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PURETIĆ SYNDROME—GINGIVAL FIBROMATOSIS WITH HYALINE FIBROMAS—

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Summary A 21-month-old Japanese boy with Puretić syndrome (gingival fibromatosis with hyaline fibromas) was reported. On the basis of the present case and 17 cases in the literature, it was concluded that the disorder was a very rare connective tissue disease with an autosomal recessive mode of inheritance.

INTRODUCTION

Puretić syndrome (gingival fibromatosis with hyaline fibromas) is a very rare congenital disorder characterized by gingival hypertrophy, small whitish papules on the skin, subcutaneous nodules and tumors on the head, chest, and abdominal wall, and multiple flexural contracture of joints (Goodman and Gorlin, 1977).

Only 17 cases from 11 families with similar clinical features have been reported in the literature, under various diagnostic names (molluscum fibrosum. Murray, 1873; unique form of mesenchymal dysplasia. Puretić *et al.*, 1962; systemic hyalinosis. Ishikawa *et al.*, 1964, 1973; fibromatosis hyalinica multiplex juvenilis. Drescher *et al.*, 1967; atypical hyalinosis cutis et mucosae. Horio *et al.*, 1968; juvenile fibromatosis. Enjoji *et al.*, 1968; juvenile hyalin fibromatosis. Kitano *et al.*, 1972; fibromatosis hialinica múltiple juvenil. Gutiérrez *et al.*, 1973; fibromatosis hialinica juvenil. Costa *et al.*, 1975; juvenile hyalin fibromatosis. Kitano, 1976; fibromatose hyaline juvénile. Gianotti *et al.*, 1977).

The present paper is concerned with an additional case and a review of the 17 cases in the literature.

CASE REPORT

A 21-month-old Japanese boy was admitted for evaluation of gingival hypertrophy, subcutaneous nodules scattered on the chest and abdominal wall, a tumor in the occipital region and multiple flexural contracture of the joints.

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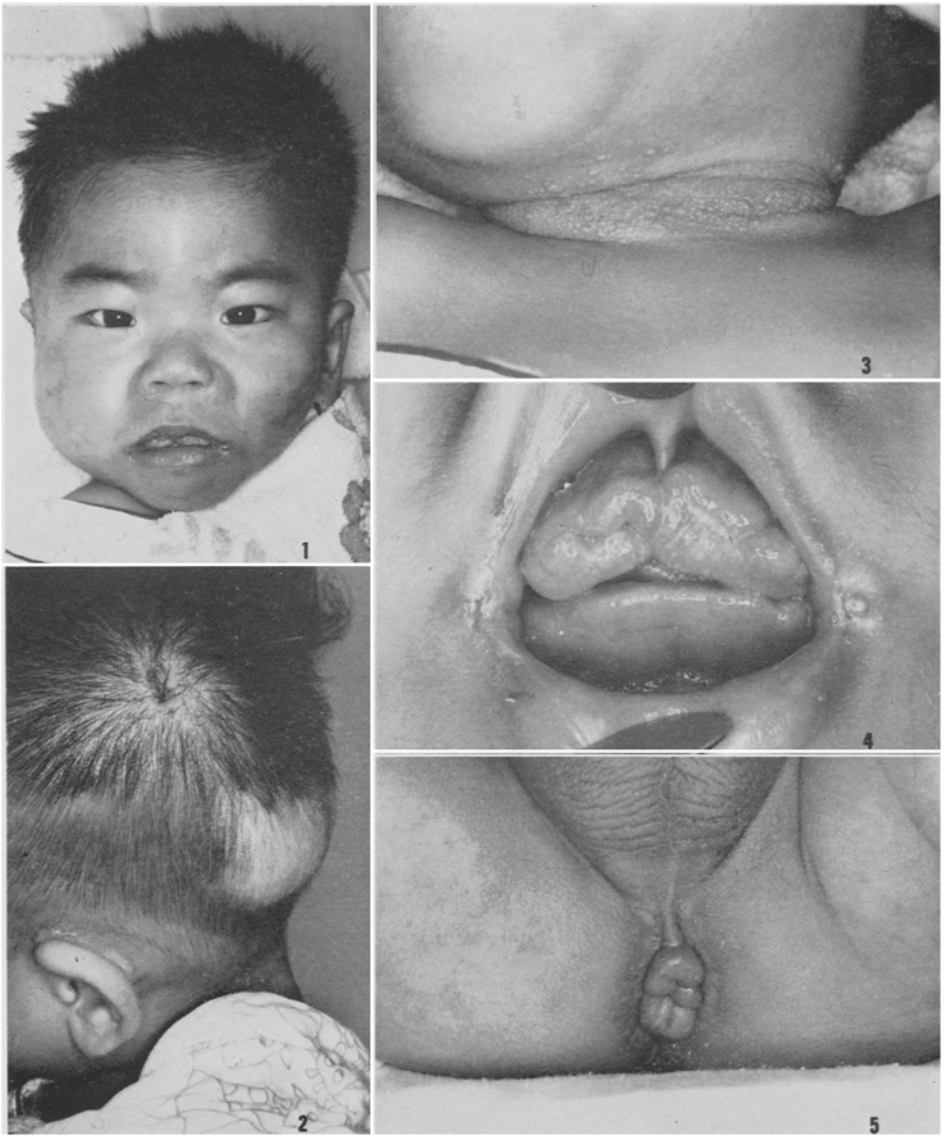

Fig. 1. Coarse facial features due to multiple skin lesions. Note nodules around alae nasi and on chin, and enlarged gingiva.

Fig. 2. Elastic soft, egg-sized tumor in the occipital region.

Fig. 3. Very small solid papules present a characteristic condition of this disorder; papules tend to appear over the area of friction such as the anterior aspect of the neck.

Fig. 4. Enlarged gingiva.

Fig. 5. Tumor at the anus.

He was the first child of three from the same parents who were first cousins. Neither the same abnormalities nor any disorder worthy of note were found in his siblings and relatives.

He was born at term weighing 2,470 g after a normal delivery. At one month of age, his left upper extremity was noted to be motionless. An X-ray examination revealed a fracture of the left humerus. Because of stiff extremities and paucity of movement, he was suspected of cerebral palsy at 3 months of age.

Sometime between 6 months to 12 months of age, he developed gingival hypertrophy, tumor in the occipital region, subcutaneous nodules on both sides of alae nasi and whitish papules in both pinnae, neck and nape. These lesions developed rapidly. Rolling over, sitting, creeping and standing were impossible due to severe flexural contracture of large joints.

On admission he was a small, ill-appearing child with a coarse, mask-like face (Fig. 1). An egg-sized and elastic soft tumor was found in the occipital region (Fig. 2). Many slightly elevated whitish papules with a flat top were noted in both pinnae, retroauricular region, external auditory meatus, neck and nape. Papules on the neck were fused and showed an eczema-like appearance (Fig. 3). Subcutaneous nodules were noted on various regions; perioral region, the alae nasi, the chest, abdominal wall and the back.

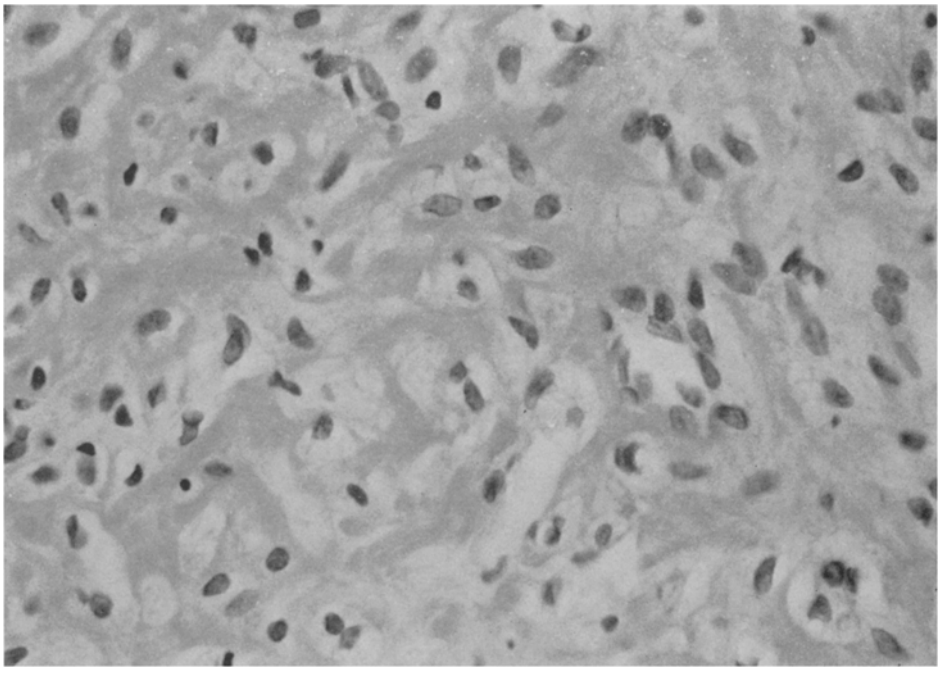

Fig. 6. Histologic picture of one of subcutaneous tumors. Spindle-shaped or oval cells embedded in profuse amorphous stroma. (H. and E. stain. ×540)

He could not open his mouth wider than one fingerbreadth due to severe contracture of the temporo-maxillary joints. Gums showed remarkable hypertrophy and enlargement (Fig. 4). Teeth were intact. The anus itself was a soft tumor (Fig. 5).

Mental development appeared normal. The deep tendon reflexes were normoactive and no pathological reflexes were elicited. He was confined to bed in supine position and could not take meals nor roll over without support due to severe contracture of large joints.

Routine laboratory tests were unremarkable except for hypochromic anemia and hypoproteinemia. Normal findings included: immunoglobulins (IgG, IgA, IgM), urinary acid mucopolysaccharides, urinary and serum amino acids and lysosomal enzyme activities in leucocytes (α-glucosidase, β-galactosidase, α-mannosidase, α-fucosidase, β-glucuronidase, *N*-acetyl-β-glucosaminidase). Roentogenographic examination revealed cortical atrophy of long bones, osteolysis of distal phalanges and delayed bone maturation.

On histological examinations, the tumor consisted of homogeneous, amorphous, eosinophilic substance and spindle-shaped or oval cells which had an oval or elliptic nucleus with fine chromatin, and foamy cytoplasm (Fig. 6). The amorphous ground substance was positive for alcian stains. Metachromasia was not observed with toluidine blue. Electron microscopic examination revealed tumor

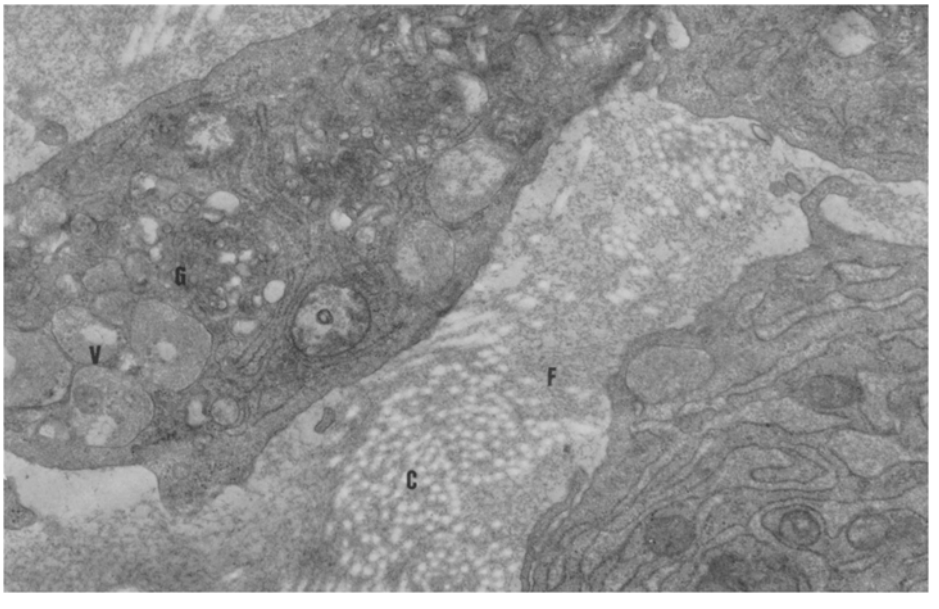

Fig. 7. Part of tumor cell with various sized fibril-filled vesicles (V). Morphologically, fibrils (F) filling the vesicles are very similar to the microfibrils forming stroma. C, collagen; G, Golgi apparatus. ×12,000.

cells embedded in profuse stroma which was composed of densely arranged delicate fibrils. The Golgi apparatus was surrounded by globular vesicles circumscribed by a single membrane and filled with densely, often concentrically arranged, delicate fibrils. The fibril-filled vesicles were of various sizes; small surrounding the Golgi apparatus and gradually enlarging towards its periphery (Fig. 7).

DISCUSSION

Clinical findings in 18 cases with Puretić syndrome including the present case are summarized in Table 1. The ratio of male to female was 9 : 9. Parental consanguinity was described in 8 cases from 5 families including the present case. There was evidence for familial occurrence in 11 cases from 5 families, showing a horizontal appearance. The segregation ratio in 16 cases, except for 2 cases (Kitano, 1976; Gianotti *et al.*, 1977), was 0.1786 ± 0.0726. These findings strongly suggest that this disorder is due to an autosomal recessive gene in agreement with Witkop (1971), Kitano *et al.* (1972) and Ishikawa *et al.* (1973). The present high incidence of reported cases among Japanese is of interest. But it is necessary to accumulate more cases before any ethnical interpretation in incidence of the disorder can be drawn.

Clinical features start early in life, ranging birth to 4 years of age. Symptoms at the onset are no limited to a few predominant ones. They include tumors, subcutaneous nodules, whitish papules on the body, gingival hypertrophy and flexural contracture of joints.

Routine laboratory tests reveal no consistent abnormalities except for hypochromic anemia described in 4 cases (Puretić *et al.*, 1962; Ishikawa *et al.*, 1964, 1973; Kitano *et al.*, 1972; present case).

As to diagnosis, well-known genetic mucopolysaccharidoses and I-cell disease can be excluded by careful examination of clinical manifestations, roentogenographic findings of bones, histological findings of the lesion and cytological findings of cultured cells (Kitano *et al.*, 1972, 1976). Especially, roentogenographic study of bones reveal numerous lesions, which are clearly different from those of well-known genetic mucopolysaccharidoses or I-cell disease (Puretić *et al.*, 1962; Ishikawa *et al.*, 1964, 1973; Horio *et al.*, 1968; Gutiérrez *et al.*, 1973; Kitano, 1976; Gianotti *et al.*, 1977, present case).

In agreement with Woyke *et al.* (1970), Kitano *et al.* (1972), Ishikawa and Mori (1973), Gutiérrez *et al.* (1973) and Costa *et al.* (1975), the histopathologic structure of the tumor in the present case was characteristic.

Biochemical analysis of the lesion disclosed that the amorphous ground substance was glycoprotein, that is, combined substance of protein fibers and mucopolysaccharides (Horiki *et al.*, 1972; Ohkubo, 1972; Ishikawa and Mori, 1973).

It seems to be necessary to accumulate further cases before any definite conclusion can be drawn about the pathogenesis of the disorder. However, a review of 18 cases

Table 1. Summary of clinical data in reported cases with Puretić syndrome.

Author	Parental consanguinity	Sex of patients (sib size)	Age of onset	Skin			Gingival hypertrophy	Flexural contracture of joints
				Tumors	Nodules	Infiltrations		
Murray (1873)	+	F,M,F (4)	3 mo.	+	+	+	+	....
Puretić *et al.* (1962)	−	M (3)	3 mo.	+	+	+	+	+
Ishikawa *et al.* (1964)	+	M (5)	2 mo.	+	+	+	+	+
Drescher *et al.* (1967)	−	M,F (6)	2 yr.	+	−	−	+	−
Horio *et al.* (1968)	+	F,F (2)	2 yr.	+	+	+	+	−
Enjoji *et al.* (1968)	−	F,F (4)	3 yr. & 4 yr.	+	−	−	−	−
Kitano *et al.* (1972)	−	M,M (2)	2 yr.	+	+	+	+	+
Gutiérrez *et al.* (1973)	−	M (3)	2 yr.	+	+	+	+	+
Costa *et al.* (1975)	−	F (6)	2 mo.	+	+	+	+	+
Kitano (1976)	+	M (1)	6 mo.	+	+	+	+	+
Gianotti *et al.* (1977)	−	F (1)	birth	+	+	+	+	+
Present case (1980)	+	M (3)	1 mo.	+	+	+	+	+

with Puretić syndrome seems to suggest that this disorder represents an example of inborn error of mucoploysaccharide metabolism in the connective tissue in agreement with Ishikawa and Mori (1973) and Costa *et al.* (1975).

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