

## CASE REPORT

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## Pigmented ameloblastic fibrodentinoma: a novel melanin-pigmented intraosseous odontogenic lesion

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**Abstract** This paper reports about an ameloblastic fibrodentinoma with macroscopically visible pigmentation, resulting in the clinical appearance of a melanotic lesion in a 21-year-old Japanese male. In addition to the characteristic histopathologic features of ameloblastic fibrodentinoma, various-formed and -sized cells, which were considered to be melanophages containing numerous aggregates of melanin pigment in their cytoplasm, were densely distributed throughout the mesenchymal component. In addition, melanin pigment was deposited in dentin. Some of the pigmented cells showed dendritic form and were regarded as melanocytes. Furthermore, pigmented cells were frequently distributed in the epithelial component, and melanin pigment was seen in some epithelial cells. Perusal of the English language literature revealed 30 cases of pigmented odontogenic tumors: 18 were calcifying odontogenic cysts, three were ameloblastic fibro-odontomas, three were adenomatoid odontogenic tumors, two were odontomas, one was an ameloblastic fibroma and one was an odontogenic fibroma. However, all of these reported lesions did not show macroscopically visible pigmentation. The possible histogenesis of melanocytes in the odontogenic lesions is discussed, although no firm conclusion could be drawn.

**Keywords** Melanocyte · Melanin pigment · Ameloblastic fibrodentinoma · Odontogenic tumor · Intra-osseous lesion

### Introduction

Melanocytes and melanin pigment are widely distributed in the skin, the nervous system, certain types of mucosa, and others, but is not normally present within the bone in mammals. Pathologically, there are very few descriptions of intra-osseous melanin-pigmented lesions other than metastases of malignant melanoma, and all reported examples have occurred within the jaw bone.

Melanin-pigmented jaw lesions include melanotic neuroectodermal tumor of infancy [16], calcifying odontogenic cyst [16], adenomatoid odontogenic tumor [2, 42], odontogenic keratocyst [4, 5], lateral periodontal cyst [6], and a few other types of odontogenic lesions. Racial pigmentation is thought to be one important factor in the occurrence of such melanin-pigmented jaw lesions, with the exception of melanotic neuroectodermal tumor of infancy.

The author has studied the occurrence and distribution of melanocytes and melanin pigment in intra-osseous odontogenic lesions from a Japanese patient and discussed their possible histogenesis and pathological significance [31, 32, 33, 34, 35, 36, 37, 38, 41]. The present paper reports a case of ameloblastic fibrodentinoma with macroscopically visible pigmentation resulting in the clinical appearance of a melanotic lesion. We believe that this represents a previously undescribed component within the spectrum of intra-osseous odontogenic tumors.

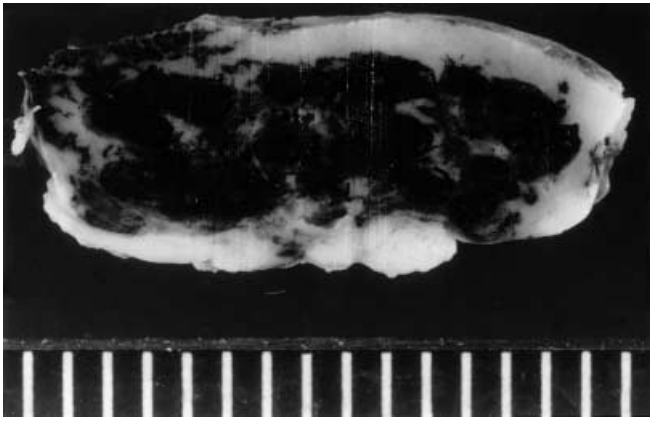
### Case report

A 21-year-old Japanese male was referred to an oral surgeon by his dentist for diagnosis and treatment of a radiolucent lesion in the mandible that was discovered during routine dental examination. Radiographic examination revealed a rather well-circumscribed, unilocular radiolucent lesion in the mandibular right retro-molar area. The lower right third molar was embedded near the lesion. A clinical diagnosis of suspected ameloblastoma was made. The patient was admitted soon afterward and underwent surgical resection of the lesion. During surgery, it was observed that the lesion was brownish-black in color and was surrounded by

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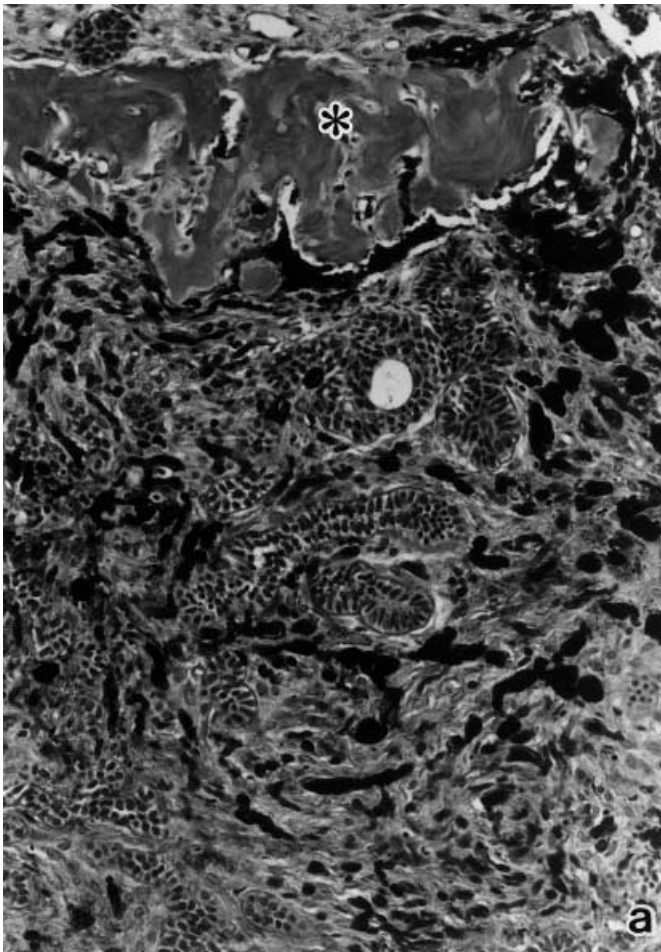
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**Fig. 1** Cut section of surgically resected specimen shows a black-colored, solid tumor with fine grittiness, surrounded by a white-colored layer;  $\times 5.1$

**Fig. 2** Microscopical findings of the tumor. **a** The tumor is composed of irregularly admixed three tissue components: strands and islands of epithelium, dysplastic dentin (*asterisk*), and fibrous tissue containing numerous numbers of pigmented cells;  $\times 100$ . **b** Well-developed enamel organ-like structure consists of a loose central area that resembles stellate reticulum with microcystic space surrounded by a layer of columnar cells that are ameloblastic in appearance (*asterisk*, dysplastic dentin);  $\times 100$



a fibrous connective tissue capsule. The impacted third molar was separated from the lesion by fibrous connective tissue. The post-operative course was uneventful.

#### Pathologic findings

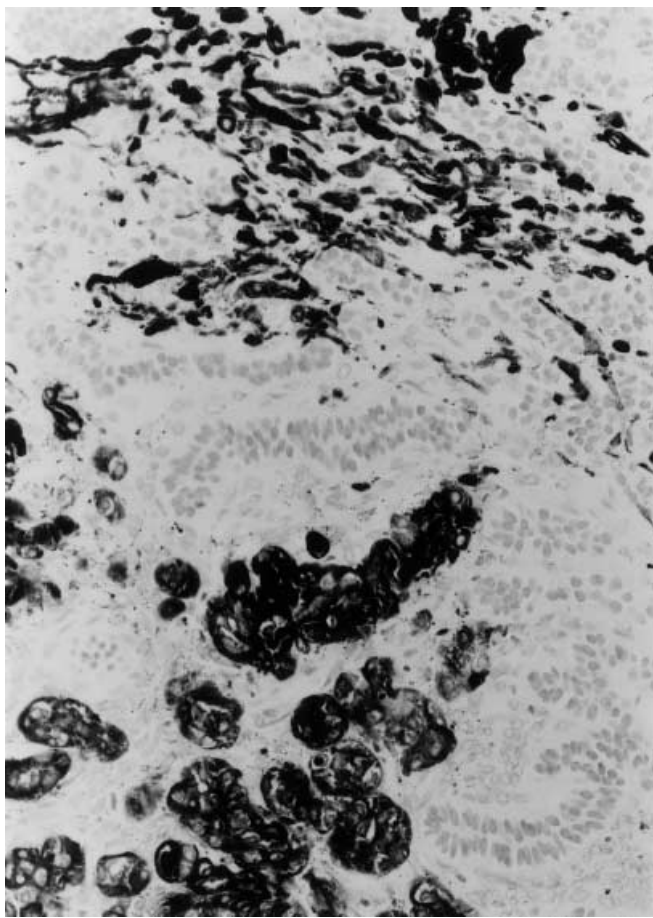
The surgical specimen was a 15 $\times$ 18 $\times$ 21-mm soft-tissue mass. Cut sections revealed a black-colored, solid tumor, which was friable, had a fine grittiness and was surrounded by a white-colored layer (Fig. 1).

Histologically, the tumor was composed of three irregularly admixed tissue components: (1) strands and islands of epithelium, (2) dysplastic dentin and (3) fibrous tissue (Fig. 2). The epithelial component resembled the enamel organ at various stages of maturation. Well-developed enamel organ-like structures consisted of a loose central area that resembled stellate reticulum with microcystic space surrounded by a layer of columnar cells that were ameloblastic in appearance (Fig. 2b). The dysplastic dentin with or without mineralization was closely associated with both epithelial and fibrous components and was apparently different from hyalinized collagenous tissue (Fig. 2a, b). There was no evidence of enamel matrix or enamel formation. The fibrous component was composed basically of tissue that resembled the primitive dental papilla in the tooth germ. An unusual histological feature was the presence of numerous spindle- and dendritic-shaped cells. In addition, swollen round-shaped cells with abundant intracytoplasmic brownish-black pigment were intermingled with fibroblastic cells evenly distributed throughout the mesenchymal area (Fig. 2a, b). These pigmented cells were frequently seen in and around the dysplastic dentin and epithelial component.

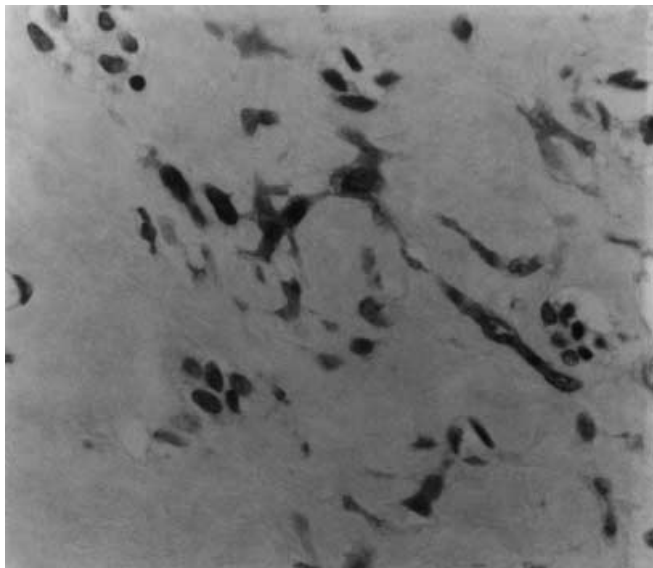
Histochemistry indicated that the brownish-black pigment in the cells intermingled with fibroblastic cells in the mesenchymal







**Fig. 3** Pigmented cells are heavily stained with Masson-Fontana's staining for melanin, and there are two types of melanin pigment-laden cells: spindle- and dendritic-shaped cells (*upper half*) and swollen round-shaped cells (*lower half*);  $\times 250$



**Fig. 4** S-100 protein immunostain using bleached section shows distinctly positive in nuclei and cytoplasm of dendritic- and spindle-shaped cells;  $\times 400$

area was melanin. The cells had strong positivity with Masson-Fontana's staining for melanin (Fig. 3) and bleaching with hydrogen peroxide and potassium permanganate solution. Periodic-acid-Schiff and stains for iron were negative. There were two types of melanin pigment-laden cells: spindle- and dendritic-shaped cells and swollen round-shaped cells. Immunohistochemistry using bleached sections showed that the former cells were reactive for S-100 protein (1:100 dilution, Dako, Japan) (Fig. 4), but not reactive for CD-68 (clone Ki-M1P, 1:100 dilution, Seikagaku Co., Japan), alpha 1-antichymotripsin (1:500 dilution, Dako, USA) and lysozyme (1:500 dilution, Dako, USA). The latter cells were reactive for alpha 1-antichymotripsin, lysozyme and CD-68, but not reactive for S-100 protein. Both types of cells were not reactive for HMB-45 (1:50 dilution, Dako, Denmark) and vimentin (1:50 dilution, Dako, Japan). Such results suggested that spindle- and dendritic-shaped cells were melanocytes and swollen round-shaped cells were melanophages.

## Discussion

It is well known that melanocytes and/or melanin pigment are observed rarely in calcifying odontogenic cysts and odontogenic keratocysts [16, 29], but it seems that the presence of melanocytes and/or melanin pigment in other intra-osseous odontogenic tumors and cysts are exceedingly rare. The review of the English language literature yields 30 well-documented cases of pigmented odontogenic tumors (Table 1): 18 were calcifying odontogenic cysts, three were adenomatoid odontogenic tumors, three were ameloblastic fibro-odontomas, two were odontomas, one was an odonto-ameloblastoma, one was an ameloblastic fibroma, one was an odontogenic fibroma, and one was an unclassified tumor (calcifying epithelial odontogenic tumor by author's suspicion). Only 12 cases of pigmented odontogenic cysts have been documented: eight were odontogenic keratocysts [4, 5, 19, 31], and there was one gingival cyst [12], one botryoid odontogenic cyst [3], one lateral periodontal cyst [6], and one dentigerous cyst [41]. Melanocytes and/or melanin pigment in these reported odontogenic lesions were microscopically observed and macroscopically showed no pigmentation, except for two cases [25, 41] with macroscopically visible mild pigmentation. To our knowledge, the present paper is the first report on the existence of melanocytes and melanin pigment in the ameloblastic fibrodentinoma. In addition, it is the first case of odontogenic tumor with visible heavy pigmentation suggesting melanocytic lesion by means of macroscopic examination of surgically-resected material. Ameloblastic fibrodentinoma is defined as "a neoplasm similar to ameloblastic fibroma, but also showing inductive changes that lead to the formation of dentin" [16]. It is thought that ameloblastic fibrodentinoma is an exceedingly rare histologic variant of ameloblastic fibroma in which dentin or dentinoid tissue has formed; however, there is a possibility that various amounts of dentinal tissue with or without calcification, in addition to characteristic histologic features of ameloblastic fibroma, might be revealed by means of precise histologic examination of extensive sampling from surgically resected specimens [40].

Numerous numbers of spindle- and dendritic-shaped cells and swollen round-shaped cells with abundant intra-

**Table 1** Reported cases of odontogenic tumors with melanin-pigment and/or melanocytes in the English language literature. *ND* not described; *CEOT* calcifying epithelial odontogenic tumor

Diagnosis	No. of cases	Race of patients [references]
Calcifying odontogenic cyst	18	8 Japanese [22, 26, 32, 38] 3 Blacks [8, 18, 24] 1 White [1] 1 Indian [7] 1 West Indian [30] 1 Hispanic [28] 3 ND [11, 14, 27]
Adenomatoid odontogenic tumor	3	1 Japanese [35] 1 Black [42] 1 Mixed (White & Indian) [2]
Ameloblastic fibro-odontoma	3	3 Japanese [9, 15, 34]
Odontoma	2	2 Japanese [33, 36]
Odonto-ameloblastoma	1	1 Japanese [37]
Ameloblastic fibroma	1	1 Black [10]
Odontogenic fibroma	1	1 ND [13]
Ameloblastic Fibrodentinoma	1	1 Japanese (present case)
Unclassified tumor (CEOT?)	1	1 Black [25]

cytoplasmic brownish-black pigment were intermingled with fibroblastic cells evenly distributed throughout the mesenchymal area. These pigmented cells were frequently seen in and around the dysplastic dentin and the epithelial component. Histochemistry, using Fontana-Masson's method, indicated that the intracytoplasmic pigment was melanin. Although it is thought that immunohistochemical reactions are damaged through bleaching of the paraffin sections [20], spindle- and dendritic-shaped cells were reactive for S-100 protein and swollen round-shaped cells were reactive for alpha 1-antichymotrypsin, lysozyme and CD-68. Such results suggested that the former cells were melanocytes and the latter cells were melanophages. HMB-45 is a well-known, diagnostically useful antibody that is a specific marker of immature and neoplastic melanocytes in paraffin sections. However, it seldom reacts with melanocytes in normal tissue and nevus cells [21]. The lack of reactivity with HMB-45 with the spindle and dendritic cells in the present case does not disprove a melanocytic origin for these cells.

The origin of the melanocytes in odontogenic lesions is speculative. Melanocytes form part of the oral epithelium. The occasional presence of melanocytes in odontogenic lesions can be expected since the dental lamina originates from the primitive oral lining. In fact, Lawson and his co-workers [17] studied the facial skeletons obtained from human fetuses, and they found melanocytes in all six Negro fetuses and in three of 11 Caucasian ones within the dental lamina and outer enamel epithelium.

Another possible origin of melanocytes in odontogenic lesions is the migration of melanocytes through the mesenchyme rather than through the ectoderm. The author's previous study [39] showed that melanocytes exist in mesenchymal tissue around the dental anlage in dog fetuses and that melanocytes appear neither in the oral epithelium nor in the epithelial element of the dental anlage at that fetal stage.

The hypothesis that a racial pigmentation may be present in the development of pigmented odontogenic lesions has been proposed in the past, although the limited

number of cases does not give any statistical value to the data. In fact, most patients with pigmented odontogenic lesions are Asians and Blacks [6, 31, 32, 33, 34, 35, 36, 37, 38]. Some investigators have thought that: (1) it is possible that inactive melanocytes are present in odontogenic lesions, similar to inactive melanocytes normally present in clinically non-pigmented oral mucosa, (2) melanocytes in the odontogenic lesions become activated and melanin pigment is produced under certain conditions, and (3) activation of the melanocytes in the odontogenic lesions may be related to factors associated with racial pigmentation [6]. However, only a few pigmented odontogenic lesions have been reported in Africans, and no such cases have been found in a review of jaw lesions in Nigerians [23].

It is interesting that all pigmented odontogenic lesions, except for cysts, are composed of odontogenic epithelium and mesenchyme with induction of dental hard tissues or calcification. Although no conclusion can be drawn as to the specific origin and pathologic significance of melanocytes in the odontogenic lesions, it may be of interest for future investigation.

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