Task specific focal dystonia: a presentation of spinocerebellar ataxia type 6

Autosomal dominant cerebellar ataxias (ADCA) are characterised by clinical and genetic heterogeneity with a substantial overlap of clinical features and a variable degree of adherence to three distinct phenotypes according to Harding’s clinical classification: ADCA type I, II, and III. The availability of molecular genetic testing has provided increasing appreciation of a wider clinical spectrum than previously thought for each ADCA subgroup. In addition there is an increasing list of genes harbouring disease causing mutations which, to date, include spinocerebellar ataxia (SCA) types 1, 2, 3, 6, 7, 8, 10, 12, and 17. SCA 6 is caused by an unstable CAG expansion in the 1-1A calcium channel gene (CACNA1A). We present a confirmed case of SCA 6 presenting with a task specific focal dystonia (writer’s cramp) predating the onset of progressive gait ataxia by five years, which further widens the clinical spectrum of SCA 6.

Case report

A 57 year old female pharmacist first presented at the age of 42 with a two month history of progressive difficulty in writing prescriptions as a result of writing induced cramp affecting the right hand. This task specific focal dystonia was aggravated by stress and fatigue. Her father was reported to have had increasing apraxia on a basis of developing tremor and gait disturbance at age 40.

On examination, the patient’s gait was normal and no focal neurological deficits were identified. Her writing, after a normal start, was interrupted by a semiflexed posture of the fingers to maintain the grasp of the pen, with the index finger and thumb appeared hyperextended and the wrist hyperflexed. This was accompanied by an ache in the hand. A working diagnosis of writer’s cramp was made using well characterised positive control the tremor. Two years later, at the age of 49, she began to experience difficulties with maintaining her balance when walking downhill, which later progressed to an increasing tendency to sway or trip. The writer’s cramp had persisted with progressive tremor and clumsiness in both arms, forcing her to swap hands when writing. A more detailed family history revealed additional information about paternal relatives who had a history of tremor and gait disturbance; however, none had developed writer’s cramp.

Neurological examination now showed evidence of gait and limb ataxia, mild intention tremor, and horizontal gaze-evoked nystagmus, with mild dysarthria and no other neurological deficit. Ancillary tests to exclude acquired ataxias were also done, and brain magnetic resonance imaging revealed evidence of marked cerebellar atrophy with sparing of cortical and brain stem structures. With informed consent, genomic DNA was extracted from peripheral blood leukocytes. Screening for trinucleotide repeat expansions for SCA 1, 2, 3, and 6 was done using polymerase chain reaction (PCR) amplification of the genomic sequences containing each trinucleotide repeat expansion site. The PCR products were size fractionated by electrophoresis in a 6% polyacrylamide gel, which was then dry blotted. After hybridisation with a gamma-32P labelled (CAG)n oligonucleotide probe, allele sizes were visualised by autoradiography. Estimations of trinucleotide repeat size for each gene was made using well characterised positive control samples. A pathological 22 repeat expansion in the CACNA1A gene and another allele of 12 repeats were detected (fig 2). Alleles within normal range were detected in the SCA 1, 2, and 3 genes.

Comment

We describe a case of SCA 6 with a focal dystonia preceding the onset of gait or limb ataxia by a period of at least five years. Recently, there has been a report of similar SCA 6 presentation but with a more progressive, disabling, and treatment resistant shoulder girdle and upper limb dystonia. In the original description of SCA 6, the most common presenting feature was a progressive cerebellar syndrome, accompanied by involuntary movements, dystonic posturing, sensory loss, and changes in the deep tendon reflexes. Other presenting features have been reported as a result of direct molecular testing, including episodic ataxia and positional vertigo associated with downbeat nystagmus. Our report provides further evidence of a wider clinical presentation of SCA 6, but may also be relevant to other ADCAs, which were previously considered to be relatively “pure” cerebellar ataxias.

This case also shows that, in the absence of a suggestive family history or presenting cerebellar features, it is unusual for clinicians to include ADCA in the differential diagnosis. Dystonia or extrapyramidal motor signs have often been associated with SCA 3, but are not specific, as overlap exists, though less frequently, with other subtypes in ADCA 1. With disease progression, the focal dystonia in our patient has partially resolved and has been predominantly replaced by a mild pan-cerebellar ataxia with very few extracerebellar signs and absence of other extrapyramidal features. The evolution of these signs and the partial resolution of the writer’s cramp persuade us that the dystonia and ataxia are part of the same pathological process rather than separate disease entities.

Ten years after the onset of gait disturbance, the patient is walking using only one stick and remains employed, consistent with the mild disease course previously reported for SCA 6 phenotype. Increasingly, the availability of molecular investigations is indicating a need to revise the prototype according to the underlying genotype. It is apparent that the majority of the inherited ataxias have a broader clinical spectrum than has previously been appreciated, particularly with ADCA. Our experience highlights the wide range of syndromic presentations as well as advocating the clinical value of testing SCA 6 alongside SCA 1, 2, and 3 which constitute ADCA 1. In addition, it may be useful to screen SCA loci in the ADCA 1 subgroup in cases of idiopathic focal dystonia who develop features of cerebellar dysfunction or who have a relevant family history.
the tegmentum of the most rostral pons.

paramedian infarct of lacuna size situated in an axial T2 weighted image showing a right

Figure 1

A 51 year old man with hypertension devel-

Case report

arthria-clumsy hand syndrome, or ataxic
dromes such as pure motor hemiparesis,

Brain magnetic resonance imaging (MRI) showed a right paramedian infarct of lacunar size situated in the tegmentum of the most rostral pons—that is, at isthmus level. From this level, the fibres of the superior cerebellar peduncle move ventromediadally towards the decussation. Serial neuro-

Comment

There have been several reports of bilateral cerebellar ataxia caused by a unilateral brain stem stroke. However, previous reports have also described associated neurological symptoms such as mild hemiparesis, dysar-

Bilateral cerebellar ataxia as the sole manifestation of a unilateral rostral pontine tegmental infarct

It has been reported that a small infarct of the pons can lead to various clinical syn-

References


Serial EEG records showed diffuse delta and theta activity with occasional prevalence of this activity in the left sided anterior regions. Cranial CT and MRI revealed diffuse oedema with hydrocephalus and dilatation of the cerebral aqueduct. No focal lesions were observed.

Treatment included dexamethasone (4 mg intravenously twice daily), doxycyclin (100 mg twice daily), rifampicin (600 mg daily), and amphotericin B, starting at doses of 20 mg intravenously per day with a progressive increase to 50 mg daily; simultaneoues intrathecal amphotericin B was given at an initial daily dose of 0.012 mg, increasing progressively to a maximum daily dose of 0.250 mg.

Despite this treatment, the clinical situation rapidly worsened and the patient died after 11 days in hospital. A necropsy examination was denied.

Comment
Free living amoebae of the genus Acanthamoeba are the causative agents of several infections usually occurring in immunocompromised, debilitated individuals and almost always resulting in death. Most cases, therefore, are diagnosed only at necropsy. Our patient was apparently immunocompetent and without any of the usual predisposing factors, such as a history of aquatic activities, treatment with immunosuppressive, chemotherapeutic, or steroid agents or broad-spectrum antibiotics, and so on. The existence of extraneural infective foci in the skin, paranasal area, or lungs—a possible point of access for amoebae—was also excluded. The most striking feature in our patient was that a firm diagnosis was made only through direct observation of the protozoan in the CSF. To our knowledge, this has not been described before in chronic amoebic meningoencephalitis and underlines the diagnostic value of CSF studies in this type of pathology. The main species reported as causing granulomatous amoebic encephalitis are A polyphaga, A castellanii, A culbertsoni, and Balamuthia mandrillaris. The diagnosis is usually made by microscopic examination of stained slices of brain specimens obtained at necropsy or biopsy and cultivation of the causal organism in an appropriate medium. This usually consists of non-nutrient agar covered with bacteria for Acanthamoeba spp or mammalian cell lines for B mandrillaris. Discrimination among species may not be easy and requires experience and the use of different methods. Morphological and ultrastructural analysis, for example, can help in discriminating acanthamoeba from balamuthia, as some differences in shape, dimensions, nuclei, and cytoplasm have been described for both cystic forms and trophozoites. Physiological characteristics such as temperature tolerance, pH dependency, and others—although they have proved useful—are not of definitive value in differentiating pathogenic from non-pathogenic strains.

More recently, molecular methods and the use of monoclonal antibodies for immunofluorescence microscopy have been developed; however, they have some limitations, such as their expense, laborious nature, and short lived reagents. Nonetheless, in spite of these various diagnostic procedures, accurate species determination may prove problematic. In our patient, we were unable to discriminate among the various species of amoebae that could have been involved in the infection. Culture tests on non-nutrient agar covered with bacteria were negative, and other cultures, serological tests, and CSF tests were not done because of the rapid progression of illness. Nonetheless, our case indicates that when an amoebic meningoencephalitis is suspected a careful search for the organisms in the CSF may be a decisive factor in the diagnosis.

In conclusion, this case report emphasises the importance of familiarising ourselves with this form of pathology and provides an example of how the identification of amoebae in the CSF may aid in making a firm diagnosis of this uncommon, undiagnosed, life threatening, and difficult to treat CNS infection. As a successful therapeutic result may sometimes be achieved, a timely diagnosis together with prompt and adequate treatment are essential.

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Identification of amoebae in the CSF in a patient with meningoencephalitis

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