PostScript

LETTERS

Pigmentary macular dystrophy in spinocerebellar ataxia type 1

Spinocerebellar ataxia type 1 (SCA1) is an autosomal-dominant, late-onset, slowly progressive disorder, primarily characterised by a gradual loss of motor coordination, resulting from dysfunction and degeneration of the cerebellum and its connecting pathways.[1 2] This disease is caused by expansion of a CAG trinucleotide repeat within the *SCA1* gene, which encodes a protein called ataxin-1.[1 2] The first and most typical neurological symptom of SCA1 is cerebellar ataxia. Additional symptoms comprise the slowing of saccades, ophthalmoplegia, dysarthria, pyramidal sign and involuntary movement.[1 2] As regards ophthalmological abnormalities of SCA1, decreased visual acuity owing to optic atrophy, attenuation of oscillatory potentials of electroretinogram and enlargement of corneal endothelial cells have been reported.[3] Hence, pigmentary macular dystrophy (PMD) has not been recognised as a clinical feature of SCA1, although it is well established as a major symptom of spinocerebellar ataxia type 7 (SCA7), which is caused by expansion of a CAG trinucleotide repeat within the *SCA7* gene.[4 5] Here, we report a patient with SCA1 who developed visual impairment due to PMD indistinguishable from that of SCA7.

The patient is a 56-year-old Japanese man, whose father died of stroke at the age of 49 years and whose mother died of gastric cancer at the age of 70 years. He has a 54-year-old sister, who was diagnosed with spinocerebellar degeneration elsewhere, although details are not known. He has no other brothers or sisters. At the age of 45 years, he noticed an unsteadiness of gait and slurred speech, both of which progressed gradually. He began to use a wheelchair by the age of 53 years. Neurological examination at the age of 56 years showed a slowing of saccadic eye movements, scanning speech, facial dyskinesia, bilateral limb ataxia and pyramidal signs. Brain magnetic resonance imaging showed atrophy of the pons and cerebellum.

The patient began to experience visual impairment at the age of 51 years. Ophthalmological examination at the age of 56 years showed that his best-corrected visual acuity was 0.2 OD and 0.1 OS. Intraocular pressures were normal and his media were clear. Fundus examination showed mild atrophy of the macular retinal pigment epithelium, with very small clumps of pigment in both eyes (fig 1). Foveal reflex was lost and a coarse granular appearance was noted in the macular region, but choroidal neovascularisation was absent. No signs of inflammation were noticed either in the anterior segment or in the retina. A relative central scotoma was detected in both eyes by Goldmann perimetry. Ishihara and panel D15 colour vision tests showed an inability to distinguish any colours. Single-flash electroretinography showed negative β wave pattern and mild attenuation of the oscillatory potentials. Phototropic electroretinography also showed mild attenuation of each wave. On the basis of these findings, we diagnosed for his visual disturbance as PMD.

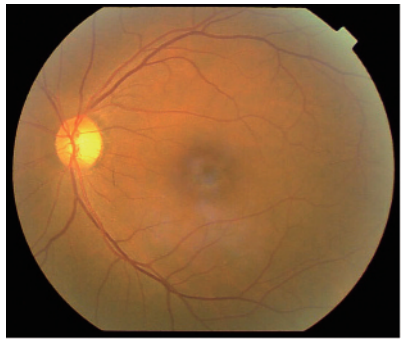

Figure 1 Photograph of the patient's left fundus. Coarse granular appearance with pale areas of pigmentary atrophy in the macular region was noted. The small clumps of pigment in pale areas were observed by fundus examination with slit-lamp biomicroscopy. No abnormalities were observed outside the macular region. Similar findings were present in the right fundus.

As both his fundoscopic and electroretinographic findings closely resembled those reported in SCA7 PMD, [4] we suspected that the patient might have SCA7. We carried out genetic diagnosis with the informed consent of the patient. We obtained a blood sample from the patient, extracted genomic DNA from the peripheral leucocytes and then analysed the CAG repeat-containing fragment in the SCA7 locus, using previously described conditions.[5] Unexpectedly, the patient had homo normal alleles with 14 CAG repeats, excluding the diagnosis of SCA7. Next, we analysed the SCA1 locus using similar methods.[1] The patient had a normal allele with 26 CAG repeats and an expanded allele with 51 CAG repeats. The sequences were as follows: $(CAG)_{13}CAT\ CAG\ CAT\ (CAG)_{10}$ in the normal allele and $(CAG)_{51}$ in the expanded allele. We diagnosed the patient's illness as SCA1 on the basis of these results.

The SCA1 patient reported here developed PMD indistinguishable from that of SCA7. At present, we do not know if the PMD observed in our patient is an unusual phenotype of SCA1 or a rare coincidental complication. For instance, an interesting possibility is that a causative gene of hereditary PMD might be located in the vicinity of the SCA1 locus and mutated in our patient. In either case, our findings indicate that SCA1, in addition to SCA7, should also be considered in the differential diagnosis of hereditary spinocerebellar degeneration complicated by PMD.

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Reinfection with Lyme borreliosis presenting as a painful polyradiculopathy: Bannwarth's, Beevor's and Borrelia

Lyme disease is caused by a tick-borne spirochaete, *Borrelia burgdorferi*. Infection may be asymptomatic, may cause only erythema migrans (spreading from the site of the tick bite) or may cause disseminated disease affecting many organs, including the nervous system. Infection with *B burgdorferi* is transmitted by ixodid ticks, which are found in many parts of the UK. Their activity is seasonal, with peaks in summer and early autumn. The risk of human infection mirrors tick activity, with peak periods in summer and early autumn, although patients may present with later-stage manifestations throughout the year.

A 53-year-old man presented in September 2004 with a 3-week history of pain in the left flank and lumbar region, associated with hypersensitivity in the left lower abdomen; 5 days before admission, the right side also became affected. Constipation and hesitancy of micturition, with preserved sensation, had been present for 3 days. No weakness in the legs, fever or rash was observed. The patient was a non-smoker and drank <30 units of alcohol a week. He was regularly exposed to the risk of tick bite owing to the area of residence and recreational activities, but he denied recent tick bites. Six years earlier, the

patient had presented with erythema migrans, fever and a painful hip. Lyme disease was confirmed serologically, with a positive serum IgM immunoblot to *Borrelia* outer surface protein C and 41-kDa protein; IgG immunoblot was negative. Treatment with doxycycline for 21 days was associated with full recovery. Since then, he has been in good health.

General examination showed no superficial lymphadenopathy, arthropathy or rash. No abnormal signs were detected in the chest, cardiovascular system and abdomen (including digital rectal examination and assessment of anal tone). Neurological examination showed normal gait and heel–toe walking. The cranial nerves were intact. In the limbs, power and sensation were normal. Reflexes were reduced in the left knee and ankle: plantar reflexes were bilaterally flexor. An attempt at sitting up from the supine position resulted in upward movement of the umbilicus (Beevor's sign).

T2-weighted MRI of the thoracic spine showed focal non-specific intramedullary abnormal signal at T9–T11, with no associated expansion of the cord. MRI of the brain and craniocervical region was normal. The CSF protein was 1.25 g/l; IgG oligoclonal bands were detected (but were not present in serum). In the CSF, 250 cells/ml were detected, which were predominantly reactive lymphocytes. No malignant cells were identified. Herpes simplex-1 and Herpes simplex-2, varicella zoster, cytomegalovirus and Epstein–Barr virus were not detected in the CSF by polymerase chain reaction (PCR). No bacteria, mycobacteria and fungi were grown in CSF. Other blood investigations showed normal results, including prostate-specific antigen and immunoglobulin electrophoresis and quantification. From serological tests on blood, negative results were obtained for syphilis (*Treponema pallidum* haemagglutination assay and rapid plasma reagin assay), rheumatoid arthritis factor, antinuclear antibodies and extractable nuclear antigen antibodies; Bence Jones protein was not detected in urine. Electrocardiograph, chest radiograph, abdominal ultrasound scan and isotope bone scan were normal.

Serum was strongly positive (optical density 1.39) in the *Borrelia* C6 peptide enzyme-linked immunoassay (Immunetics, Boston, Massachusetts, USA). This synthetic peptide antigen-based test has greater specificity than some screening tests based on whole-cell lysate antigens. Serum IgM immunoblot was positive (bands at *Borrelia* outer surface protein C and at 39 and 41 kDa proteins), IgG immunoblot was negative. In CSF (tested at 1:10 dilution), IgG immunoblot was positive (bands at *Borrelia* outer surface protein C and at 20, 39, 41 and 58 kDa proteins). Insufficient CSF was available for borrelial DNA detection tests by PCR or for IgM immunoblot and more detailed assessment of intrathecal antibody synthesis.

The patient was treated with ceftriaxone 2 g a day intravenously for 10 days. Seven days after admission to hospital, he developed a left VII cranial nerve palsy: this was treated with a 10-day course of oral prednisolone and the patient fully recovered from the palsy. In May 2005 (after 8 months of follow up), serum *Borrelia* C6 peptide enzyme-linked immunoassay was positive (optical density 1.17) and IgG immunoblot was positive (bands at *Borrelia* outer surface protein C and at 20, 39, 41 and 58 kDa proteins). In July 2005, after 15 months of follow up, the patient had no residual neurological deficit. His serum showed a C6 peptide enzyme-linked immunoassay reading of optical density 0.87. IgG immunoblot was positive, but with weaker reactions than in May 2005 (tested in parallel). IgM immunoblot was negative.

This patient presented with a painful inflammatory thoracic motor and sensory polyradiculopathy (Bannwarth's syndrome).[1] The positive Beevor's sign (weakness of the lower abdominal muscles, due to a cord or root lesion at or below T10)[2] was confirmed by MRI. Other causes of a positive Beevor's sign include facioscapulohumeral dystrophy and myopathy, which were absent in this patient. The initial differential diagnosis based on the magnetic resonance appearances was malignant infiltration or varicella zoster infection, sine herpete. These possibilities were excluded by the negative findings from CSF cytology and PCR studies, by isotope bone scanning and by other investigations. Instead, Lyme borreliosis was diagnosed on the basis of the patient's history, residence in an endemic area and serological results indicating reinfection.[3] Development of facial weakness supported a diagnosis of neuroborreliosis. The CSF lymphocytosis and raised levels of CSF protein were also typical findings for acute neuroborreliosis. Neuroborreliosis with malignancy simulating meningopolyneuritis has been described previously,[4] but has not been reported as a presentation of reinfection with *B burgdorferi*.

This case serves to underscore several clinical points. Firstly, Lyme borreliosis may present by mimicking a malignancy. Secondly, a previous episode of borrelial infection may not confer immunity. Reinfection is uncommon, but is more likely to occur in patients whose previous episode was promptly treated rather than in those with longstanding infection, who have a well-developed antibody response before treatment.[5] Thirdly, patients may not specifically recall a tick bite. Thus, it is important that a history of tick exposure risk, which may be residential, occupational or recreational, is sought from patients. Finally, Beevor's sign has a useful localisation value.

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Informed consent was obtained for publication of the patient's details in this report.

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What's in a name—familial rectal pain syndrome becomes paroxysmal extreme pain disorder

The condition generally known as familial rectal pain syndrome is a rare autosomal dominant disorder that was first described by Hayden and Grossman.[1] The term familial rectal pain, was coined by Dugan.[2] The OMIM database (http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id = 167400) uses the term ''pain, submandibular, ocular and rectal, with flushing''.

The disorder starts in the neonatal period (possibly in utero) and is lifelong. Its most characteristic clinical features are attacks of excruciating pain that affect various parts of the body, including the rectum, genitalia, face and limbs. In addition, other features reflecting autonomic dysfunction occur, including harlequin colour changes and pupillary abnormalities. Some patients with the disorder experience non-epileptic tonic seizures during severe episodes of pain. These may be associated with cardiac asystole.

Over the past decade, a worldwide consortium of clinicians, geneticists and scientists have been attempting to find the cause of familial rectal pain and recently discovered that it is caused by mutations in the sodium channel *SCN9A*.[3] The consortium has worked closely with patients affected by the disorder and their families. During this collaboration there was considerable dissatisfaction with the name ''familial rectal pain syndrome''.

Consequently, a conference was arranged at the offices of the charity called Contact a Family (http://www.cafamily.org.uk) in London on 6 September 2005. Members of the consortium, along with affected people and their families, debated whether the name should be changed and, if so, to what. Others participated by email.

Whether the condition should be named according to its clinical features or on a more scientific basis reflecting the new knowledge that it is a channelopathy or that it appears to be a disorder principally affecting the autonomic nervous system was discussed initially. All preferred the first approach, partly because it was felt that a name should have meaning for the general public and also for the medical and scientific communities and partly because mutations in the sodium channel have not been found in all those affected with the disorder.

There was near unanimity that the term rectal should be dropped. This was partly because its inclusion seems to imply that the pain is confined to the rectum, when in fact this is only one affected site. In addition,