

법랑모세포섬유-치아종으로부터 발생한 법랑모세포섬유육종

-종례 보고-

Bazarsad Shadavlonjid^{1),3)}, 조은애¹⁾, 남웅²⁾, 김현실¹⁾, 육종인¹⁾, 김진^{1)*}

연세대학교 치과대학 구강병리학교실, 구강종양연구소¹⁾, 연세대학교 치과대학 구강악안면외과학교실²⁾

Dental School of Mongolian National University of Medical Science, Ulaanbaatar, Mongolia³⁾

〈Abstract〉

A case of Ameloblastic Fibrosarcoma Transformed from Ameloblastic Fibro-odontoma

Bazarsad Shadavlonjid^{1),3)}, Eunae Cho¹⁾, Woong Nam²⁾, Hyun Sil Kim¹⁾, Jong In Yook¹⁾, Jin Kim^{1)}*

¹⁾Department of Oral Pathology, Oral Cancer Research Institute, Yonsei University College of Dentistry, Seoul, South Korea

²⁾Department of Oral and Maxillofacial Surgery, Yonsei University College of Dentistry, Seoul, South Korea.

³⁾Dental School of Mongolian National University of Medical Science, Ulaanbaatar, Mongolia

Ameloblastic fibrosarcoma (AFS) is an extremely rare malignant odontogenic tumor characterized with benign ameloblastic cells islands and malignant mesenchymal component. While two-thirds of AFS seem to arise de novo, but one-third develops from recurrent ameloblastic fibroma (AF) or ameloblastic fibro-odontomas (AFO). Pathological distinction of malignant transformation is essential for appropriate treatment. The patient was a 28 years old man. Since the primary tumor was excised, the mass recurred 2 years later. The recurrent tumor was diagnosed as AFS. Chief complaint was pain in the right mandible. Computer tomography finding revealed multilocular intrabony lesion with radiopaque substance in the primary lesion. In the recurrent lesion cortical bone destruction was found. Microscopically, both the primary and recurrent lesions showed benign ameloblastic follicles with myxoid or highly cellular mesenchymal proliferation. The histological difference between primary and recurrent lesions were that foci of dental hard tissue composed of enamel and dentin were found only in the primary lesion, whereas nuclear pleomorphism was aggravated in the recurrent lesion. The histological criteria determining malignancy were discussed.

Key words: Ameloblastic fibro-odontoma, Ameloblastic fibrosarcoma, Malignant transformation

I. INTRODUCTION

Ameloblastic fibrosarcoma (AFS) is an extremely rare malignant odontogenic tumor with the general features of a benign ameloblastic cells and malignant mesenchymal component¹⁾. To our knowledge, about 90 cases have been described in literature. 50% of all AFS are described as malignant transformation from AF²⁾. Malignant transformation of AFO is rarely reported, but 2 cases of AFS transformed

* Correspondence: Professor Jin Kim, Department of Oral Pathology, Oral Cancer Research Institute, Yonsei University College of Dentistry, Seodaemun-gu, Yonsei-ro 50, Seoul, 03722, South Korea, Tel: +82-2-2228-3031
E-mail: jink@yuhs.ac

ORCID : 0000-0001-5398-8989

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from AFO were reported by Howell and Burkes³⁾. The tumor usually develops in the mandible, presenting locally aggressive behavior causing pain and swelling⁴⁾. Pathological distinction of malignant transformation is essential for appropriate treatment. The aim of this report is to present a new case of this rare entity with reference to diagnostic criteria of malignant transformation of AFO.

II. CASE REPORT

The 28 years old man was referred to Dental Hospital of Yonsei University complaining of the right mandibular swelling. The panoramic radiograph of the primary lesion revealed an ill-defined multilocular intrabony lesion expanded from the right mandibular premolar to the angular area. Several foci of radiopaque substance were found. The root resorption of the involved teeth was found. Computer tomography showed expansion of the alveolar ridge with discontinuity of cortical bone and presence of radiopaque foci in the mandible (Fig. 1A and B). The surgical excision specimen showed benign epithelial components made up of columnar cells arranged in a palisaded pattern with a central area of stellate reticulum-like cells (Fig. 1C). The mesenchymal component showed a myxoid or highly cellular areas alternately; the myxoid portion composed of stellate or spindle shaped cells and the highly cellular portion composed of spindle or polygonal cells with slight nuclear atypia (Fig. 1E, F). Characteristically, foci of dental hard tissue composed of enamel and dentin were found (Fig. 1D). With these histological findings, the primary lesion was diagnosed as AFO with a note of the possibility of recurrence due to highly cellular area.

During 2 years follow up period, pathological mandible fracture occurred and even after close reduction, the patient had discomfort in ascending ramus area. The computer

tomography revealed multilocular intrabony lesion with cortical bone erosion (Fig. 2A). The tumor resection was conducted. Microscopically, the recurred mass revealed the similar histological findings with the primary tumor. Comparing to the primary tumor, the epithelial component of the recurred mass was reduced (Fig. 2B, C). Particularly, the deposits of odontogenic hard tissue materials disappeared. In addition, highly cellular stromal portion showed nuclear pleomorphism (Fig. 2C, D, E). Despite the increased cellularity of the recurrent tumor, the mitotic index showed the same value with the primary tumor. The myxoid areas showed 0/10 high power field (hpf), whereas the highly cellular areas showed 3-4/10 hpf. The proliferating activity was measured by immunohistochemical staining for Ki-67. The primary antibody was purchased from Abcam (Cambridge, UK) and was diluted to be 1:100. The proliferating index showed the same value to be 6.8% in the primary tumor and 6.3% in the secondary tumor (Fig. 3). Considering increased cellularity and nuclear pleomorphism with devoid of odontogenic matrix, the recurred mass was diagnosed as AFS.

III. DISCUSSION

The current 2005 WHO classification distinguished ameloblastic fibro-dentino- and fibro-odontosarcomas (AFOS), separately from AFS. AFOS is defined as a tumor with histological features of AFS, together with dysplastic dentin and/or enamel/enameloid and dentin/dentinoid. Therefore, the recurrent tumor of this case was diagnosed as AFS because of no enameloid or dentinoid materials¹⁵⁾.

The definitive diagnosis of AFS has been established based on histopathologic evaluation of the mesenchymal component which usually demonstrates various features of malignancy including hypercellularity, nuclear pleomorphism, and mitotic

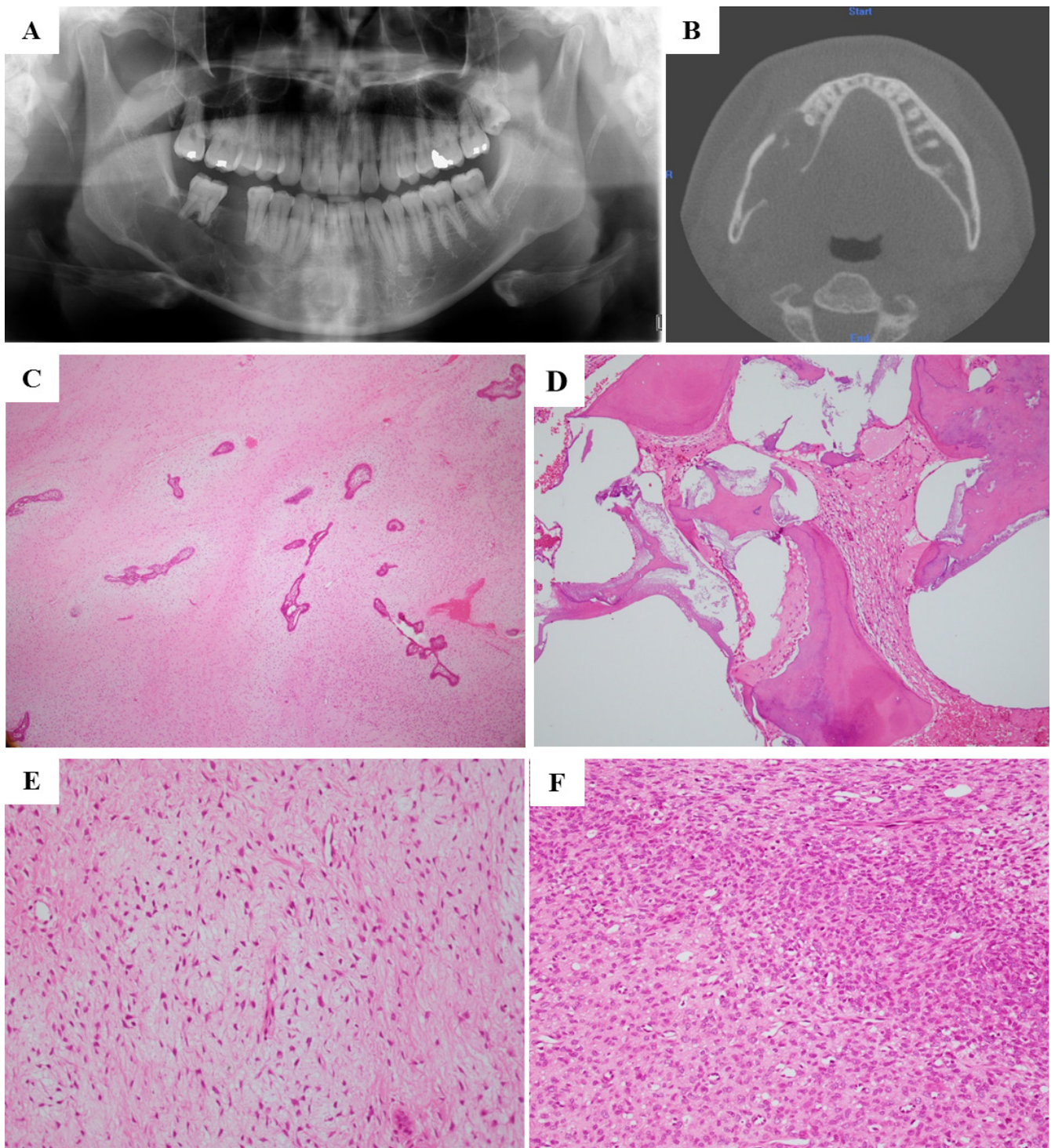


Fig. 1. (A and B) A panoramic radiograph and coronal computed tomographic sections of the mandible showing a neoplasm in 2013. (C) AFO, sparsely cellular and myxoid dental papille like stroma surrounding benign epithelial component (x40). (D) Irregular masses of dental hard tissue composed of dentinoid structures accompanied with enamel matrix (x40). (E) Myxoid mesenchymal components showing spindle or stellate shaped cells (x200). (F) Closely packed mesenchymal component arranged hyperchromatic plump ovoid or spindle shaped cells (x200).

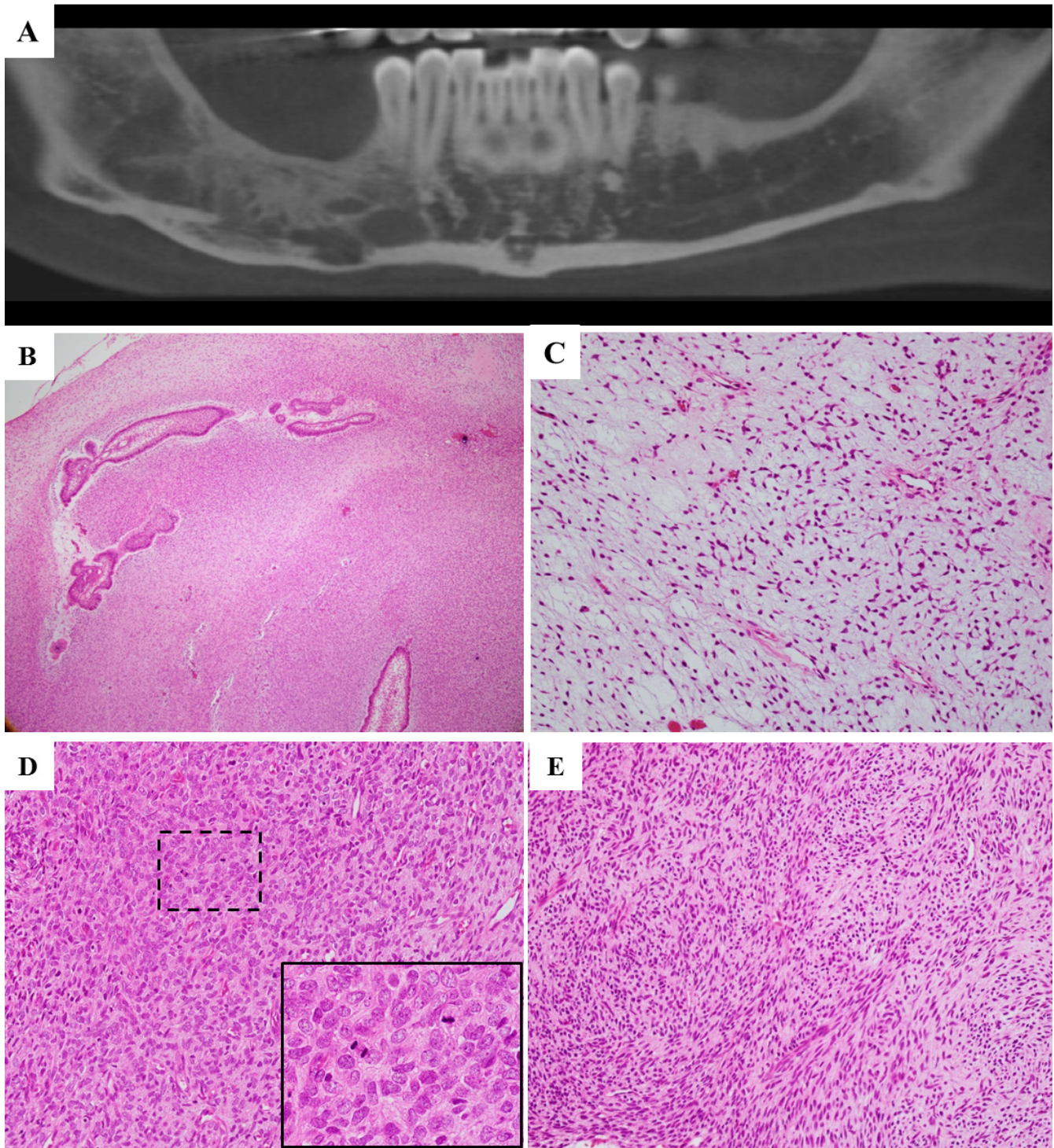


Fig. 2. (A) The panoramic radiograph showing a multilocular intrabony lesion with evidence of breaking down of cortical bone (arrows) in 2015. (B) Ameloblastic follicles with highly cellular stroma (x40). (C) Myxoid mesenchymal tissue with hyperchromatic nucleated spindle cells (x200). (D) Closely packed mesenchymal component with pleomorphic polygonal cells with mitosis (x200) (inset x1000). (E) Highly cellular proliferation of spindle cells resembling fibrosarcoma, exhibiting moderate to marked nuclear pleomorphism and hyperchromatism (x200).

figures⁶⁾. In our cases, the decision of malignancy of the recurrent tumor was not difficult based on relatively uniform high cellularity, nuclear pleomorphism with mitotic activity. However, the decision of biological behavior of the primary tumor was problematic. Although the primary tumor showed the stereotyped histological features of AFO such as definite differentiation of odontogenic matrix and benign natured ameloblastic epithelial islands and myxoid mesenchymal components, the primary tumor included highly cellular areas with mitotic activity, suggesting foci of malignant transformation.

The measurement of mitotic activity has been a histological criterion to determine malignancy in both carcinoma and sarcoma. For determining malignancy in fibroblast proliferating lesions, high mitotic counts (>1 per 10HPF) throughout a tumor should arouse suspicion of fibrosarcoma⁷⁾. In terms of differentiating AFS from AF, most reports described that mitoses should not be a feature of AF^{8,9)}. The presence of a large number of cells in mitosis and atypical mitosis supports malignancy^{10,11)}. Considering the guideline of mitotic activity, the primary tumor included foci of malignant transformation. However, besides mitotic activity, other histological findings of the primary tumor were insufficient

to be treated as malignancy. Furthermore, a wide spectrum of mitotic indices in AFS from 2/10 hpf to more than 100/10 hpf have been reported. Furthermore, few mitoses can be present even in AF¹¹⁾, in contrast, there are reports that well-differentiated malignant areas are relatively hypocellular, with few mitotic figures in AFS¹²⁾.

Proliferating activity has been a reliable marker to confirm malignant tumors¹³⁾. However, likewise to mitotic activities, proliferation activity varies among the reported cases from 47% to less than 10%^{11,13,14)}. In our cases, Ki67 expression was found less than 10% in both primary and recurrent tumors.

As a general rule, smooth muscle tumors without necrosis and little to no nuclear atypia may be diagnosed as "leiomyoma of uncertain malignant potential (UMP)" when the mitotic rate is $<1/50$ hpf (soft tissue location) or $<10/50$ hpf (retroperitoneum)^{15,16)}. That is, developmental site has been one of the main criteria for determining malignancy. For the decision of malignancy of odontogenic mesenchymal tumors, we proposed that odontogenic differentiation can be another factor to determine malignancy. In this case report, one crucial decision factor to determine malignancy was the fact that odontogenic differentiation shown in the

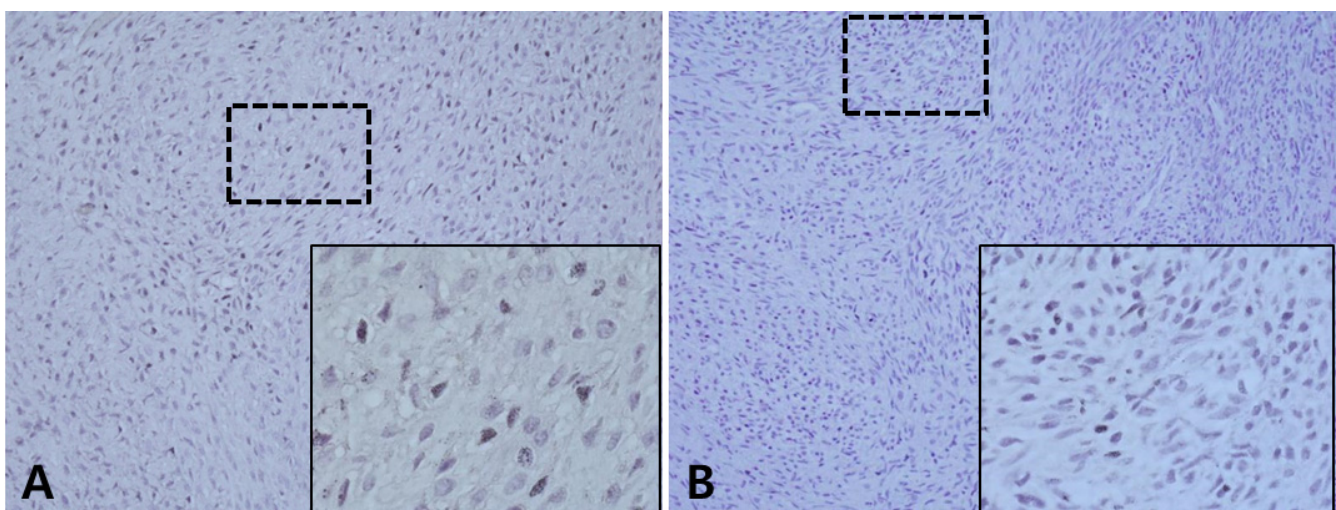


Fig. 3. Ki-67 expression in the primary and recurrent tumors (x200) (inset x1000). (A) The primary tumor, AFO. (B) The recurrent tumor, AFS.

primary tumor was diminished with increased nuclear pleomorphism and cellularity in the recurrent tumor. Considering the primary tumor shown stereotyped AFO with transforming foci to sarcoma, AFO should be treated as one of the odontogenic tumors with the potentiality promoting to malignancy. Accumulated data with clinical follow-up of long periods should be required to establish more accurate criteria to determine malignancy. Currently, one year after the surgical procedure, the patient has been clinically disease-free.

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