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Research Letter

Spontaneous osteosarcoma transformation of fibrous dysplasia in maxilla

KEYWORDS
Osteosarcoma;
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Fibrous dysplasia (FD), with possible *GNAS* (guanine nucleotide-binding protein/a-subunit)-I gene mutations, is typically a benign fibro-osseous lesion that chiefly affects maxillofacial area causing facial deformity.[1] Sarcomatous change of FD is rare and the frequency of sarcomatous transformation differs from less than 1% (monostotic/polyostotic cases) to 4% (McCune-Albright/Jaffe-Lichtenstein syndrome). Osteosarcoma is the major histologic type of malignant transformation of FD, followed by fibrosarcoma, chondrosarcoma, and malignant fibrous histiocytoma, with most cases reported years after radiation treatments[2,3] Here, we reported an osteosarcoma spontaneous occurring in a Taiwanese patient with maxilla FD without prior radiotherapy with pertinent literature review.

A 65-year-old female patient complained a sudden painful ulcerated swelling over the left palate for 12 months (Fig. 1A). A long-standing stabilized FD over the left maxilla was diagnosed in another hospital with neither surgical nor radiation treatment before. Extraoral examination revealed a bony swelling over the left maxilla (Fig. 1B). Panoramic radiography showed an ill-defined mixed radiolucent and radiopaque lesion over the left upper edentulous area up to the left maxillary sinus (Fig. 1C). 3D-cone beam computed tomography (CBCT) revealed an extensive bony swelling over left maxilla (Fig. 1D). Reformatted CBCT images showed full occupation of the left maxillary sinus by a mixed radiolucent-radiopaque destructive mass extending below the infraorbital area (Fig. 1E). No alteration of eyesight was complained. Increased level of serum alkaline phosphatase (111 IU/L) was noted. A bony malignancy associated with pre-existing FD was considered. Incisional biopsy revealed a high-grade osteosarcoma characterized with osteoid tissues showing highly pleomorphic cells with bizarre nuclei (Fig. 1F). Subsequently, radical resection was performed (Fig. 1G and H). Histopathological examination of the surgical specimen showed bizarre osteoid tissues adjacent to and infiltrated into areas featured with FD with irregular-shaped trabeculae of woven bone within fibrous stroma (Fig. 1I–K). A high-grade osteosarcoma arising from pre-existing maxilla FD has been rendered. *GNAS*-I mutations of the malignant tissues revealed negative result. The patient died of tumor after 11-month follow-up.

Reviewing English literature, to our knowledge, 15 spontaneous osteosarcoma cases in pre-existing non-syndromic maxillofacial FD without previous irradiation are identified for the recent ten years (2010–2019);[3–8] the clinical features (together with the current case) are summarized in Table 1. Briefly, the male-to-female ratio was 1:1.67 and the age of the patients ranged from 8 to 65 years with the mean age of 42.7 years. The present case is the oldest of such disease and is the first case in Taiwan. The majority of patients were belonged to the 6th decade (five cases)[4,7] As high as 14 cases reported from Asian countries (China, 11 cases;[3,7] one case each from Taiwan (our case), Korea,[4] and Irian[6]); the remaining two cases documented each from UK[5] and USA.[8] There were ten polyostotic cases[3,7] with only six cases including our case)[3,5,6,8] of monostotic form. The time-interval between initial FD and later malignant change was available for nine cases[3,4,7,8]

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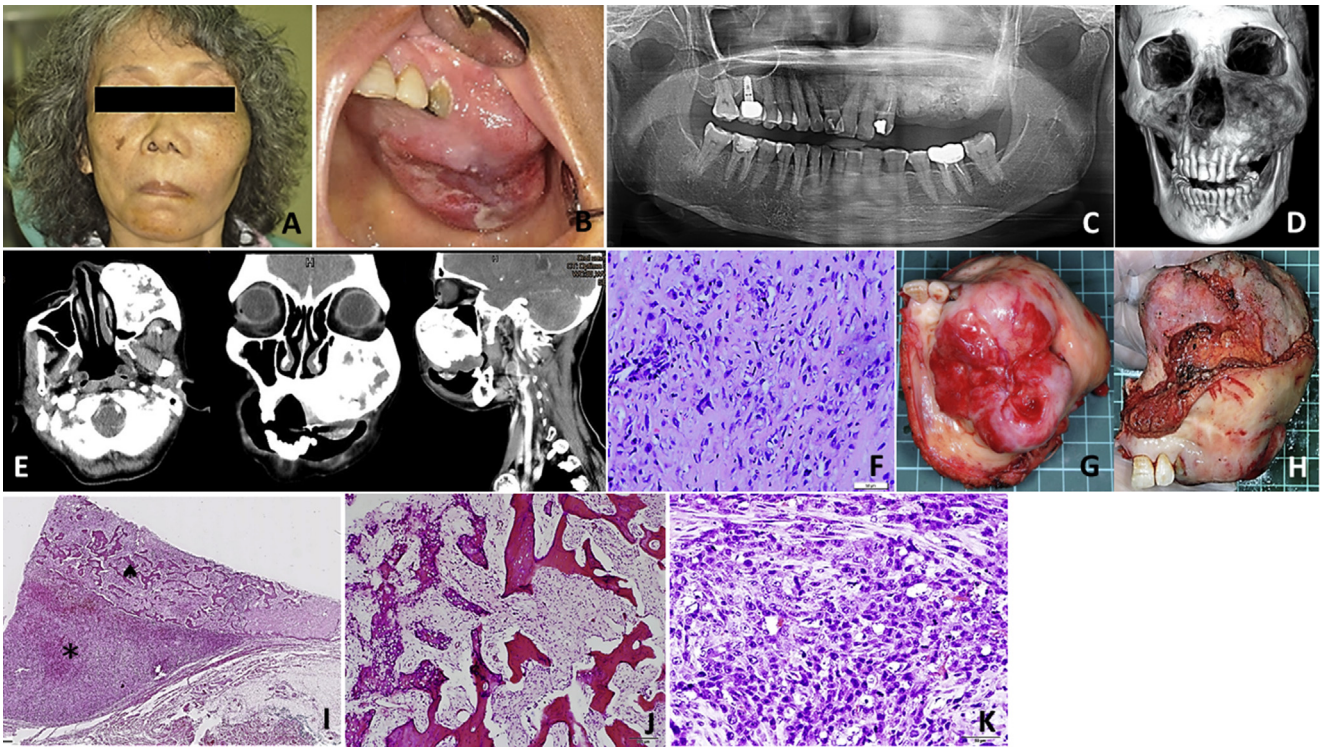

Figure 1 Clinical, radiographic, and microscopic pictures of the current case of spontaneous osteosarcoma arising from pre-existing fibrous dysplasia (FD) without prior irradiation. (A) Ulcerated swelling over the left palate. (B) Facial asymmetry with bony swelling over the left maxilla. (C) Panoramic radiography: an ill-defined mixed radiolucent-radiopaque expansion extending from the upper-left edentulous area to maxillary sinus. (D) 3D-cone beam computed tomography (CBCT) revealed an extensive bony swelling over the left maxilla. (E) Reformatted axial, coronal, and sagittal CBCT images showed total occupation of the left maxillary sinus by a mixed radiolucent-radiopaque destructive mass. (F) Incisional biopsy: high-grade osteosarcoma characterized with malignant osteoid tissues showing highly pleomorphic cells with bizarre nuclei (hematoxylin and eosin stain, H&E; magnification, 200 ×). (G, H) Surgical specimen upon radical resection: oral (G) and frontal (H) view. (I—K) Histopathological examination of surgical specimens: sarcomatous (*) and FD (♠) areas (H&E; magnification, 4 ×) (I); bizarre osteoid tissues (left portion) adjacent to area featured with FD with irregular-shaped trabeculae of woven bone within fibrous stroma (right portion) (H&E; magnification, 100 ×) (J); tumor cells within sarcomatous area showing highly cellular atypia with numerous abnormal mitoses (H&E; magnification, 100 ×) (K).

with the mean duration being 30 years (range: 8—50 years); two cases (including our case),[5] despite without exact duration, were judged as long-standing FD according to the given case history, whereas the remaining five cases[3,6] were diagnosed simultaneously implicating that the delayed detection of FD, which was noted until the occurrence of malignant transformation. Most common clinical presentations included rapid-increased/sudden swelling (all cases including our case),[3—8] pain (6 cases including our case),[3,5,7,8] local numbness (6 cases),[3,7] and intraoral ulceration (4 cases including our case).[3,5,7] Eyesight problem was noted in two cases.[3,6] Osteosarcoma predominantly involved the left maxilla (10 cases including our case),[3,5—7] followed by the left mandible (4 cases),[3,8] and the right mandible (2 cases)[3,4] All (including our case)[3—8] but one patient receiving radical resection with/without chemotherapy and/or radiotherapy.[3] Fourteen patients including our case[3—7] had available follow-up data indicating very poor prognosis with only 3 alive[3,4,7] and 11 patients including our case[3,5—8] died of disease during the follow-up period (several-week—101-month).

The genetic etiology of FD is well-documented being resulted from two-point mutation in GNAS-I protein;[9] however, such mutations do not contribute to the malignant change of FD.[9] The lack of *GNAS*-I mutation in the current case is concurred to the findings of Pollandt et al.[9] who demonstrated constant absence of the *GNAS*-I mutation in an osteosarcomatous variant of FD, indicating a different genetic etiology for malignant change of FD.

Additionally, albeit rare, spontaneous malignant transformation of FD without prior radiotherapy is well-confirmed;[3—8] hence, dental practitioners should aware the happening of spontaneous sarcomatous change, particularly osteosarcoma, when FD patients presented with above-mentioned symptoms and radiological features of malignancy.

Table 1 Summary of clinical features of reported cases (2000—2019) of spontaneous osteosarcoma in maxillofacial fibrous dysplasia (FD) without prior radiation treatment.

Authors (year)	Country	Age, years	Gender	Primary site of malignancy	Type of FD	[a]Duration of FD, years	Symptoms of malignancy	Treatment of malignancy	Follow-up
Kim et al. (2010)[4]	Korea	50	Female	Right mandible	Monostotic	25	Swelling, 1 month	Neoadjuvant chemotherapy, radical resection, postoperative adjuvant chemotherapy	24 months, alive, no evidence of disease
Varghese et al. (2010)[5]	UK	47	Male	Left maxilla	Monostotic	[b]Not available	Pain, rapid enlarged swelling, intraoral ulceration; 1.5 month	Frozen section, palliative radiotherapy	A few weeks, died of tumor
Sadeghi et al. (2011)[6]	Iran	16	Male	Left maxilla	Monostotic	0	Rapid swelling, diplopia, 4 months	Radical resection; CCRT	18 months, died of tumor
Cheng et al. (2013)[7]	China	55	Male	Left maxilla	Polyostotic	45	Pain, local numbness, trismus	Incisional biopsy	6 months, died of tumor
Cheng et al. (2013)[7]	China	57	Female	Left maxilla	Polyostotic	43	Facial swelling, intraoral ulceration, bleeding	Radical resection	23 months, alive, no evidence of disease
Cheng et al. (2013)[7]	China	26	Female	Left maxilla	Polyostotic	20	Accelerated growth, local numbness, pain	Radical resection & postoperative radiotherapy	16 months, died of tumor
Sun et al. (2014)[3]	China	55	Male	Left mandible	Polyostotic	50	Swelling, pain, local numbness; 1 month	Radical resection	44 months, died of tumor
Sun et al. (2014)[3]	China	55	Male	Left maxilla	Polyostotic	38	Swelling, intraoral ulceration; 2 months	Radical resection	57 months, died of tumor
Sun et al. (2014)[3]	China	31	Female	Left mandible	Polyostotic	8	Swelling, local numbness; 0.5 month	Radical resection	15 months, alive with lung metastasis
Sun et al. (2014)[3]	China	28	Female	Left maxilla	Polyostotic	20	Swelling, local numbness, headache; 6 months	Radical resection, radiotherapy	62 months, died of tumor
Sun et al. (2014)[3]	China	41	Female	Left maxilla	Polyostotic	0	Swelling, pain, decreased visual acuity; 1 month	Radical resection, radiotherapy	57 months, died of tumor
Sun et al. (2014)[3]	China	26	Female	Left maxilla	Polyostotic	0	Swelling, local numbness; 0.5 month	Radical resection	77 months, died of tumor
Sun et al. (2014)[3]	China	41	Female	Right mandible	Monostotic	0	Swelling; 2 months	Radical resection	101 months, died of tumor
Sun et al. (2014)[3]	China	8	Male	Left mandible	Polyostotic	0	Swelling; 2 months	Incisional biopsy	Unknown, lost to follow-up
Pack et al. (2016)[8]	USA	39	Female	Left mandible	Monostotic	21	Swelling, pain, paresthesia	Radical resection	Not available
Su et al. (present case)	Taiwan	65	Female	Left maxilla	Monostotic	[b]Not available	Swelling, pain, intraoral ulceration, 12 months	Radical resection	11 months, died of tumor

[a] Duration between initial presentation of FD and later osteosarcoma occurrence.
[b] Long-standing FD but the exact duration has not been given.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jds.2019.04.002.

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