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Case Report
Clinical Pathology

Clinicopathological investigation of odontogenic fibroma in tuberous sclerosis complex

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Abstract. Tuberous sclerosis complex (TSC) is an autosomal dominant inherited disease characterized by systemic hamartoma and diverse systemic features. TSC1 and TSC2 are the causative genes, and mental retardation, epileptic seizures, and facial angiofibroma develop in many patients with the disease. The case of a patient with TSC who developed a central odontogenic fibroma of the mandible is reported here. The patient was a 21-year-old woman who was referred with a swelling of the labial gingiva in the region of the right lower lateral incisor and canine. Dental radiography revealed a multilocular radiolucent region with a clear boundary. The right lower lateral incisor and canine were continuous with the lesion and thus were excised en bloc. The lesion was encapsulated and easily dissected. The diagnosis on immunohistological staining was odontogenic fibroma without an epithelial component. TSC1/2 gene mutation causes abnormal activation of mammalian target of rapamycin (mTOR) downstream of the PI3K–AKT pathway. The odontogenic fibroma in this patient was positive for mTOR, suggesting that the development of the odontogenic fibroma was the result of abnormal activation of mTOR, as in angiofibroma. The clinical course of this patient is presented and the developmental mechanism of central odontogenic fibroma is discussed.

Key words: mammalian target of rapamycin; odontogenic fibroma; tuberous sclerosis complex.

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Tuberous sclerosis complex (TSC) is an autosomal dominant inherited disease characterized by systemic hamartoma and diverse systemic symptoms[1]. TSC1 and TSC2 have been identified as the causative genes, and mental retardation, epileptic seizures, and facial angiofibroma develop in many patients with the condition. The development of symptoms in the oral cavity, including gingival fibroma and dental enamel pits, has also been reported in these patients[2]. The case of a patient with TSC who developed a central odontogenic fibroma of the mandible and dental enamel pits is described here.

Case report

A 21-year-old woman visited her dental clinic with a chief complaint of mobility of the right lower lateral incisor tooth. Swelling of the labial gingiva in the right lower lateral incisor and canine regions was noted, and a multilocular radiolucent region with a clear boundary was observed on dental radiography. She was referred to the Department of Oral and Maxillofacial Surgery, Gunma University Hospital, for more detailed examination and treatment. She had an established diagnosis of TSC

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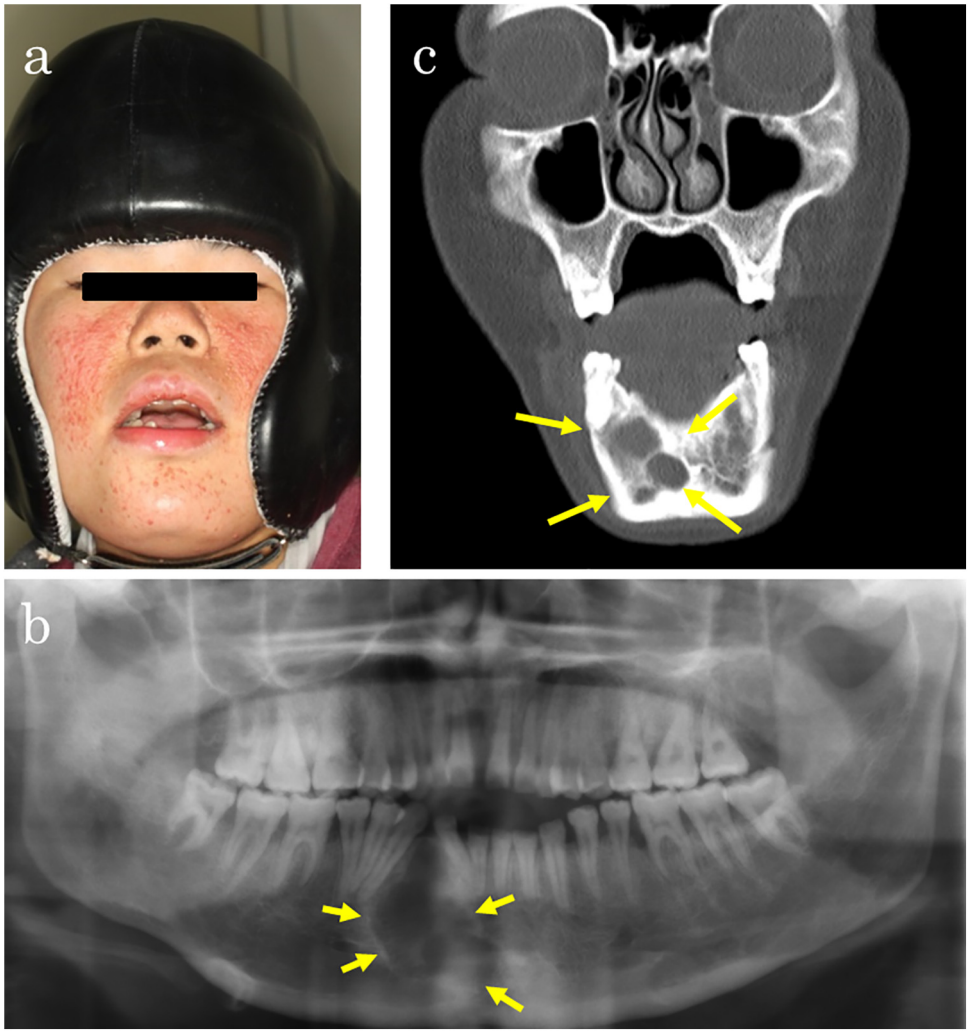

Fig. 1. (a) Photograph showing the patient's multiple facial angiofibromas. (b) Panoramic radiograph showing a multiloculated cyst-like lesion. (c) Computed tomography image showing a mass measuring 27 mm × 23 mm × 19 mm in the mandibular gingiva.

with concomitant mental retardation and epilepsy. Her nutritional status was satisfactory.

Findings on examination included multiple facial angiofibromas associated with TSC (Fig. 1). In the oral cavity, there was a bone-like hard enlargement of the labial gingiva with a normal surface mucosa in the region corresponding to the right lower lateral incisor and canine tooth (Fig. 1). On panoramic radiography, the roots of the right lower lateral incisor and canine were separated, and a multilocular cyst-like radiolucent region with a clear boundary was present in the space between these teeth (Fig. 1). Computed tomography revealed a radiolucent region with a clear boundary and partial thinning of the labial cortical bone (Fig. 1).

The suspected clinical diagnosis was mandibular tumour, so a biopsy was performed. The content of the lesion was whitish and solid. The histopathological diagnosis was odontogenic fibroma. The tumour was excised by surgical extirpation and curettage under general anaesthesia. The right lower lateral incisor and canine were continuous with the lesion and thus were excised en bloc (Fig. 2). The lesion was encapsulated and easily dissected. After excision, one layer of the intrabony defect was removed, after which the wound was closed.

Histopathological analysis revealed proliferating spindle-shaped fibroblast-like cells accompanied by collagen fibres. Immunohistological staining was negative for CAM5.2, S-100, and CD34, and weakly positive for β-catenin; the MIB-1 index was less than 1%. There were no findings suggestive of malignancy (Fig. 3). This case was also positive for mammalian target of rapamycin (mTOR) (Fig. 3). The odontogenic epithelium was absent, and the lesion was diagnosed as odontogenic fibroma without an epithelial component. There has been no recurrence in the 36 months since surgery (Fig. 4).

Discussion

The diagnostic criteria for TSC are both genetic and clinical. Although the causative gene (TSC1 or TSC2) has been identified, the detection rate of TSC gene mutation on genetic diagnosis is only 75–90%, and cases without a gene mutation have been reported[1]. Therefore, it is not possible to make a definitive diagnosis based on the presence or absence of the TSC gene mutation and genotype alone, and TSC is diagnosed based on a combination of clinical features. The 2012 International Tuberous Sclerosis Complex Consensus Conference proposed updated clinical diagnostic criteria for TSC. Among these criteria, hypopigmented macules and facial angiofibroma are considered to be major criteria and enamel pits

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