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The Primrose syndrome with progressive neurological involvement and cerebral calcification

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Sirs: The Primrose syndrome is a rare disorder, first described in 1982 in a man with mental retardation, progressive muscle wasting, ossified ear cartilage, cystic changes in the humeral and femoral heads, paracentral posterior cataract and hearing loss [4]. Two other cases were later described [1, 3]. We report a new case, the first described in a woman, with the classical features of the Primrose syndrome, associated with late-onset progressive gait ataxia, pyramidal signs and cerebral calcification.

The patient, a 49-year-old woman with delayed motor developmental milestones and severe mental retardation, was born from non-consanguineous parents. The mother is reported to have had a clumsy gait since adolescence. At 40 years of age, diabetes was diagnosed in the patient. Six years later, she underwent cataract surgery on the right eye. At that time, gait problems appeared. At 49 years of age, she was admitted to our department because of progressive worsening of gait disturbances, with inability to walk unaided. General examination showed mild dysmorphic features (Fig. 1) with smooth skin of the legs and numerous dyschromic spots, sparse and thin hair, bilateral enophthalmos, pseudophakia of the right eye, ptosis and cataract in the left eye, depressed nasal bridge, prognathism, completely rigid helices and bilateral pes cavus. Neurological examination revealed severe mental retardation, frequent confabulation, mild deafness, severely impaired spastic-ataxic gait, positive Romberg sign, slight hypertonia, mild muscular atrophy of the limbs, upper limb areflexia, brisk tendon reflexes in the legs, bilateral ankle clonus and Babinski sign.

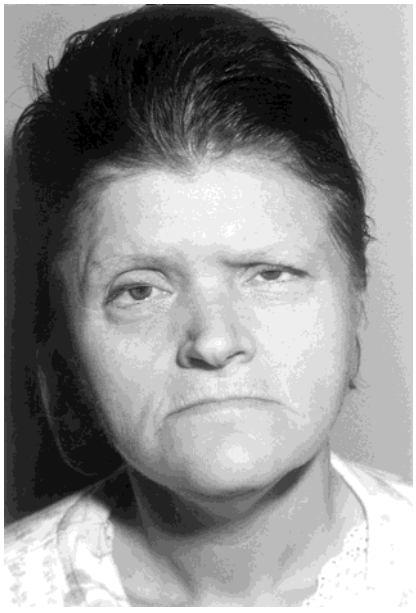

Fig. 1 Facial dysmorphism with evidence of palpebral ptosis, slight enophthalmos, depressed nasal bridge and prognathism

Laboratory investigations revealed normal values for routine chemistry and the following blood test results: thyroxine, thyroid-stimulating hormone, folate, vitamin B12, ceruloplasmin, amino acids, lactic and pyruvic acid, cholestanol, lysosomal enzymes activity (α-fucosidase, α-mannosidase, α-galactosidase, hexosaminidase A and B; arylsulfatase A and B; β-glucuronidase; galactocerebrosidase), seroly for syphilis, urinary phosphate and calcium levels were all normal.

EEG, ECG and the chromosome map were normal. Dermatological examination showed hypopigmented atrophic lesions with slight sclerosis of the limbs. Total body radiography of the skeleton showed generalized, severe osteopenia (Fig. 2 a, b). Electroneurography showed mild, mainly sensory axonal neuropathy.

Brain CT showed areas of dense calcification in both heads of the caudate nuclei while areas of less dense calcification were seen in both globi pallidi and in the anterior limb of the left internal capsule; dense calcification of both external ears was also evident (Fig. 3 a, b). Brain MRI failed to show further abnormalities. A muscle biopsy specimen was suggestive of neurogenic atrophy.

The clinical and radiological hallmarks of the patient reported here strongly suggest a diagnosis of Primrose syndrome [4]. The only three previously reported cases were men with a negative family history. Beside the classical signs of Primrose syndrome, they all showed common craniofacial dysmorphism and a slowly progressive neurological course with gait disturbances particularly severe in Primrose's original patient [4]. However, the neurological involvement was neither well documented nor considered a characterizing feature.

The female patient described here adds to the other few cases and suggests that: i) Primrose syndrome is not confined to males; ii) facial dysmorphism and late-onset, progressive neurological manifestations are part of the clinical phenotype; iii) neurological involvement is also proved by the presence of cerebral calcification, reported for the first time in our patient. In this regard, we recommend that CT be performed to search for cerebral

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