few months, a feature uncommon for gnathic lesions[1, 25]

IV. Conclusion

It can be concluded that misdiagnosis is very common in osteosarcoma of the jaw as this case exhibited unusual features like changing radiographic patterns ,de novo origin, recurrence, extraction as predisposing factor, a rare fibroblastic variant with scanty osteoid resulted in missing classical sign of osteosarcoma .Besides adding this case of osteosarcoma of the mandible in the dental literature, this article would catch the attention of the dental professionals so that they may approach such cases with greater concern and diagnose them at an early stage for better prognosis.

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