been implicated in the past, but symptoms appeared approximately four weeks after the last dose of gentamicin. It is possible that one or more of the previously administered cyclophosphamide may have been responsible, but this has not been reported before, and the last course of treatment was eight weeks before the onset of her neurological symptoms. The possibility is that our patient developed OM as a direct manifestation of Hodgkin's disease, but at the time of development of OM the extent of her disease had considerably reduced following high dose chemotherapy. Furthermore, before the onset of neurological symptoms she had had clinical and radiological evidence of regression of her disease. Normal CT and MRI scans of her brain excludes a diagnosis of cerebral Hodgkin's disease. A metabolic abnormality resulting from destruction of Hodgkin's disease tissue is also unlikely, although it has been previously postulated that production of neurotoxic amines and/or peptides might be responsible.1 This report, however, failed to show any correlation between the presence or severity of OM and the routinely available antitumour antibodies. Support for an autoimmune basis to paraneoplastic OM has come from reports of a specific antineuronal autobody (anti-Ri) in the serum of patients with opsonolus and breast carcinoma.6 The presence of the Ri antigen in tumour tissue of these patients suggests that it is the body's immune response to a tumour antigen that elicits the antibody response. There was no evidence of an autoimmune serological data to support such a response in our patient, it is possible that breakdown of lymphomatous tissue resulting from effective chemotherapy led to the production of antineuronal antibodies and the subsequent development of OM.

Treatment for opsonolus from whatever cause remains uncertain. While some authors recommend ACTH or steroids,7 this is by no means proven beneficial. At least, very least, it is imperative to treat the underlying condition.

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9 Bolstbauer E, Deonna T, Hirt HR. Myclonic encephalopathy of infants, or 'dancing syndrome'. Helv Paediatr Acta 1979;34:119-33.

Very late onset X-linked recessive bulbospinal neuromopathy: mild clinical features and a mild increase in the size of tandem CAG repeat in androgen receptor gene

X-linked recessive bulbospinal neuromopathy (X-BSNP) is an adult-onset hereditary motor neuronopathy characterised by bulbar symptoms, slow, progressive proximal muscular atrophy, and endocrinological abnormalities.1,4 Generally, the age at onset of X-BSNP ranges from the third to fifth decade,5,6 and activities of daily living of most patients with this disease significantly decline within fifteen years of onset.7 Recently, patients with X-BSNP were found to have an abnormally elongated tandem CAG repeat in the first exon of the androgen receptor (AR) gene.8 The increased number of CAG repeats in AR gene is, however, considerably variable among patients. We report a very late onset and very mild case, and the abnormal elongation in his AR gene was also mild. An 84 year old Japanese man with no family history of any related disease, noted mild difficulty in climbing stairs when he was in his mid seventies. In 1991, at the age of 83, painful muscular cramp in the calves and difficulty in walking was more apparent, although he could ride a bicycle and work in the field. He was referred to our hospital in January 1992. A neurological examination showed diffuse muscular weakness and remarkable atrophy in his four extremities as well as in the truncal and facial muscles. The tongue was mildly atrophied, but there was no hyperpigmentation of the skin. Deep tendon reflexes were generally absent and there were no pathological reflexes. Fasciculation was remarkable in his face, tongue, neck, anterior chest, arm and leg muscles, and there were no mild voluntary contractions. There was neither apparent sensory disturbance, cerebellar ataxia, nor nystagmus. The plasma creatine kinase level was mildly increased. Oestrone sensitivity was noted. Glucose tolerance was normal. There was no hyperlipidaemia nor liver dysfunction. The endocrinological studies showed that the steady-state level of plasma testosterone was normal but plasma oestrone and oestradiol were mildly elevated. The suppression test conducted by oral administration of fluoxymesterone for six days showed a normal suppression to testosterone luteinizing hormone (LH) and follicle-stimulating hormone (FSH). Needle EMG studies showed generalised high amplitude NMU potentials with reduced NMU interference in the muscles examined. A nerve conduction study conducted showed normal motor conduction velocities in the median and tibial nerves, but no sensory action potential in the sural nerve. Nerve biopsy revealed moderate reduction of large myelinated fibre density, and a muscle biopsy of the vastus lateralis showed scattered grouped atrophy, clusters of picnotic nuclear clumps, and hypertrophic fibres which often contained internal nuclei.

The number of tandem CAG repeats in the first exon of his AR gene was determined on genomic DNA obtained from his peripheral blood leukocytes, using polymerase chain reaction and cycle sequencing technique. In the number of tandem CAG repeat was 40, which was the shortest in our series of patients with X-BSNP (45 cases with a range from 40 to 55; the normal range being from 17 to 24 in our series).9

The extremely late onset of illness and well preserved function were quite unusual for X-BSNP, although diffuse muscular wasting in the limb muscles, contraction fasciculation and mild tongue atrophy of this patient suggested motor neuron disease. Moreover, absence of familial inheritance, and lack of glycaemia, glucose intolerance, hyperlipidaemia and liver dysfunction were incompatible with this disease. However, detection of AR gene mutations with an abnormally increased size of a polymorphic tandem CAG repeat10 clearly confirmed a diagnosis of X-BSNP. Determination of AR gene mutations is useful not only for the pre-onset diagnosis or carrier detection of X-BSNP11 but for the clinical diagnosis of atypical patients as seen in the present case.

In a majority of patients with X-BSNP, plasma testosterone, LH and FSH are poorly suppressed after oral administration of fluoxymesterone (Morishima et al, unpublished data). The study of Oestrone suppressibility in this disease is known to be varied among the patients. We have shown that the number of CAG repeats in AR gene is correlated with age at onset of illness. The mild clinical severity of the age-adjusted muscular weakness, suggesting that the size of an abnormally elongated CAG repeat in AR gene is one of the factors determining the clinical severity of X-BSNP, as was recently documented in fragile X syndrome12 and myotonic dystrophy.13 These correlations among age at onset, clinical severity and increased size of the tandem CAG repeat were confirmed in our controls, although the precise mechanism of the fluoxymesterone suppression on these gonadal and gonadotropic hormones is not clear, it may reflect some aspect of androgen target organ sensitivity.13 The normal suppression pattern of plasma testosterone, LH and FSH in this patient could also be explained by the mildest elongation of tandem CAG repeat in AR gene.
Transient musical hallucinosis

Paquier et al reported a patient who, following a subarachnoid haemorrhage, developed musical hallucinosis. Based on a literature review, they suggested that musical hallucinosis, formed auditory perceptions that occur in the absence of an external acoustic stimulus while the patient is aware of their non-real nature, may result from lesions of either side of the brain, and not necessarily from the limbic system, as previously proposed.1 A patient recently seen by us reinforces the authors’ conclusion.

A 75 year old right handed woman had been suffering from severe hearing loss due to senile otosclerosis for 30 years. Her past history revealed no insulin dependent diabetes mellitus, ischaemic heart disease, peripheral vascular disease and paroxysmal atrial fibrillation. In September 1992, she suddenly developed right hemiparesis and dysphasia which recovered within a few weeks. Her CT scan revealed a left thalamic infarction, mild cortical atrophy and ventricular dilatation. A few days after the event, she started hearing a melody, which seemed in the first days to originate extraneously and was heard bilaterally. The melody she heard was extremely loud, leading her to ask surrounding people to turn off the radio, which she believed to be the source of the tune. The melody was sudden, weak, slow, clear and reminiscent of popular songs that she had heard in her youth, but were still unknown to her. She was able to sing this melody. Shortly after the onset of this phenomenon, she gained full insight into the problem and realised that this incessant tune originated in her own mind. The volume was variable and sometimes the melody was enjoyable; the volume was mostly high, especially during the night, disturbing her sleep, and severely interfering with her daily activities. Amitriptyline partially helped her sleep. The intensity of the music diminished during the following weeks, but the same melody persisted.

Musical hallucinations after stroke are reported rarely. Only three cases, all with right hemispheric pathology, were quoted in a recent review.1 Our patient illustrates the fact that dominant hemispheric stroke can also result in musical hallucinations.

As with so many reported cases, including that of Paquier et al, our patient had suffered from hearing loss for many years. Berrios in a review, pointed out that musical hallucinations are far more common in elderly, hearing impaired, female patients.1 It is possible to assume that the musical hallucinations represent a “deafferentation” phenomenon, reminiscent of visual hallucinations in the blind, thalamic pains or phantoms limb. It appears that both central and end organ pathology contribute to the appearance of musical hallucinations.1 The prolonged lack of normal input to cortical areas involved in hearing, due to peripheral disease, might cause a specific vulnerability which results in the generation of this abnormal sensation following a central insult. Appropriately, Wengel et al entitled their manuscript “musical hallucinations, the sounds of silence”,4 as they occur when the mind is chronically deprived from music and sound.

The inhibition was revealed in our studies during a period of voluntary contraction by stimulating the motor cortex at a strength lower than that required to produce excitation under the same conditions. A recent study has reported that the discharge of motor neurons in the first dorsal interosseous muscle of the hand of a patient with multiple sclerosis could be suppressed by transcranial magnetic stimulation of the motor cortex, but this was not observed in normal subjects.1 In our previous studies1 we averaged the rectified surface electromyogram (EMG) to reveal inhibition of voluntary contraction in a number of different arm and hand muscles. We have now re-investigated one of our subjects to examine the effect of transcranial magnetic stimulation on the probability of discharge of single motor units in the first dorsal interosseous muscle. We can confirm that transcranial magnetic stimulation at a strength which causes a reduction in gross surface EMG, and is sub-threshold for excitation, does lower the probability of discharge of individual motor units in normal humans.

The subject was a right handed male (age 49 years) with no history of neurological illness. Local ethical approval was obtained and the subject gave his informed consent to the procedures. Two forms of electromyographic recordings were made from the first dorsal interosseus muscle of the right (dominant) hand. Gross EMG, surface electrodes were placed over the belly of the muscle and at an indifferent point over the proximal interphalangeal joint of the first digit. A concentric needle electrode was inserted percutaneously into the first dorsal interosseous muscle to record the discharges of single motor unit. The subject was required to make a weak voluntary contraction of the muscle. Auditory feedback of the signal was provided to enable the subject to recruit and maintain the discharges of a motor unit that could be reliably identified and selected for peri-stimulus time histogram analysis. Transcranial magnetic stimulation was delivered from a Novametrix 200 stimulator using a 9 cm round coil centered over the vertex. The initial direction of current flow in the coil was anti-clockwise and adequate stimuli preferentially excited muscles on the right side.

The threshold transcranial magnetic stimulation required to produce an initial excitatory response, gauged from the surface EMG recording, was 40% of maximum output. The response had a latency of 23 ms and was followed 5–8 ms later by a period of suppressed EMG lasting 30 ms and culminating in a late period of increased EMG activity. Part A of the figure shows the average of the full-wave rectified surface EMG response to 50 magnetic stimuli at 77% of output. The occurrence of the reason for any suggestion that anesthesia of the penis occurs on transplantation of the organ is suggested. A prominent feature of the period of the negative EMG response was its dependence on the number of stimuli.
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