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OCULOCEREBRAL HYPOPIGMENTATION SYNDROME (CROSS SYNDROME)*

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A typical case of Cross syndrome with hypopigmentation, mental and psychomotor retardation, spasticity, bilateral optic atrophy and dental defects in a three-year-old boy is presented. The clinical features of this rare syndrome are discussed. *Key words: Cross syndrome, albinism.*

The oculocerebral hypopigmentation syndrome, also known as Cross syndrome, is an extremely rare form of albinism which is associated with mental retardation, spasticity, athetoid movements, and ocular and stomatologic anomalies[1]. It appears to be transmitted as an autosomal recessive trait.

This report presents a three-year-old child affected with ocular, stomatologic and neurologic disturbances including hypopigmentation.

Case Report

A three-year-old boy was admitted to our department with failure-to-thrive. The child was the product of a third-degree consanguineous marriage. The father aged 27, and the mother, aged 22, are healthy, and normally pigmented. The patient's one-year-old sister, who was blonde with blue eyes and white skin, evidenced hypopigmentation. She was mentally retarded and both her upper and lower extremities were spastic. Her head remained in a hyperextended position and she had a weak, high-pitched cry.

The patient, who was born in a hospital evidenced cyanosis of the extremities during the first five-ten minutes postnatally. He did not cry for a while. After receiving oxygen he returned to normal. At 11 months of age, he was first admitted to a university hospital because of failure-to-thrive, and his delayed psychomotor development was first recorded there. He was then reportedly unable to sit unaided. Physical examination (Figs. 1, 2) revealed a weight of 7850 g (below the third percentile), a height of 92 cm (between 10th-25th percentiles) and a head circumference of 45 cm (below the third percentile). There was

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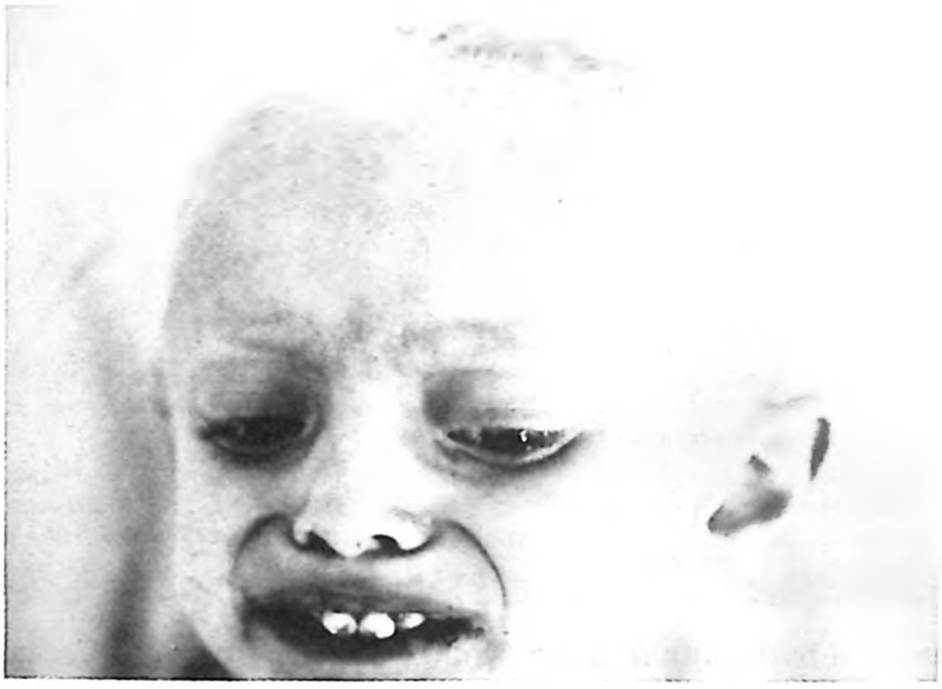

Fig. 1: A three-year-old boy exhibiting oculocerebral hypopigmentation syndrome (Cross syndrome).

Fig. 2: Cross syndrome in a three-year-old male child.

significant hypopigmentation, the hair was extremely blond, the skin was white, and the eyes were light blue. He was severely retarded. Interaction with the environment was poor and undifferentiated. He was able to sit unaided, but was unable to stand up or walk. He was generally hypertonic. The deep tendon reflexes were symmetrically normal. Stomatologic examination revealed widely spaced discolored teeth. He also had gingival hypertrophy and grinding and rumination movements. The ophthalmologic examination revealed bilateral optic atrophy. Routine laboratory tests were normal including blood cell counts, blood electrolytes, urea and glucose. Plasma and urinary amino acid chromatography, serum iron and iron binding capacity, copper, ceruloplasmin, magnesium and thyroid function tests were within normal limits. Screening for intrauterine-acquired infections such as toxoplasmosis, rubella, cytomegalovirus and syphilis were negative. Although the bones were normal structurally, skeletal X-ray examination demonstrated a bone age of six months. The computerized tomographic scan of the brain showed calcification in the basal ganglia (Fig. 3).

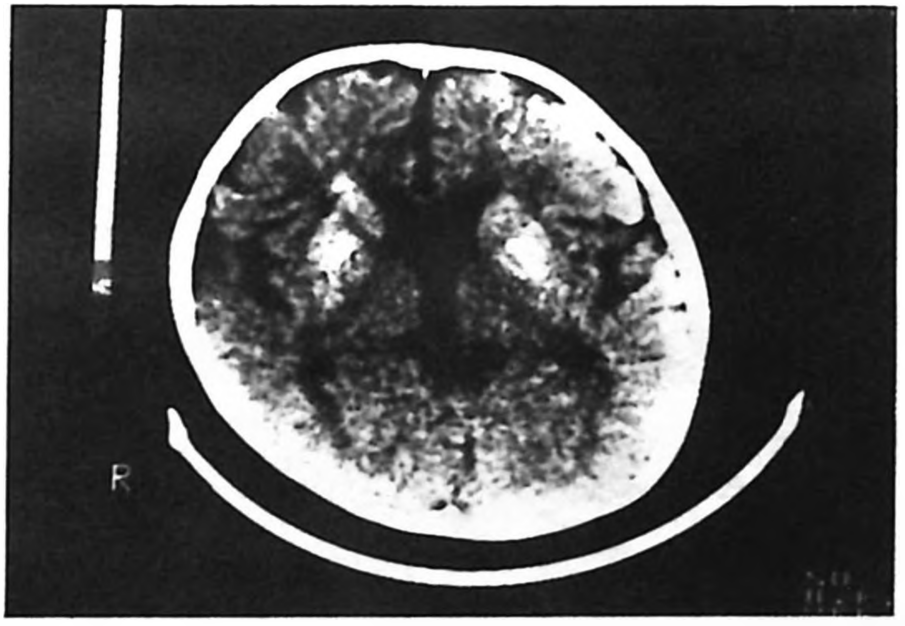

Fig. 3: A computerized tomographic scan of the brain revealing calcification in the basal ganglia.

Biopsy of the sural nerve showed no metachromatic substances. A skin biopsy was performed in order to confirm the clinical diagnosis of oculocutaneous albinism. There was amelanosis in the epidermis as seen by hematoxylin-eosin and Fontana staining (Fig. 4). The biopsy material stained with a tyrosinase stain, was positive (Figs. 5, 6).

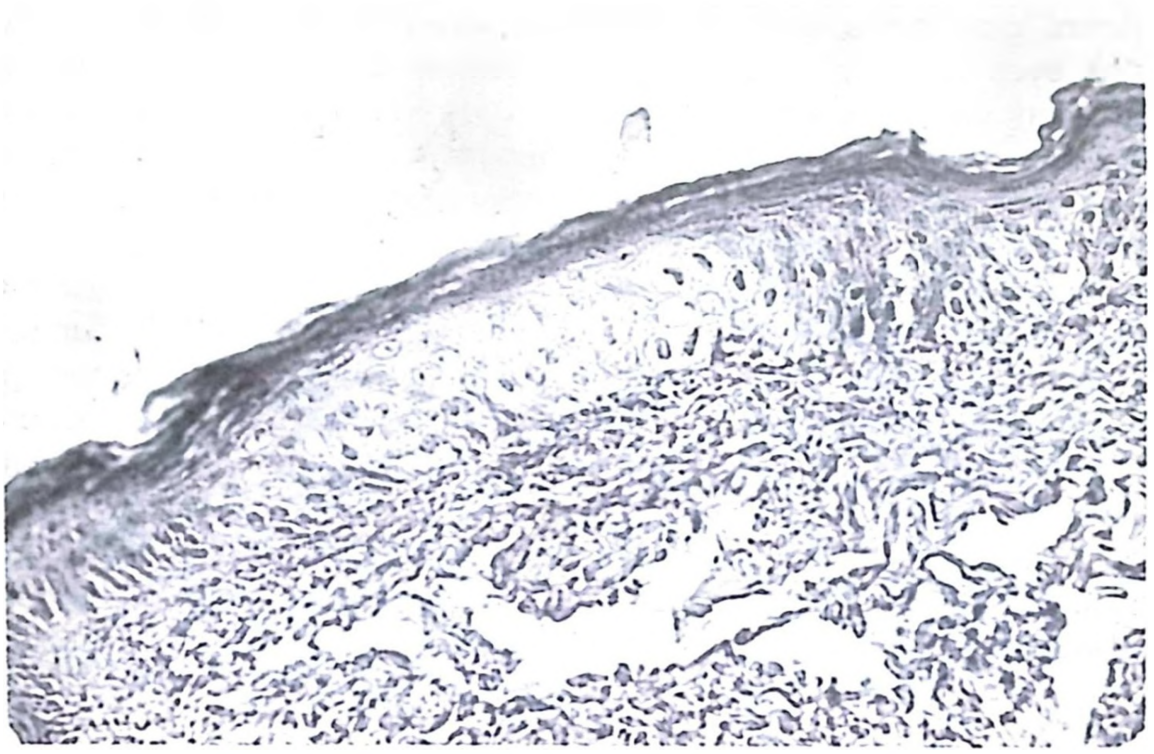

Fig. 4: Hematoxylin-eosin and Fontana staining illustrating amelanosis in the epidermis.

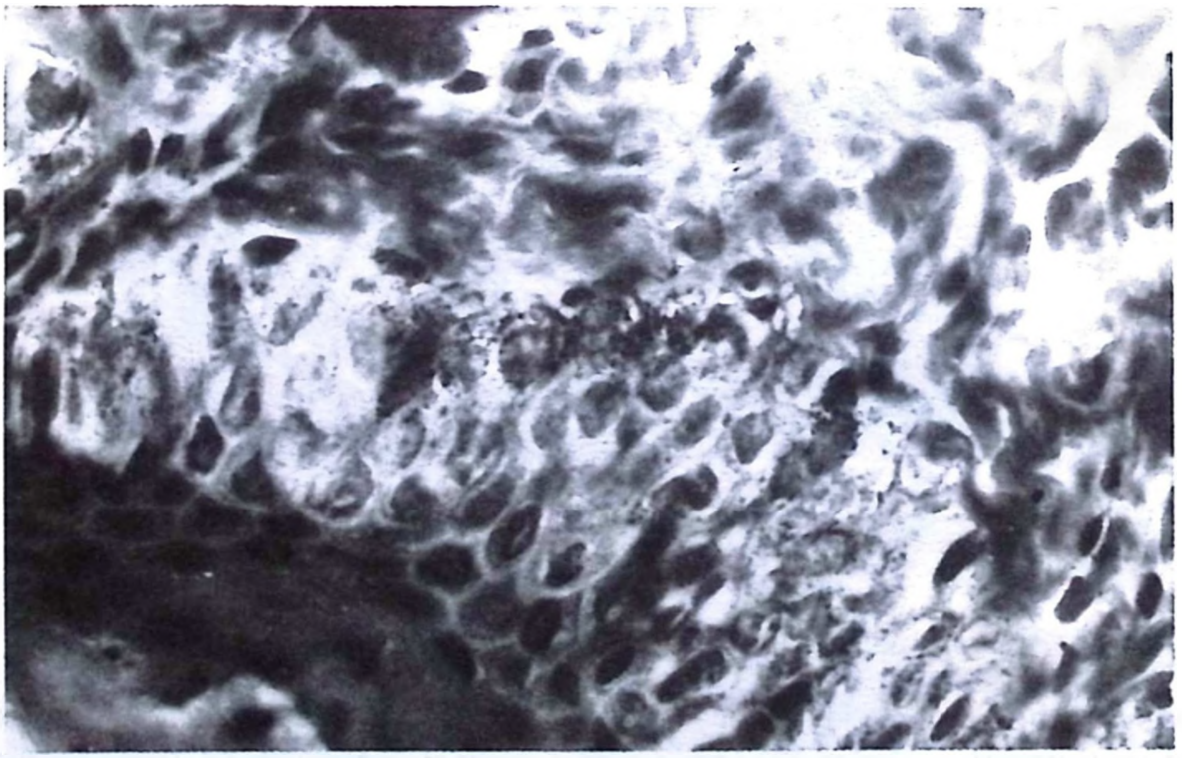

Fig. 5: The biopsy material stained with a tyrosinase stain yielding positive results.

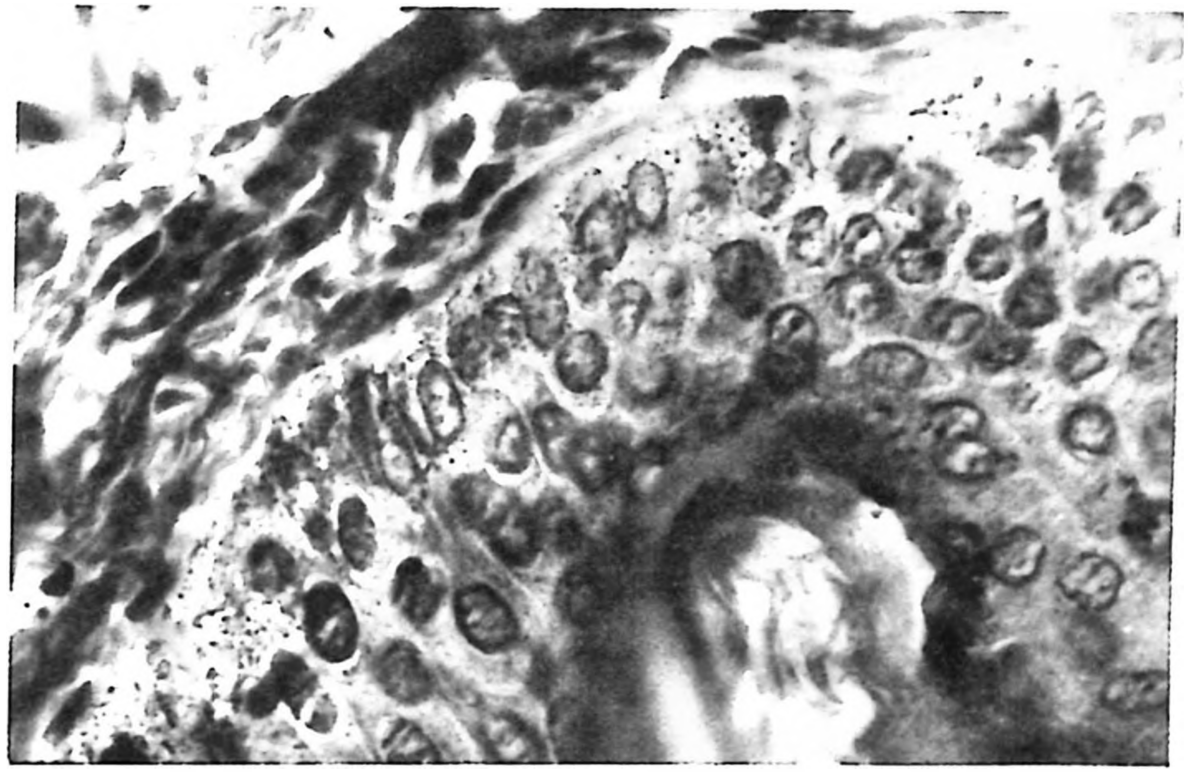

Fig. 6: Tyrosinase staining used on biopsy material yielding a positive result.

Discussion

The patient's findings including motor and mental retardation, significant hypopigmentation of the eyes and skin, bilateral optic atrophy, neurologic abnormalities such as spasticity, widely spaced and discolored teeth and gingival hypertrophy suggested the oculocerebral hypopigmentation syndrome. This very rare syndrome was first reported in three siblings in an Amish family in Ohio[1]. Later, several cases were reported from Germany, Italy, Great Britain and Belgium[2,3]. The clinical features observed in our patient were similar to those seen in nine previously reported cases[1-3]. All the patients presented with hypopigmentation, severe psychomotor retardation and neurologic and ocular disturbances. In addition, dental anomalies and consanguinity were present, as in the cases reported from Ohio, Italy and Belgium[1-3]. Computerized tomographic scan of the brain of our patient showed basal ganglia calcification in a pattern similar to that seen in hypoparathyroidism, pseudohypoparathyroidism (Albright's syndrome), familial calcification of the basal ganglia, Fahr's syndrome, Cockayne's syndrome, lead and carbon monoxide poisoning, and irradiation with methotrexate therapy[5]. We excluded such etiologies of basal ganglia calcification because of past history, physical examination and laboratory results. Tyrosinase staining of the skin biopsy revealed enzyme activity. This feature of pigment disorder resembles that found in patients with Cross syndrome[1-4]. Therefore, albinism

associated with neurologic, ocular and dental defects strongly supports the diagnosis of Cross syndrome in our patient.

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