Acta Neurol. Belg., 2009, **109**, 38-39

Cerebral oedema in episodic ataxia

L. Crevits, M. Cambron and S. Anseeuw
Department of Neurology, Oto-neuro-ophthalmology, Ghent University Hospital, Ghent, Belgium

Abstract

We report a patient with episodic ataxia (presumably of type 2) who developed cerebral oedema secondary to a common infection (presumably viral). Cerebral oedema may be a part of the clinical spectrum of familial episodic ataxia and argues for an overlap with hemiplegic migraine. It is suggested to consider a diagnosis of episodic ataxia or familial hemiplegic migraine in catastrophic reactions to apparent trivial trauma or infection.

Key words : Cerebral oedema ; coma ; intracranial hypertension ; episodic ataxia.

Introduction

The familial episodic ataxias represent a heterogeneous group of inherited syndromes affecting the cerebellum and manifesting with intermittent ataxia. Episodic ataxia type 2 (EA2) is an autosomal dominant disorder with episodes of ataxia lasting hours, with typical interictal eye movement abnormalities (Jen *et al.*, 2004).

We report a family with a clinical diagnosis of EA2. One of the members of the family presented with rapidly evolving coma, intracranial hypertension and fatal brain oedema. Familial hemiplegic migraine (FHM) may also be complicated by cerebral oedema (Kors *et al.*, 2001). A relation of EA2 and FHM is discussed, both at a genetic and phenotypic level.

Case report

This patient complained from his 18th year of recurrent bouts of vertigo lasting about one hour and occurring weekly. No apparent trigger could be revealed. At age 22, a craniopharyngioma was partially removed. Because of recurrence, a total resection of the tumour was carried out 5 years later and hormonal replacement therapy was administered.

The patient presented again at 30 years because of unsteadiness persisting between his known vertiginous attacks. Apart from mild cerebellar gait ataxia, interictal neurological examination revealed a rebound nystagmus and failure to visually suppress the horizontal vestibular ocular reflex. Magnetic resonance imaging (MRI) showed the signs of previous brain surgery, but no cerebellar pathology. The frequency of the vertiginous attacks could be reduced dramatically by flunarizine 10 mg a day.

One year later, the patient was admitted to Ghent University Hospital because of diffuse rash, cough, diarrhoea and somnolence starting two days earlier. Apart from a temperature of 39°C, clinical examination, extensive biochemical analysis including hormone levels, bacterial cultures, chest radiography and brain imaging were all non-contributory. In the next hours, the patient developed coma with papilloedema. A computed tomography of the brain was not contributively. A lumbar puncture revealed clear cerebrospinal fluid (CSF) with an elevated opening pressure of 30 cm water. In CSF, glucose was 0.7 g/L (glycaemia 1.10 g/L), protein 0.40 g/L and cells 4/mm^3 (all lymphocytes). Bacterial and virological results were negative. The clinical situation further deteriorated although broad spectrum antibiotics were administered. The EEG showed a burst suppression pattern and multiple organ failure developed. MRI could not be performed due to the critical clinical situation. The patient died five days after admission. Post mortem examination of the brain revealed no abnormalities apart from diffuse parenchymal oedema.

Family history

The mother of the patient suffered from episodic dizziness and had developed pronounced permanent ataxia during adulthood. Neuro-ophthalmological data were not available. The father was in good health.

The four years younger sister of the patient was known by one of us (LC) with episodic ataxia and migraine without aura (according to IHS-criteria, 2004). Her episodes of ataxia had started in childhood and occurred with a variable interval, sometimes weekly. They lasted up to one day. Migraine was treated with valproate. Interictal neurological examination at the age of 24 years revealed gaze evoked nystagmus to the left and to the right, with a rebound nystagmus. Failure to visually suppress the horizontal vestibular ocular reflex was manifest. MRI of the brain was normal, especially no cerebellar alterations could be detected. Acetazolamide proved to be the only medication that could reduce the frequency of the attacks.

Discussion

Based on clinical symptoms and signs in the patient and his sister, and the positive history of the mother, a diagnosis of familial episodic ataxia can be considered. The apparent autosomal dominant mode of transmission, the typical clinical presentation and the response to acetazolamide in the sister suggest episodic ataxia type 2 (EA2, OMIM # 108500). Unfortunately, informed consent for genetic confirmation was not obtained. Association with a craniopharyngioma has not been described and is thought to be a chance occurrence.

EA2 is an autosomal dominant disorder with episodes of vertigo and ataxia lasting for hours. Interictal eye movement abnormalities typically consist of gaze evoked and rebound nystagmus or downbeating nystagmus, and impaired vestibular ocular reflex suppression. The episodes of ataxia respond to acetazolamide but flunarizine can also be applied as a treatment (Boel and Casaer, 1998). There may be a gradual baseline ataxia with evidence of cerebellar atrophy. Affected patients also may have migraine, and some of them suffer from hemiplegic migraine. Several different mutations in the calcium ion channel gene CACNA1A on chromosome 19p13 can cause EA2 (Ophoff *et al.*, 1996). Familial hemiplegic migraine (FHM) is another disorder linked to CACNA1A gene mutation. FHM, EA2 and SCA6 are considered to be allelic ion channel disorders.

Delayed cerebral oedema and fatal coma after minor head trauma have been described in hemiplegic migraine. The S218L mutation in CACNA1A has been associated with the dramatic coma in FHM. Some members of the family reported by Kors *et al.* (2001) had progressive ataxia, but typical episodic ataxia had not been described. A minor brain injury is sufficient to provoke fatal oedema in FHM. Possibly, a depolarizing stimulus that is irrelevant to healthy subjects may induce hyperexcitability in patients with that kind of channelopathy. Therefore, it is hypothesised in the present patient that a viral infection may have elicited cytotoxic brain oedema leading to intracranial hypertension. However, it can not be excluded that a trauma had not been mentioned because it was too trivial. The interval between infection and coma ("delayed cerebral oedema") is another similarity with fatal coma after a minor head trauma in FHM. Thus, the context of cerebral oedema in EA is very comparable to fatal coma after head trauma in FHM.

The present report suggests that cerebral oedema may be an overlapping manifestation of episodic ataxia and FHM. These associations may be considered in unexpected cerebral reaction to apparent trivial head trauma or infection.

REFERENCES

Boel M., Casaer P. Familial periodic ataxia responsive to flunarizine. *Neuropediatrics*, 1998, **19** : 218-220.

Headache Classification Committee of the International Headache Society. The international classification of headache disorders. *Cephalalgia*, 2004, **24** (Suppl. 1) : 1-160.

Jen J., Kim G. W., Baloh R. W. Clinical spectrum of episodic ataxia type 2. *Neurology*, 2004, **62** : 17-22.

Kors E. E., Terwindt G. M., Vermeulen F. L., Fitzsimons R. B., Jardine P. E., Heywood P., Love S., van den Maagdenberg A. M., Haan J., Frants R. R., Ferrari M. D. Delayed cerebral edema and fatal coma after minor head trauma : role of the CACNA1A calcium channel subunit gene and relationship with familial hemiplegic migraine. *Ann. Neurol.*, 2001, **49** : 753-760.

Ophoff R. A., Terwindt G. M., Vergouwe M. N., van Eijk R., Oefner P. J., Hoffman S. M., Lamerdin J. E., Mohrenweiser H. W., Bulman D. E., Ferrari M., Haan J., Lindhout D., van Ommen G. J., Hofker M. H., Ferrari M. D., Frants R. R. Familial hemiplegic migraine and episodic ataxia type-2 are caused by mutations in the Ca2+ channel gene CACNL1A4. *Cell*, 1996, **87** : 543-52.

Luc Crevits,
Department of Neurology,
Oto-neuro-ophthalmology,
Ghent University Hospital,
De Pintelaan 185,
B-9000 Ghent (Belgium).
E-mail : luc.crevits@ugent.be