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# Ameloblastic fibrosarcoma in the maxilla, malignant transformation of ameloblastic fibroma

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**Summary.** This report presents a fatal case of ameloblastic fibrosarcoma arising from an ameloblastic fibroma, originating in the maxilla of 19-year-old Japanese male. An analysis of previously reported fatal cases of ameloblastic fibrosarcoma is included.
In the course of the disease, the mesenchymal component of ameloblastic fibroma showed a dramatic histopathological transformation into sarcoma following multiple recurrence and the patient died of uncontrollable local infiltration of the cranial base. Although many cases have seemed to show disappearance of the epithelial component as malignant transformation progressed, many benign appearing ameloblastoid epithelial masses were scattered throughout the sarcomatous area even in the fatal stage in the present case. No distant metastases were found at autopsy. During multiple recurrences of the lesion, a little dysplastic dentin which was closely associated with both epithelial and mesenchymal components was found, though it could not be observed in autopsy material. Ultrastructural findings in autopsy material showed that the mesenchymal component consisted of undifferentiated mesenchymal cells, fibroblastic and fibrocytic cells with marked cellular and nuclear pleomorphism and that the epithelial component closely resembled the enamel organ.

**Key words.** Ameloblastic fibrosarcoma – Histogenesis – Histopathology – Ultrastructure – Fatal case

The ameloblastic fibrosarcoma (ameloblastic sarcoma) is an exceedingly rare mixed odontogenic tumour. It is regarded as the malignant counterpart of the benign ameloblastic fibroma; the mesenchymal component becoming malignent, while the epithelial component does not show any signs of cancer (Pindborg and Kramer 1971). The first survey of the literature on ameloblas-

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tic fibrosarcoma (Pindborg 1960) was followed by another (Leider et al. 1972) which included previously reported cases and added new examples. Other individual cases have been reported in the English literature (Peychl and Sazama 1971; Mori et al. 1972; Hatzifotiadis and Economou 1973; Goldstein et al. 1976; Howell and Burkes 1977; Adekeye et al. 1978; Reichart and Zobl 1978; Daramola et al. 1979; Prein et al. 1979), however, there have been only two reports of the ultrastructural examination of ameloblastic fibrosarcoma (Eda et al. 1976; Nasu et al. 1984). According to the reported cases, the ameloblastic fibrosarcoma occurs in both sexes and all ages, however, it is more common in young adults. The lesion occurs more frequently in the mandible than in the maxilla. The prognosis is guarded, since recurrence may occur even after a considerable length of time. Several cases of ameloblastic fibrosarcoma with uncontrollable local invasion have been documented (Pindborg 1960; Cina et al. 1962; Peychl and Sazama 1971; Mori et al. 1972; Hatzifotiadis and Economou 1973; Howell and Burkes 1977).

We have seen a patient who had maxillary tumour diagnosed previously as benign ameloblastic fibroma that underwent transformation to ameloblastic fibrosarcoma. The purpose of this article is to show its detailed clinical course and the histopathological findings of biopsy, operation and autopsy material with ultrastructural investigation.

## Case report

*Clinical course.* A 19-year-old Japanes male visited the otolaryngology service of Iwate Medical University on December, 1973, complaining a swelling on his gingiva of maxillary left molar region with mild pain. The patient had noticed the gingival swelling for the fist time four weeks previously. Examination revealed a projecting lesion measuring in 6 mm in diameter on the buccal gingiva of the left maxillary molar area and rentogenogram revealed a radiolucent area measuring in 7 mm in diameter in the alveolar bone. Following an interpretation of a benign cystic lesion, surgical removal of the lesion was performed. At the surgical treatment, the lesion was completely enucleated glossly and the wall of maxillary sinus was intact. The histopathological diagnosis at that time was ameloblastic fibroma.

**Table 1.** Fatal cases of ameloblastic fibrosarcoma

| Case No. | | Age at onset | Sex | Location | Duration |
|---|---|---|---|---|---|
| 1.[a] | Pindborg (1960) | 17 | M | lt. mand. | 2 years 6 months |
| 2. | Cina et al. (1962) | 32 | F | rt. mand. | 2 years 2 months |
| 3.[a] | Peychl and Sazama (1971) | 17 | M | rt. max. | 4 years 6 months |
| 4. | Mori et al. (1972) | 3 | F | rt. mand. | 6 years |
| 5. | Mori et al. (1972) | 23 | F | lt. mand. | 19 years |
| 6. | Hatzifotiadis and Economou (1973) | 15 | M | lt. max. | 1 year 9 months |
| 7. | Howell and Burkes (1977) | 18 | F | lt. mand. | 4 years |
| 8.[a] | Takeda et al. (1984) | 19 | M | lt. max. | 9 years 6 months |

[a] Autopsy was performed

In April, 1975, the patient returned with a recurrence. Enucleation of the tumour was carried out at that time and a histopathological diagnosis of ameloblastic fibroma was again made from the operation material. By December, 1976, there was a recurrent tumour mass filling in the left maxillary sinus, and resection of the left maxilla including the tumour-bearing area was performed. Subsequent recurrent lesions were removed on 1978 and 1980. In January, 1983, swelling of the region of left lateral ocular angle appeared, and it rapidly increased in size. At the last admission, May, 1983, there was an infant's head-sized tumour mass (measuring in 30 by 24 by 15 cm) in the forehead of the left side, involving in the base of skull, the middle face and the epipharynx. Cranioectomy and partial resection of the tumour was performed, but his general condition progressively deteriorated and he died in June, 1983. Total duration of his illness was 9 years and 6 months.

*Autopsy findings.* The autopsy was performed 12 h after death and revealed diffuse invasion of grayish-white tumour to the cranial base (i.e. sphenoidal bone, ethmoidal bone, basilar part of the occipital bone, left orbital part of the frontal bone) and the epidular space, left orbit, nasal cavity and epipharynx. No distant metastases were found in any other organs. The direct cause of death was respiratory disturbance due to bronchopneumonia of the bilateral lung with congestion and oedema.

### *Histopathological findings*

The first histopathological examination of the surgical specimen obtained in December, 1973, revealed a tumour composed of anastmosing islands and strands of benign epithelial cells, the more peripheral of which were ameloblast-like in appearance with a loose central area simulating stellate reticulum (Fig. 1a). The background consisted of a loosely cellular mesenchymal tissue that resembled the dental papilla of a tooth germ (Fig. 1b). There was no evidence of stromal cell pleomorphism. A histopathological diagnosis of ameloblastic fibroma was made. The operation material of the first recurrence, at April 1975, revealed similar histopathological findings. The specimen of the second recurrence, at December, 1976, revealed similar islands of epithelial component but a more abundant, and increased cellularity of the mesenchymal component (Fig. 2a). Although cells of the mesenchymal component showed minimal pleomorphism and a fine fibrillar background was observed (Fig. 2b), the lesion still suggested a benign ameloblastic fibroma. Subsequent recurrent lesions in 1978 and 1980 revealed both epithelial and mesenchymal patterns identical to those previously noted, but the cellularity of the mesenchymal component was increased gradually.

In May, 1983, rapid-grown tumour revealed a dramatic histopathological difference. The mesenchymal component showed a great increase in cellularity and showed a sarcomatous character; it was extremely cellular and nuclear pleomorphism, distinct nucleoli and frequent mitotic figures were evident (Fig. 3a and b). The degree of differentiation of sarcomatous mesenchymal cells varied from area to area (Fig. 3a and b). There were no evidence of malignancy in the epithelial component. Furthermore, a small amount of hard tissue resembling dysplastic dentin closely associated with both epithelial and mesenchymal components was found in some parts (Fig. 4a and b) but no enamel like substance was found. At autopsy, the histopathological findings of the tumour were identical to those previously noted (Fig. 5a and b), but hard tissue resembling dysplastic dentin was not demonstrated in the sections of available materials. In part of the tumour invading bone, marked hyalinosis of the mesenchymal component was noted (Fig. 5c). In such areas, epithelial cells tended to show squamous metaplasia.

### *Ultrastructural findings*

Specimen for ultrastructural examination was taken at autopsy, though postmortem changes had progressed. The mesenchymal cells were composed of fibroblastic and fibrocytic cells (Fig. 6a and b), and undifferentiated cells, though the details of the cytoplasmic structure were unclear due to autolysis. The epithelial component was differed significantly from the mesenchymal component by the presence of basal lamina. The epithelial cells at the periphery were columnar or cubical in shape, the cells in one row underneath the peripheral cells were

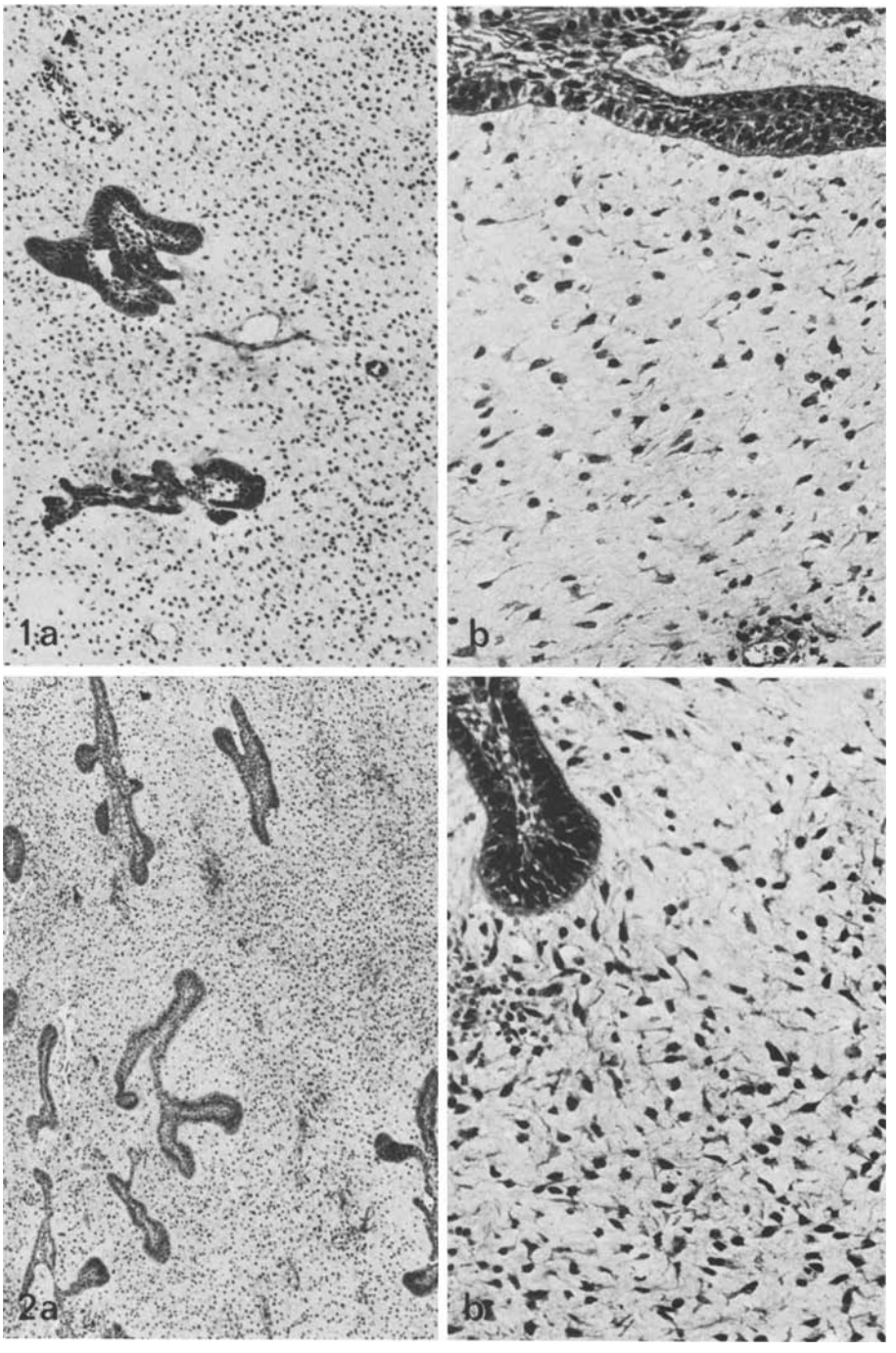


**Fig. 1 a, b.** Photomicrographs of the first histopathological examination, initially diagnosed as an ameloblastic fibroma, showing islands of ameloblastic epithelium within loosely cellular mesenchymal tissue. Haematoxylin and eosin, (**a**) × 40 and (**b**) × 200

**Fig. 2 a, b.** Photomicrographs of recurrent lesion 3 years after the first operation, showing abundant epithelial islands and increased cellularity of the mesenchymal component. Haematoxylin and eosin, (**a**) × 40 and (**b**) × 200

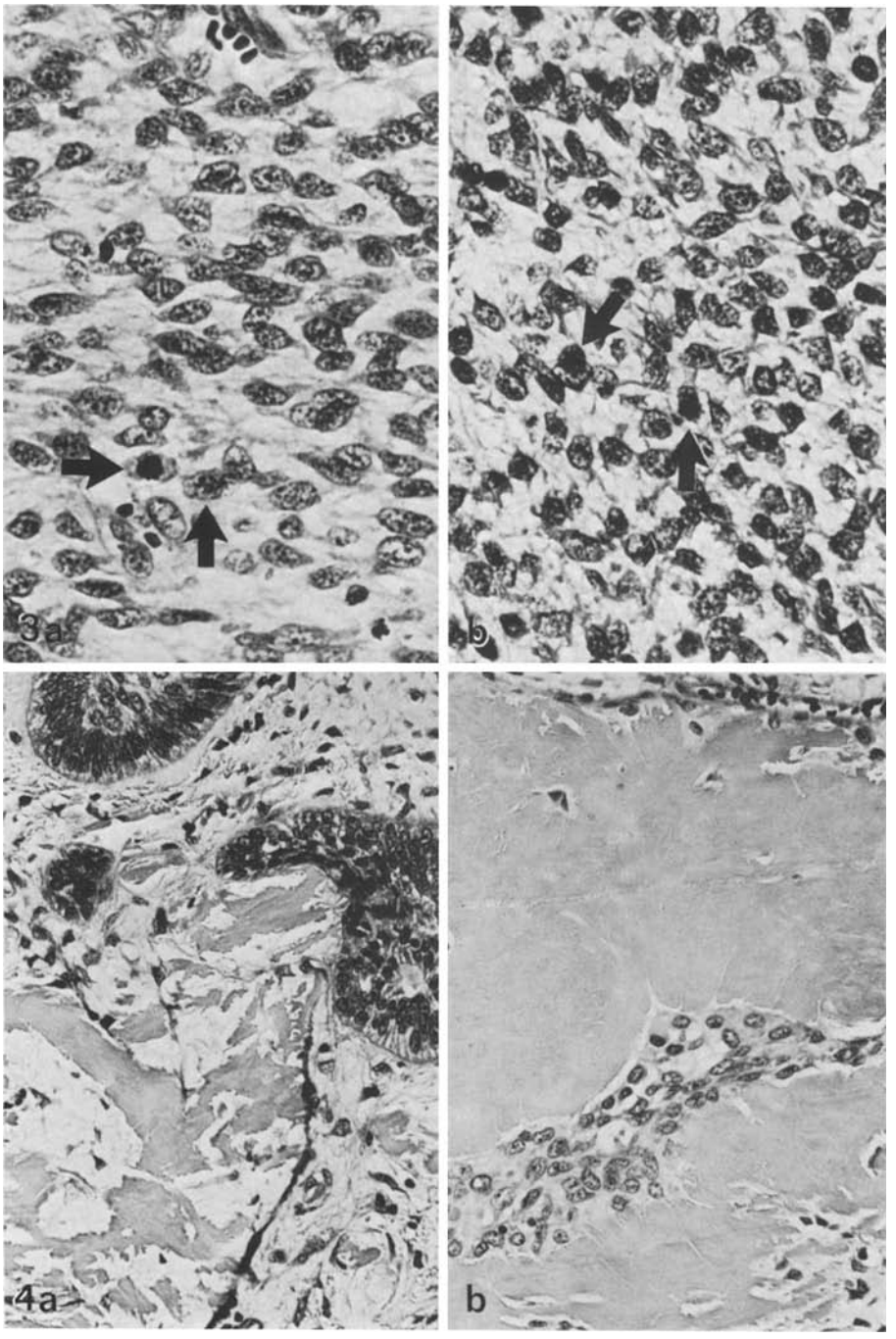


**Fig. 3a, b.** Photomicrographs of recurrent lesion 9 years after the first operation, showing fibrosarcomatous pattern of the mesenchymal component with marked cellular pleomorphism and many mitoses (*arrows*). (**a**) well-differentiated fibrosarcoma and (**b**) poorly differentiated one. Haematoxylin and eosin, (**a**) and (**b**) $\times 400$

**Fig. 4a, b.** Photomicrographs of dysplastic dentin found in some parts of the lesion. Haematoxylin and eosin, (**a**) $\times 200$ and (**b**) $\times 400$

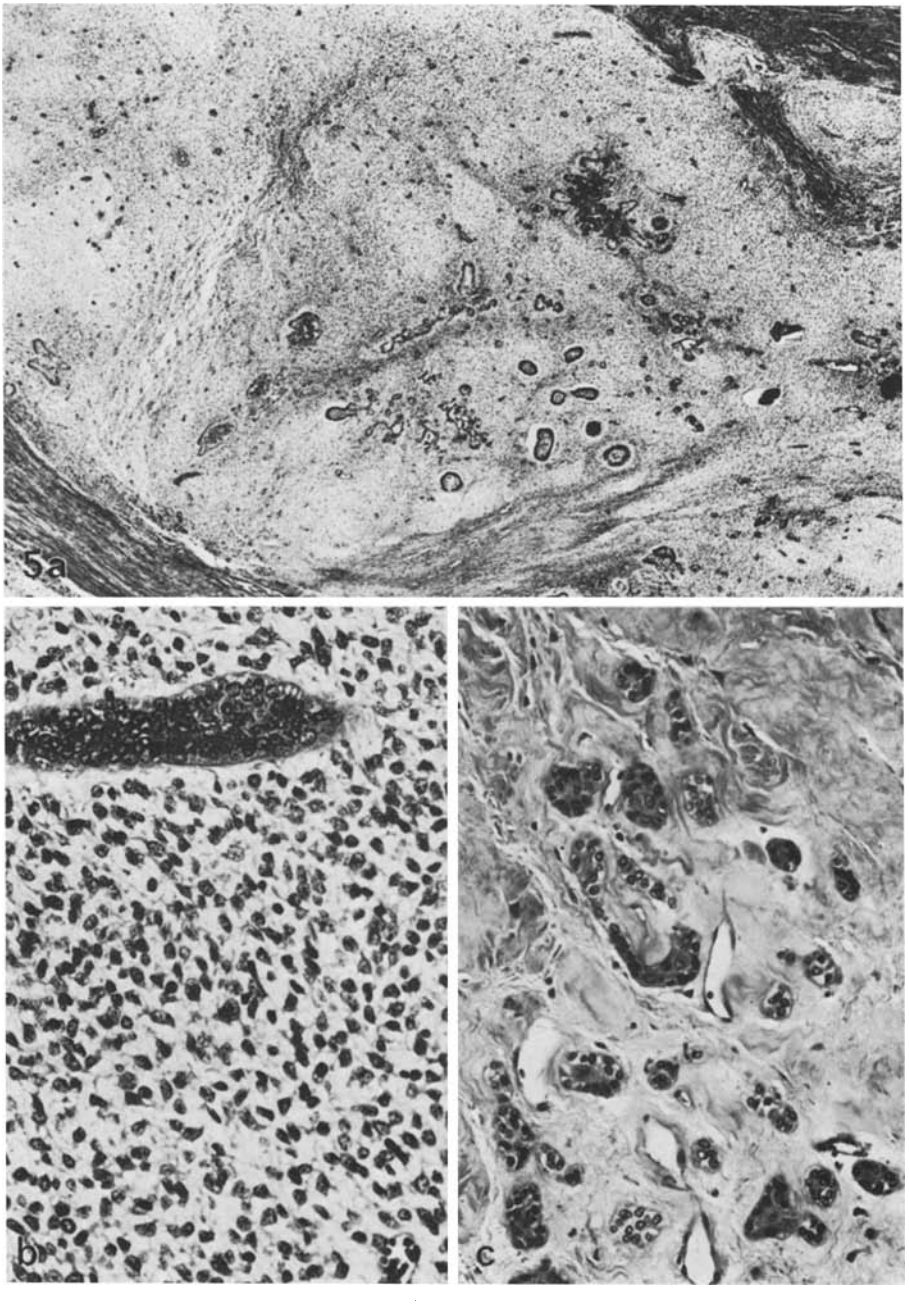


**Fig. 5a–c.** Photomicrographs of autopsy material invading to the base of the skull. (**a**) scattered numerous epithelial islands with various sizes throughout sarcomatous area. (**b**) sarcomatous area showing similar findings to that of previously noted in Fig. 3, (**c**) hyalinosis of mesenchymal component in part, Haematoxylin and eosin, (**a**) $\times 20$, (**b**) and (**c**) $\times 200$

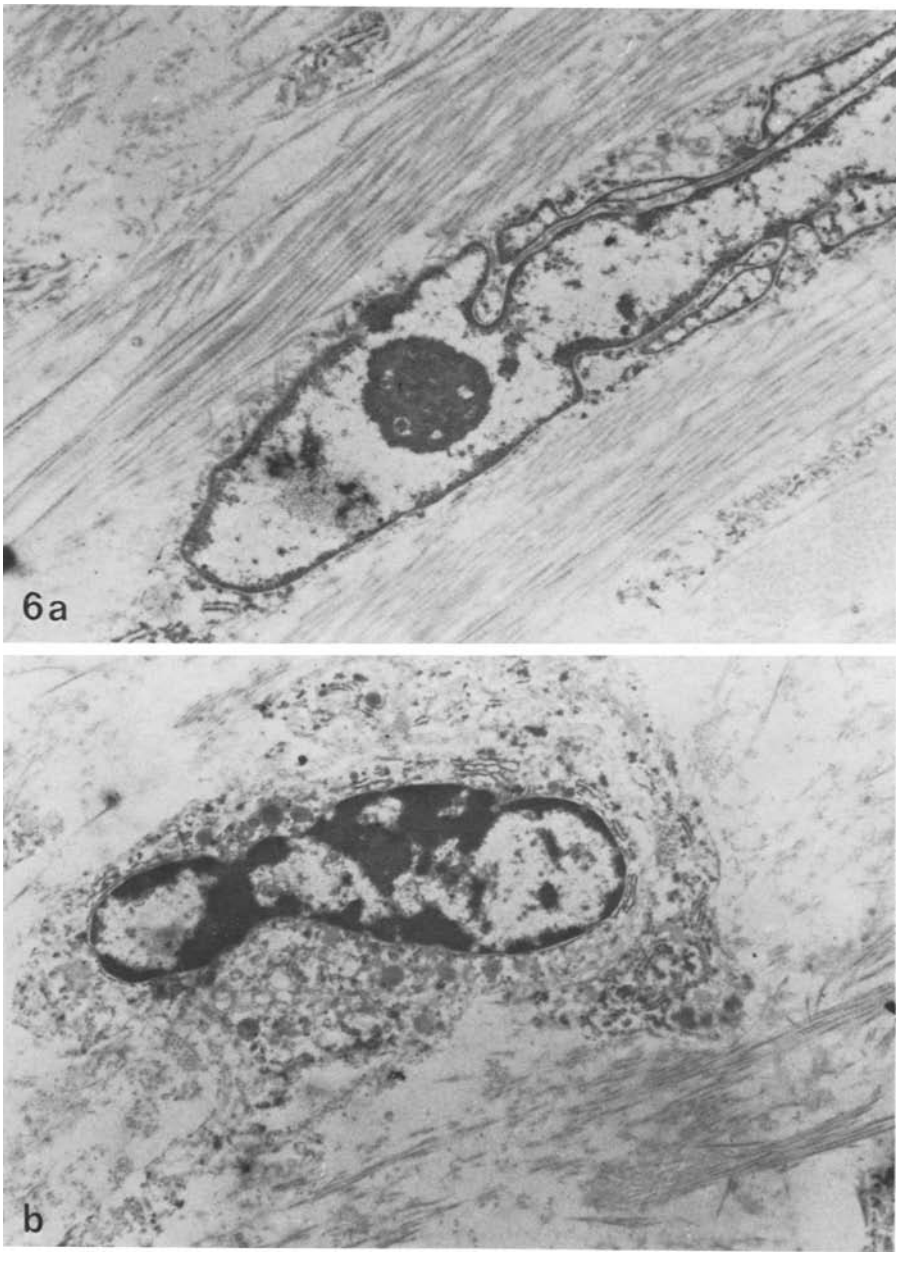


**Fig. 6a, b.** Ultrastructure of fibrocytic cell in dense collagenous stroma (**a**), and fibroblastic cell in loose collagenous one (**b**). (**a**) ×12,000 and (**b**) ×7,000

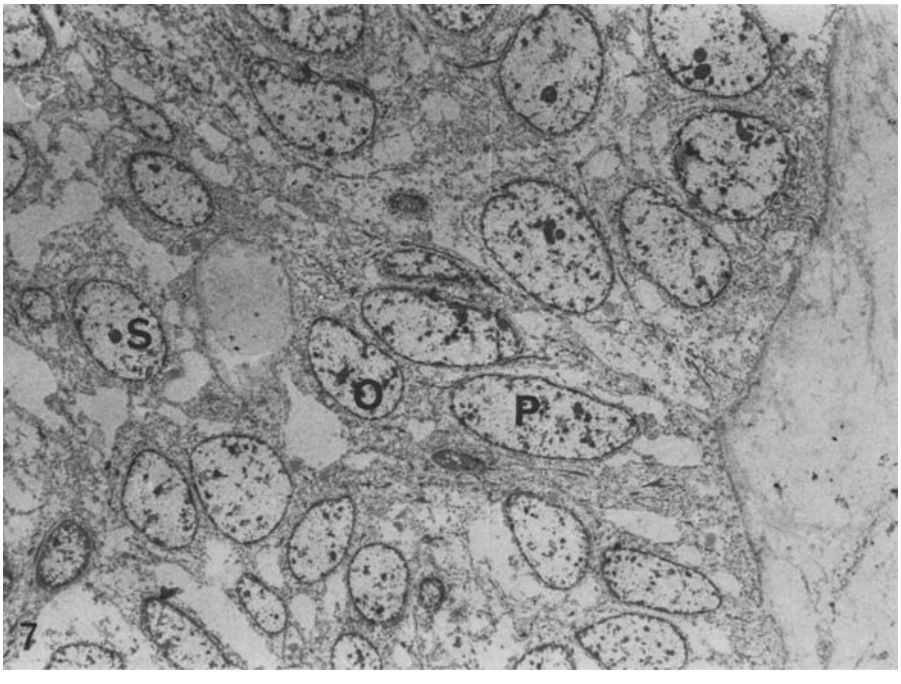


**Fig. 7.** Ultrastructure of epithelial component showing enamel organ-like structure: peripheral columnar cells (C), oval cells in one row underneath the peripheral cells (*O*), and stellate-shaped cells (*S*). ×2,500

oval or polyhedral resembling the stratum intermedium, and innermost cells were stellate like stellate reticulum cells (Fig. 7).

## Discussion

Ameloblastic fibrosarcoma is defined as "a neoplasm with a similar structure to the ameloblastic fibroma, but in which the stromal mesenchymal component shows the features of a sarcoma" (Pindborg and Kramer 1971). While cases of ameloblastic fibrosarcoma have been observed as arising *de novo* (Cataldo et al. 1963; Peychl and Sazama 1971; Hatzifotiadis and Economou 1973; Daramola et al. 1979; others), several authors have demonstrated an ameloblastic fibroma or an ameloblastic fibro-odontoma to be the pre-existing lesion of the ameloblastic fibrosarcoma (Cina et al. 1962; Leider et al. 1972; Goldstein et al. 1976; Howell and Burkes 1977; Reichart and Zobl 1978). Our present case appears to substantiate that the transformation of ameloblastic fibroma to ameloblastic fibrosarcoma. Although the mechanism of malignant transformation of ameloblastic fibroma and other benign mixed odontogenic tumours remains unsettled, multiple surgical procedures seem to be one of the important factors in their malignant

transformation (Kegal 1932; Dahlin and Ivins 1969; Leider et al. 1972; Howell and Burkes 1977).

Of the reported cases of ameloblastic fibrosarcoma, about one-half of the patients had one or more recurrence, though a number were lost to follow-up. Metastasis is not a feature of the lession, and fatal cases usually have been associated with uncontrollable local infiltration following numerous recurrences. Table 1 lists fatal cases of ameloblastic fibrosarcoma. Five are located in the mandible and three are located in the maxilla. There is no sex predilection. The average age of the patients at onset of symptom are 18 years, and the age range is three to 32 years. This average age is approximately 10 years younger than those of all cases of ameloblastic fibrosarcoma (Leider et al. 1972). The duration of disease from onset of symptom to death ranges one year and nine months to 19 years. In Case 5, 7, and 8, the lesion arose in pre-existing benign odontogenic tumours; ameloblastoma in Case 5, ameloblastic fibro-odontoma in Case 7 and ameloblastic fibroma in Case 8.

In reviewing the literature, many instances show that the epithelial component seems to disappear as malignant transformation progresses so that eventually all traces of the odontogenic origin may be lost and the histopathological features become those of a central fibrosarcoma of jaw bone (Dahlin and Ivins 1969; Peychl and Sazama 1971; Leider et al. 1972; Hatzifotiadis and Economou 1973; Reichart and Zobl 1980). On the other hand, there are some cases showing that many ameloblastoid epithelial masses are scattered throughout the sarcomatous mesenchymal area even in the fatal stage (Pindborg 1960; Cina et al. 1962; Mori et al. 1972), and this is true in the present case. Whether the epithelial component is seen in the sarcomatous mesenchymal area or not, ameloblastic fibrosarcoma seems to show a different clinical behavior to the conventional fibrosarcoma. In the analysis of conventional fibrosarcoma in the head and neck, metastases were detected in 25 per cent (Swain et al. 1974), and five year-survival rate was about 30 per cent (Huvos and Higinbotham 1975). This contrasts with the cases of ameloblastic fibrosarcoma, because metastases usually do not occur in spite of anaplastic histological features of the mesenchymal component of ameloblastic fibrosarcoma. Related to this is the suggestion that ameloblastic fibrosarcoma is a low grade malignancy of fibrosarcoma (Leider et al. 1972; Reichart and Zobl 1978) or a semimalignant lesion (Prein et al. 1979). We speculate that the epithelial component of the tumour exerts an organizational effect over the mesenchymal component, in both benign mixed odontogenic tumours and malignant ones.

It has been stated that the presence of induced dentin and enamel does not alter the basic nature of odontogenic sarcoma and that subclassification into those lesions containing dental hard tissues is unnecessary (Cina et al. 1962; Leider et al. 1972). However, other workers have agreed on a subclassification of ondontogenic sarcoma, since a distinction should be drawn in order to facilitate correct histopathological diagnosis by pathologists. If the inductive process leads to the formation of dentin-like substance or both dentin- and enamel-like substances, then the former should be called

an ameloblastic dentinosarcoma and the latter is called an ameloblastic odontosarcoma (Pindborg 1960; Gorlin and Goldman 1970; Altini and Smith 1976; Shear and Altini 1982). In the present case, dysplastic dentin which was closely associated with both epithelial and mesenchymal components was found in some parts. The present case was diagnosed finally as ameloblastic fibrosarcoma according to WHO's classification (Pindborg and Kramer 1971), however, this case might be called ameloblastic dentinosarcoma as a more appropriate designation.

The ultrastructural study of ameloblastic fibrosarcoma has been reported by Eda et al. (1976) and Nasu et al. (1984). They reported that the mesenchymal component of ameloblastic fibrosarcoma was made up predominantly of fibroblastic cells and undifferentiated cells, and the features of epithelial component were similar to those of the enamel organ. In the present study, the mesenchyal component was consisted of fibroblastic cells, fibrocytic cells and undifferentiated mesenchymal cells, though their exact cytoplasmic structures were not demonstrated due to autolytic changes. The epithelial component showed a similarity to that of enamel organ, since the epithelial component was composed of columnar cells, cells resembling stratum intermedium and stellate-shaped cells.

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