Juvenile hyaline fibromatosis complicated with oral squamous cell carcinoma: A case report

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A 45-year-old woman was referred because of swelling of the palate, gingival hypertrophy, and multiple cutaneous tumors. She had many cutaneous tumors, which covered most of her body, and she also displayed contractures of the major joints. Maxillary and mandibular gingival hypertrophy, malposition of the teeth, and swelling of the hard palate were the oral findings. The histopathologic features of the cutaneous and gingival tumors were consistent with hyaline fibromatosis, and the swelling of the palate proved to be a squamous cell carcinoma. The carcinoma was treated with tegafur/uracil and seemed to respond to this therapy. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001;91:200-4)

Juvenile hyaline fibromatosis (JHF) is an extremely rare autosomal recessive disease that is characterized by hypertrophy of the gingiva, cutaneous nodules, and flexural contractures of the large joints. The term juvenile hyaline fibromatosis was introduced by Kitano et al in 1972. The disease was previously referred to as mesenchymal dysplasia, molluscum fibrosum, systematic hyalinosis, and fibromatosis hyalinica multiplex juvenilis. Although some patients with this disease have survived into adulthood, previous reports almost exclusively describe affected children.

We report a case of adult systemic hyaline fibromatosis with concurrent squamous cell carcinoma of the hard palate.

CASE REPORT

A 45-year-old woman was referred to our clinic by her dentist because of swelling of the hard palate. When she was 1 year old, a subcutaneous tumor appeared in the occipital region, and it was excised. Although a new tumor of the head appeared several months after that operation, her parents were not willing to allow this lesion to be treated. For approximately 20 years, numerous new tumors had continually appeared on many regions of her body, and by 20 years of age she had become bedridden because of joint contractures. None of the tumors had been treated, and she had not previously been evaluated when she came to our hospital.

The patient was the product of a consanguineous marriage, her parents being cousins. She had one younger sister and one younger brother; the siblings were without similar clinical findings.

On her admission to our hospital, subcutaneous nodules ranging in size from 0.5 cm to 10 cm were seen in the occipital region, neck, back, and large joints (Figs 1 and 2). Many tumors occurred at the joints, but they did not seem to come directly from the underlying bone. The tumors were hard, and some were ulcerated. On oral examination, many tumors resembling the skin lesions were seen on the maxillary and mandibular...
gingiva (Fig 3). The teeth had been displaced by the tumors. A 3.5-cm swelling was observed on the hard palate. The lesion was tender on palpation, and it had an irregular surface with ill-defined margins (Fig 4). Routine blood tests revealed no abnormalities, and the patient's mental state was normal.

Radiographic findings revealed calcification in the subcutaneous tumors (Figs 5 and 6), and cortical erosions of the humerus and femur were evident. Computed tomography (CT) revealed calcifications within the subcutaneous tumors, and a soft tissue mass extended from the hard palate into the nasal cavity and maxillary sinus (Fig 7). Enhanced CT revealed uptake in the submandibular and cervical lymph nodes bilaterally.

The patient was given a local anesthetic, and an incisional biopsy was performed. Routine microscopic examination disclosed that the subcutaneous tumors and gingival tumors consisted of hyalinized connective tissue (Fig 8). The histopathologic features of the tumor of the hard palate were diagnostic for well-differentiated squamous cell carcinoma (Fig 9).

These findings confirmed the diagnosis of JHF complicated by squamous cell carcinoma of the hard palate. The patient was hospitalized, receiving 300 mg a day of tegafur/uracil (UFT) daily, and the palatal tumor appeared to be shrinking. Unfortunately, on September 30, 1999, she died in our hospital because of aspiration pneumonia.

**DISCUSSION**

JHF is a rare autosomal recessive disorder largely affecting connective tissue and characterized by the production and deposition of an unidentified "hyaline" material in the skin and other organs. Described by Murray in 1873, the disease is still not well understood, even though approximately 30 cases have now been reported. Typically, JHF consists of multiple cutaneous papules, nodules, or tumor masses that vary in size from 1 mm to approximately 5 cm, grow slowly and painlessly, and are found mainly in the regions of the head, back, and extremities, with a predilection for the nose, ears, scalp, back, and knees. Associated mental retardation is not unknown, but most patients are intellectually quite normal, as was the case with our patient.

With respect to oral findings, generalized gingival enlargement begins during the first year or so of life. The gingival hypertrophy often extends onto the
occlusal surfaces of the teeth. Gingival biopsies have yielded findings similar to those of the skin.12,14

Roentgenographic studies almost always show abnormalities,1 including all of the following: osteoporosis; osteolytic lesions, particularly of the skull, long bones, and phalanges; and cortical erosions, often symmetric, at the proximal ends of femora, tibiae, and humeri. Calcification of the soft tissue around joint capsules has been reported.1 Our patient had evidence of cortical erosion of the femora and humeri, and calcification of the cutaneous tumors was also seen.

Histopathologically, the tumors produce a homogeneous, amorphous, eosinophilic, periodic acid-Schiff-positive ground substance that is sometimes chondroid in appearance. Spindle-shaped fibroblasts are present in this matrix in a streaklike pattern. The proportion of cells to ground substance varies from one tumor to another.12,15 Some investigators believe that hyaline fibromatosis represents an error in glycosaminoglycans metabolism.7,8,16 Ishikawa and Mori5 found an increased amount of chondroitin-6-sulfate in these tumors.

Although many reports are of childhood cases, 6 of 22 patients reported in the literature survived into adolescence.7 There were no reports of cases complicated by carcinoma. Affected siblings born to healthy parents and a high rate of parental consanguinity indicate that inheritance is autosomal recessive.1 In the case of our patient, the parents had a consanguineous relationship.

In general, the prognosis for such patients is poor,17,18 and the only treatment is palliative—pain relief and control of infection and diarrhea. However, the quality of life is obviously important, and the surgical removal of some tumors to improve function is justified.

Treatment with UFT was effective for shrinking the carcinoma in our patient. UFT is an oral antineoplastic