FUCOSIDOSIS: CLINICAL, PATHOLOGIC, AND BIOCHEMICAL

STUDIES OF FIVE PATIENTS

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INTRODUCTION

Fucosidosis is an inherited metabolic disorder in which deficiency of a-l-fucosidase activity results in accumulation of fucosyl compounds in lysosomes (6,7,24). Clinical manifestations reported include progressive motor and mental deterioration, coarseness of facial features, cardiomegaly, hepatomegaly, skeletal abnormalities and short stature (1,5,6,8,13). Initially many of the patients exhibit hypotonia, but progressive spasticity develops with time.

The enzyme a-l-fucosidase is widely distributed in the body. All patients with fucosidosis have very low a-l-fucosidase activity in plasma, in leucocytes and in other tissues. However, some clinically normal individuals have low plasma activity as a hereditary property, and assay of this enzyme in plasma is not a reliable criterion for diagnosis of fucosidosis (16). Confirmation of diagnosis thus depends on assay of enzyme activity in leucocytes, cultured fibroblasts, or other tissues.

CLINICAL SUMMARIES: We have studied five patients with fucosidosis from three families (Table 1). The first seen were two male siblings (#s 1 and 2), whose parents are first cousins of Italian origin (Formia, north of Naples). The elder, born in 1961, was first seen at age 2 years because of muscular weakness. Muscle biopsy showed small vacuoles or granules in the fibers, but no specific diagnosis could be made. Rectal biopsy at 5½ years showed cytoplasmic granu-
lation of myenteric plexus neurons, and vacuolar histiocytosis of colonic lamina propria and submucosa. Polyps removed from the right antrum in 1971 showed vacuolate cytoplasm of epithelial and stromal cells, again suggestive of lysosomal storage disease.

At age 12 years, he had his first grand mal seizure. At this time, he could stand with support, but was unable to walk or talk. He had marked kyphosis, dull facies, protruding tongue and heavy eyebrows. Punctate macular lesions which blanched on pressure were present over the soles and the palms. Examination of lungs, heart and abdomen was unrevealing. He had bilateral hamstring shortening and diffuse muscle weakness, but the deep tendon reflexes were hyperactive. Cranial nerve functions appeared intact.

The younger sibling, born in 1963, was first seen at 3 years of age for generalized muscle weakness. Like his brother's, his course was progressive. At 7 years of age, he had dull facies, protruding tongue, open mouth with drooling, and mild kyphosis. All the extremities were spastic, but he was able to walk with a scissor gait when supported. By 10 years of age he required complete nursing care.

The coarse features, progressive mental retardation, kyphosis, and the presence of cytoplasmic vacuolation of a number of cell types suggested fucosidosis, among other possible lysosomal storage diseases, in these children. The diagnosis of fucosidosis was established by demonstrating the absence of α-1-fucosidase activity in plasma and in cultured fibroblasts (28, 29).

Patient #3 was found in a survey of patients in an institution for the retarded. He was the product of young Mexican-American parents; the mother subsequently had two normal children by a second marriage. Pregnancy was uncomplicated and delivery was described as normal. He held his head up at 8 months and started to walk at 15 months. He was able to say a few single words at 18 months, but at 19 months retardation was suspected and at 2 years he did not speak nor feed himself. At age 9, his IQ was less than 35. He was first seen by us at age 17, with severe mental and physical retardation, coarse features, thick eyebrows and very large tongue. The anteroposterior diameter of the chest was increased, and dorsal kyphosis was present. There were no skin lesions suggestive of angiokeratoma. He could walk by himself, but with awkward gait. He was aggressive and bit, scratched and pinched other patients.

In our third family there are two affected males (#s 4 and 5). The parents are Mexican-American and there is no known consanguinity. Each child had been the product of a normal pregnancy and delivery. The elder was 3 9/12 years old when first seen for delayed speech and abnormal gait. He had recurrent respiratory infections in early life, and was developmentally slower than an older normal