Fragile X premutation presenting as essential tremor

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swelling and inflammatory infiltrates as the patient did not complain of back pain or radiculopathy, and his EMG and conduction studies were normal.

We were successful in the identification of Sphingomonas paucimobilis gene sequences from our patient’s muscle DNA. Sphingomonas paucimobilis (formerly Pseudomonas paucimobilis) is a strictly aerobic, gram negative bacillus that is widely distributed in water and soil. This microorganism is responsible for a variety of community acquired and nosocomial infections but, to our knowledge, there are no clinical reports of skeletal muscle infection in the literature. The origin of the infection could not be established in our patient: he was not immunocompromised or debilitated, and had no history of recent wounds. It may be that Sphingomonas paucimobilis acted as an opportunistic pathogen given the mild upper respiratory tract infection that preceded the onset of muscle pain and that may have been responsible for a mild decrease in immunological defences. Infection with Sphingomonas paucimobilis appears to have limited inherent virulence and no deaths related to this entity have been reported in the literature. Thus the benign disease course in this patient may have been a result of the combination of the limited virulence of Sphingomonas paucimobilis itself, the antibiotic treatment and the short course of prednisone he had received. Unfortunately, we did not culture the patient’s muscle biopsy to isolate causative bacteria, and thus we cannot be conclusive about the aetiological role of Sphingomonas paucimobilis in localised myositis. However, the possibility of contamination either during biopsy or in the procedure of DNA extraction and analyses is unlikely because of the strictly aseptic sterile techniques we routinely use. Moreover, if contamination were the cause, more common bacterial sequences should have been identified.

At this point, a casual conclusive relationship between the observed Sphingomonas paucimobilis genome and myositis remains to be demonstrated. However, we do feel that the aetio-pathogenesis of localised myositis is heterogeneous, and although uncommon, Sphingomonas paucimobilis infection must be considered in the differential diagnosis of patients presenting with focal inflammatory muscle disease.

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CASE REPORT

A 62-year-old right-handed man presented with an action (kinetic) tremor initially affecting his left hand. This progressed over 5 years to involve both his hands and legs, interfering with writing and fine motor activities. Alcohol had no effect on the tremor. He complained of being unsteady but denied any falls or slowing of movement. His medical history was significant for ischaemic heart disease and previous myocardial infarction. There was no family history of tremor or movement disorder. His sister’s grandson has fragile X syndrome, and the case described here was found to carry an unmethylated expansion within the premutation range of the FMR1 gene through cascade screening 7 years ago (88 repeats). There was no history of a neurological disorder or premature ovarian failure in the female carriers. Two months after this man’s result was reported, his own grandson was shown to have fragile X syndrome.

Neurological examination revealed a bilateral postural tremor more evident on the right than the left, and a 4–6 Hz intention tremor with finger-to-nose testing. Handwriting was large but legible. The tremor interfered with his ability to draw an Archimedes spiral and led to corruptions of a straight line drawn on the page. Examination of the cranial nerves showed subtle facial masking, mild dysarthria but no may mimic this condition. Here we describe a 62-year-old right-handed man with an action (kinetic) tremor fulfilling diagnostic criteria for ET which was the presenting feature of the fragile X associated tremor/ataxia syndrome. His sister’s grandchildren were the clue to the diagnosis, illustrating the importance of a detailed medical history in descendants as well as ancestors in the context of late onset neurological disorders.

ET, typically a symmetric bilateral postural tremor with fluctuating amplitude, can be asymmetric and varies both in severity and functional impact. It classically begins in the fourth and fifth decades of life, is frequently associated with a family history and affects 0.8/1000 (95% confidence interval 0.5 to 1) of the general population, with a prevalence that increases with age. ET is one of the most common movement disorders seen in routine neurological practice, and the diagnosis is usually straightforward. The challenge is to recognise often subtle features that point towards an alternative cause of the tremor, which can have important implications for treatment, prognosis and genetic counselling. The fragile X associated tremor/ataxia syndrome (FXTAS) is one recently described disorder that enters the differential diagnosis of ET.1–3 In this video case report, we show the features of FXTAS which may lead to a possible diagnosis of ET, demonstrate that additional often subtle clues point towards an underlying genetic cause and emphasise the importance of thorough history taking.

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Essential tremor (ET) is one of the most common movement disorders seen in routine neurological practice, but other diseases

Figure 2 Slow tau inversion recovery MRI of the upper third of the patient’s legs. (A, B) Diffuse hyperintensity of the medial head of the gastrocnemius. (C, D) Normalised picture 10 months later.
rigidity. Nystagmus was evident on extreme lateral gaze only. He had bilateral pes cavus and was areflexic. Tandem gait was impaired. Romberg’s test was negative (see video, available online).

Preliminary investigations, including routine bloods, thyroid function tests and nerve conduction studies were within normal limits. Formal cognitive testing was within normal limits (Addenbrooke’s cognitive examination score 97/100, Mini-Mental State Examination (MMSE) 28/30). MRI of the brain revealed generalised atrophy, particularly affecting the frontal lobes and cerebellum, with characteristic low signal in the middle cerebellar peduncles on T1 and high signal on T2 sequences (fig 1).

DISCUSSION
Clinically, the patient fulfilled the diagnostic criteria for ET, and given the prevalence of ET, could the association with ET simply be a chance finding? The patient described here also had the classical clinical and imaging features of FXTAS, with a postural tremor developing in mid-adult life, high signal in the middle cerebellar peduncle on MRI and an unmethylated expansion within the premutation range of the FMR1 gene. He therefore shares core features with other patients with FXTAS, falling within the “probable” FXTAS group in recent proposed diagnostic criteria. It is therefore highly likely that his movement disorder is due to the FMR1 expansion. The gait ataxia, mild dysarthria and areflexia are subtle clinical clues that the diagnosis was not ET. Subsequent neurophysiological studies were within normal limits. All of these features have been described in FXTAS, and point away from ET as the diagnosis. The normal Addenbrooke’s cognitive profile and MMSE highlight the relative insensitivity of these tests to frontal/subcortical deficits. This case highlights the importance of considering FXTAS in cases of ET, particularly if there are atypical features, and stresses the value of taking a detailed family history, even though neurodevelopmental difficulties in the grandchildren or nephews may not appear to be relevant.

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> Video material is available online only at http://jnnp.bmj.com/content/vol79/issue10

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