Cognitive, motor and sensory involvement in a suspect inherited metabolic disease

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Introduction

A progressive neurological syndrome with juvenile-onset can pose a difficult challenge to a clinician. Many of these disorders are caused by genetic defects, although a clear pattern of inheritance is not always appearent. Furthermore, their prognosis is difficult to assess, in that what initially presents as an isolated deficit may subsequently evolve into a complex multisystemic syndrome. Here we describe a case in which the absence of familiarity and a complex clinical picture led us to an extensive investigation.

Presentation and history

- A 36-year-old man was brought to our observation. His familial history was negative; his birth and development had been normal and he had been healthy until the age of fifteen.
- At that age, he started complaining of **visual loss**. Subsequent ophthalmological consultations revealed a progressive reduction in visual acuity in both eyes and a concentric restriction of both visual fields. By the age of thirty he was **completely blind**.
- During the fourth decade he had also developed a **behavioural and cognitive syndrome** with apathy, anhedonia and a speech impairment; urinary and fecal incontinence was also present.

General and Neurological Examination

- He was able to stand and walk on his own; his gait was slow, short-stepped, and uncertain, with a small base.
- His optic discs were pale. **Bilateral amaurosis was noted, with ophtalmoplegia**. Photic reflexes were absent.
- Speech was severely hypophonic and dysarthric; it was also poor in content.
- Rinne and Weber's tests revealed a moderate neurosensorial hypoacusis.
- Muscle trophism was globally reduced. Strength was reduced in the upper limbs (Medical Research Council: 4/5) and in the lower limbs (MRC: 3/5). Axial dystonia was present, with head and neck left lateroversion. Muscle tone in the limbs was normal.
- Tendon reflexes were moderately increased; Epstein sign was present.
- A moderate degree of ataxia was present, as evidenced in the finger-nose pointing test. A slight degree of bradykinesia was also present.
- Cognitive testing, performed via **Mini Mental State Examination**, led to a score of 21,75/30. **Frontal Assessment Battery** score was 13/18.
- Urinary and fecal incontinence was noted.

MRI images

- The cerebral hemispheres appeared to be severely and simmetrically reduced in size **(fig. 1, A)**, and ex vacuo dilatation of the lateral ventricles was present. Supratentorial white matter and the posterior arms of the internal capsule appeared faintly hyperintense in FLAIR images **(fig. 1, C)**.
- The cerebellum also appeared severely reduced in size **(fig. 1, B)**; the folia appeared hyperintense in FLAIR section **(fig. 1, D)**; a similarly marked degree of atrophy was also evident in the the pons, the medium cerebellar peduncles and in the midbrain. This diffuse atrophy was accompanied by a marked dilatation of the fourth cerebral ventricle and of the liquoral spaces in the posterior cerebral fossa.

Fig. 1

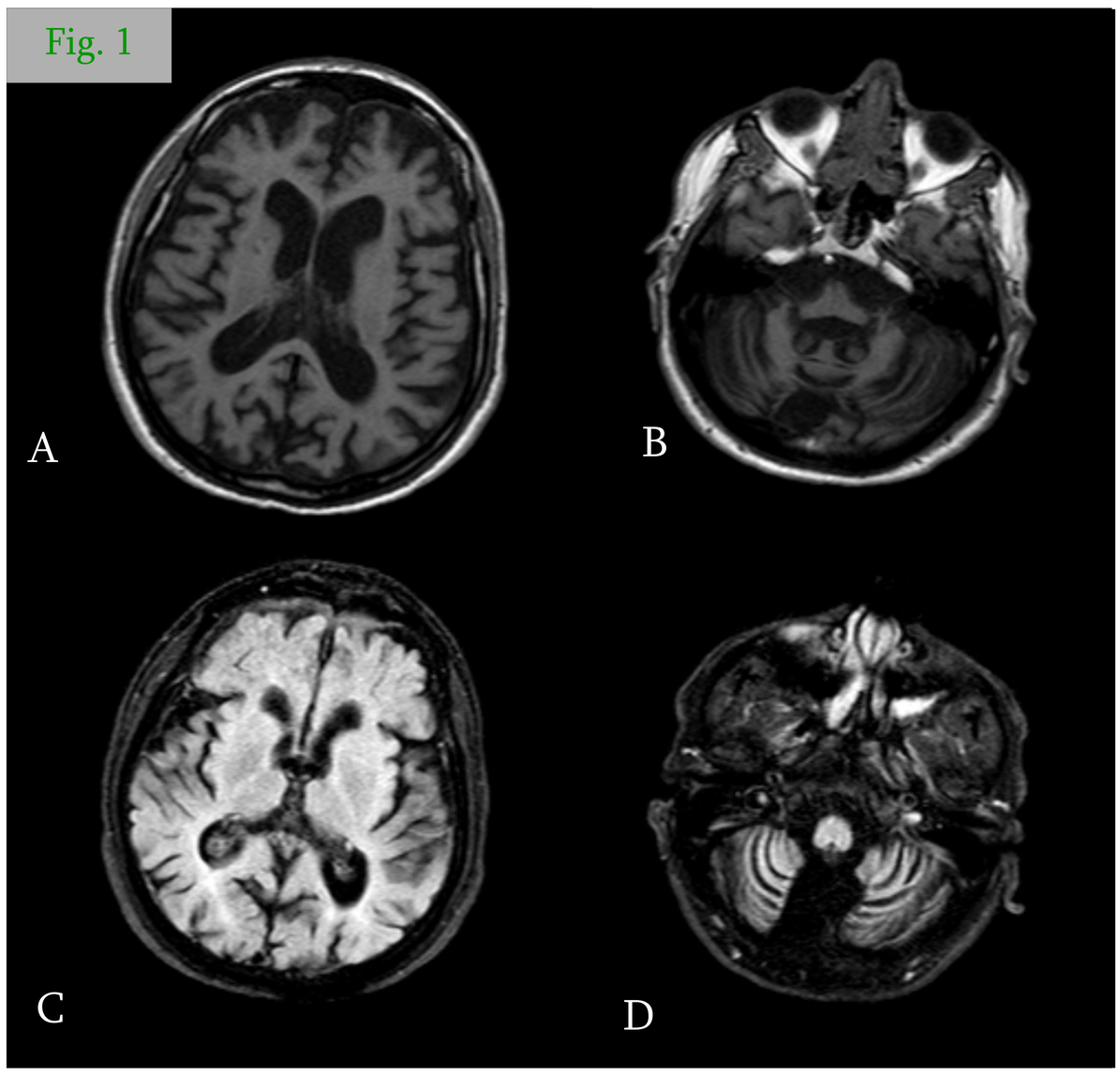
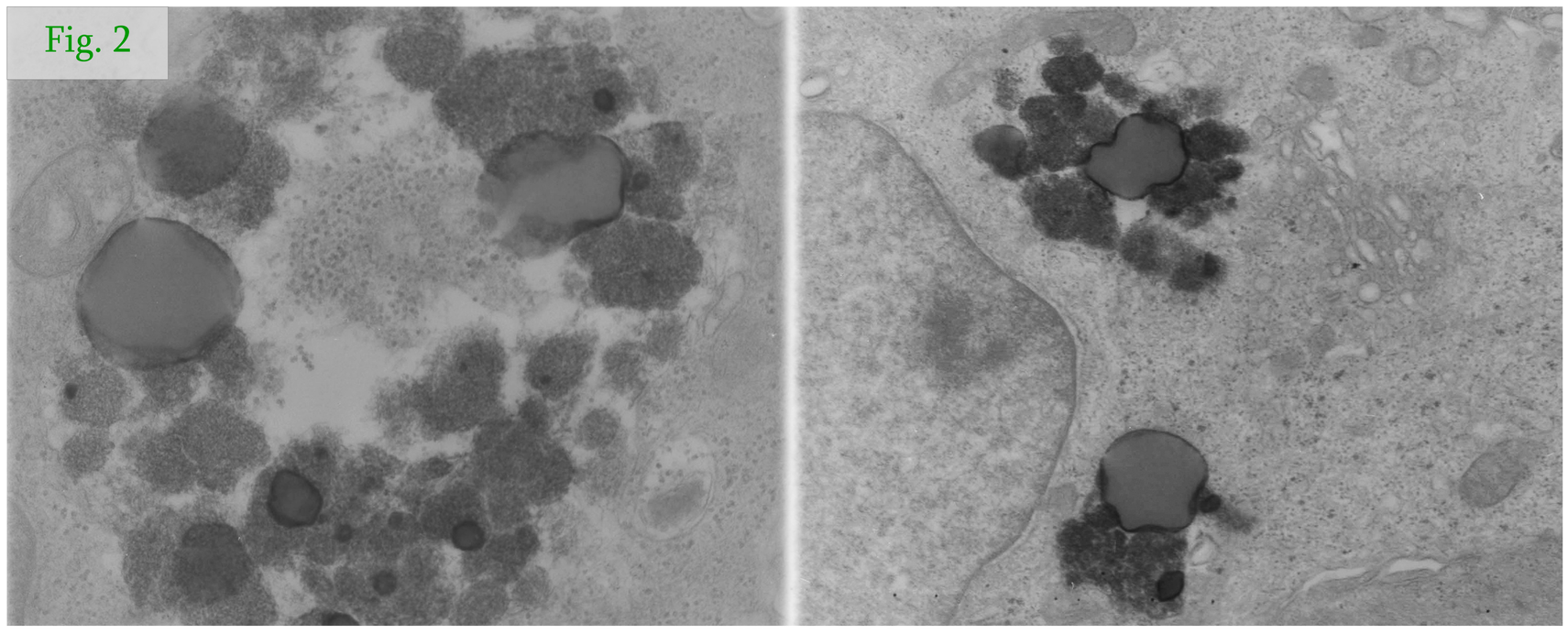


Fig. 2



Skin Biopsy

- A skin biopsy (fig. 2) produced a skin fragment with reduced but well-differentiated cellular components (glands, vasa, smooth muscle); no inflammatory alterations were present.
- Insides fibrocyte processes and gland cell, there were variable-sized lysosomes, containing either a dense osmophilic, floccular matrix, or round osmophilic bodies with a thick granular component; these inclusions were associated with lipid material that was recognized as ceroid. In conclusion, an increase in the lysosomal components was found.

Other tests

- Electroencephalographic testing revealed sporadic generalized anomalies. Electroneuromyographic testing was normal in all explored districts.
- An electroretinogram showed abolished scotopic (rod), photopic (cone), 30-Hz flicker and maximal responses, in both eyes.
- Audiometric testing confirmed the presence of bilateral neurosensorial hypoacusis, which was moderate for deep frequencies and severe for acute frequencies. Brainstem auditory evoked potentials showed increased latency in both ears.
- A urodynamic exam showed bladder hyperactivity to low capacity and high pressure, with a post-voiding residual volume of 30 mL.

Conclusion

This case is of interest because it shows a case of juvenile-onset retinopathy developing into a complex, multisystemic neurological syndrome. We believe that gene testing for the genes associated with juvenile-onset ceroid lipofuscinosis may shed light on this complex case.

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XLVI CONGRESSO NAZIONALE
10-13 OTTOBRE 2015 – GENOVA

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