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Letters

Metachromatic leukodystrophy: conduct disorder progressing to dementia

Sir: Metachromatic leukodystrophy (MLD) is an inherited autosomal recessive disorder of myelin metabolism, characterised by the accumulation of galactosyl sulfatide in the central and peripheral nervous system due to deficiency of arylsulfatase A activity.[1] Four varieties are described: congenital, infantile, juvenile and adult. In the adult form a psychotic disorder or dementia typically precedes the onset of neurological symptoms. The earliest age of onset of the adult form is variously given as 21[2] or 16.[1] A 5–10 year survival is common, but the course may progress over several decades.[2–4] A general trend appears to be that the earlier the age of onset, then the earlier the appearance of neurological symptoms.

We report a case with early onset, a prolonged course and eventual presentation with psychiatric features, but no abnormal neurological signs.

The patient, aged 29 years, was referred for a second opinion in 1985, having been admitted 2½ years earlier to a psychiatric hospital with a provisional diagnosis of schizophrenia. Certain organic features in her mental state had then given rise to concern.

Her birth and early development had proceeded entirely normally. At school she was said at first to be sociable, reliable, proficient at reading and writing and was of average academic ability. However, at the age of 11 yr she changed, becoming increasingly disruptive, attention seeking, and unable to maintain friendships. By the age of 16 she was seen by a child psychiatrist who concluded that though of average intelligence she suffered from a severe personality disorder. Causal factors for this could not be identified. She appeared to lead a "fantasy life", sometimes behaving in a dangerously abnormal manner, for example on one occasion walking across a busy motorway. On leaving home at the age of 16 she held jobs for a short time only and led increasingly the life of a vagrant, moving from town to town, and obtaining money from petty theft or prostitution. She proved incapable of maintaining personal relationships and was increasingly erratic in her behaviour. She gave birth to two illegitimate children, whom she was unable and unwilling to care for. All of this was in contrast to a family background of good stability, with no family history of psychiatric or neurological illness. Her two younger siblings now aged 23 and 19 years, remained socially well adjusted.

On a number of occasions, while on remand, she was examined by prison medical officers and at all times gave the impression of being of average intelligence. A label of psychopathic personality disorder was repeatedly applied. This pattern of behaviour continued until her admission at the age of 26 to High Royds Hospital, Leeds, having been found wandering the area in a dishevelled state and unable to give an account of herself. On examination she was shabby and childlike in her appearance, and spoke in a variety of regional accents, swore frequently and repeated stereotyped phrases such as "egg but no bacon". She would smile fatuously, laugh or cry for no apparent reason and was uncooperative with cognitive testing. The initial diagnosis was of schizophrenia. Ultimately it was possible to demonstrate grossly impaired short term memory, poor writing and constructional apraxia. Primitive reflexes were elicited but no other abnormality of the central or peripheral nervous system was reported. CT scan showed cerebral atrophy with periventricular white matter change around the anterior and posterior horns. Lumbar puncture showed a raised CSF protein. She had WAIS (IQ) scores of: Verbal 59, Performance (Prorated) 40 and Full Scale (Prorated) 48.

She was transferred to the Bethlem Royal Hospital for further investigations and opinions on diagnosis. Her mental state appeared largely unchanged, although right-left disorientation, difficulty in following complex instructions and nominal dysphasia were now noted. However, neuropsychological opinion was that such features were in keeping with her level of global intellectual deficit. Occasional urinary incontinence had also developed. Consultant neurological opinion confirmed the absence of other abnormal neurological signs. The differential diagnosis appeared to lie between Huntington's chorea, Wilson's disease, or metachromatic leukodystrophy to account for the undoubted dementia at such a young age.

Routine biochemical and haematological investigations were normal, as was a search for abnormal amino-acidurias, heavy metals in the urine, and chromosome studies. Arylsulfatase A activity, however, assayed in leukocytes was 20% of control levels with a synthetic substrate (nitrocatechol sulphate), and was completely absent with natural substrate; similar results were found using cultured skin fibroblasts. Metachromatic granules were present in the urine. EMG showed slightly reduced sensory conduction velocity in the lower limbs, but EEG was normal, as was repeat CSF protein. A repeat CT scan showed similar but more marked changes than before and was reported to be consistent with metachromatic leukodystrophy.[5] MRI scan showed a symmetrical abnormal signal in the periventricular white matter occurring diffusely in the hemispheres, but most particularly in the frontal regions (fig).

We believe this case to be unusual in two respects. First, the apparent age of onset at 11 years, and second the prolonged insidious presentation as a change in personality.

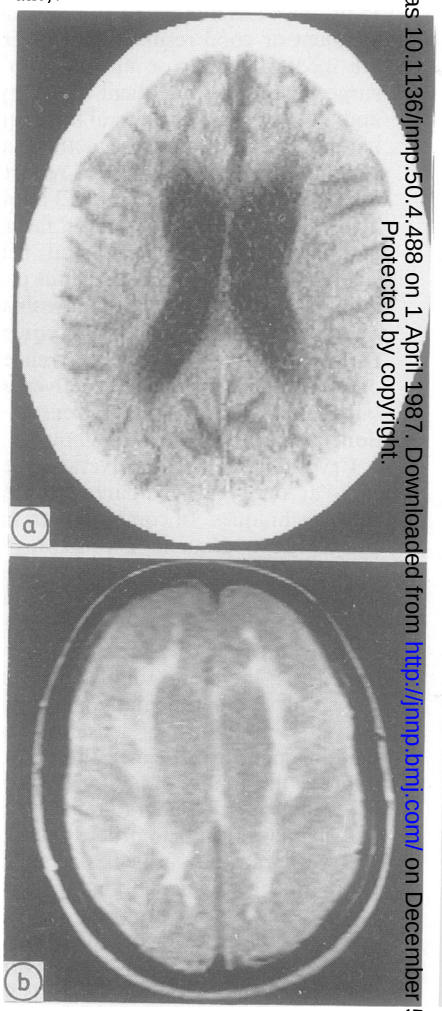

Fig *CT scan and MR scan of patient (CT above, MR below). See text.*

It might be argued that this woman suffered from two distinct disorders, initially a personality disorder, and then later and coincidentally developing metachromatic leukodystrophy. However, the changes in her personality are very much of the type described in other cases of adult metachromatic leukodystrophy.[2-4 6 7] The extended period before clearly organic symptoms appeared is, however, atypical. An alternative is to suggest that she had juvenile metachromatic leukodystrophy. However, the pattern of onset, especially the lack of neurological signs after 18 years of illness and the normal EEG, make this highly unlikely.

Adult metachromatic leukodystrophy is a rare condition, with 15 cases reported between 1977 and 1983,[1] and it is therefore not surprising that the natural history is incompletely documented. At present there is no biological marker to distinguish the adult form from other metachromatic leukodystrophy subtypes, although the assay of intracellular cerebroside sulphatase activity[8 9] may prove to be of value when sufficient data have been collected. Thus, when subdividing the disease we should rely more on the pattern of clinical features and investigations, using age of onset and time course as a rough guide only, accepting that in these areas there will be an overlap with other subtypes.

It seems possible that as psychiatrists become more aware of the condition, and of the availability of an enzyme marker test for it, other examples similar to the patient just described may come to light.

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Tremors of the smile

Sir: It is our observation that facial tremors on muscle contraction can occur in conditions producing generalised tremors; for example, multiple sclerosis, valproate toxicity, alcohol withdrawal and anxiety. Recently we encountered an unusual case of a patient exhibiting isolated bilateral idiopathic tremor of the face induced only by spontaneous or volitional contraction of the risori muscles.

A 27 year old female had a 9 year history of progressive tremor of the perioral facial muscles induced either by spontaneous smiling or volitional contraction. Forceful smiling abolished the tremor and seemingly there was a set point of contraction effort (motor unit recruitment) required for tremor production. Fatigue during contraction and stress increased the intensity (amplitude) of the tremor but reduced its frequency. Unilateral muscle contraction of the risorius induced ipsilateral tremor only. Her late father had a similar lifelong tremor. She had no other neurological symptoms, and examinations were normal except for the tremor described. Computed tomography of the brain with selective thin sectioning of the posterior fossa showed no abnormalities and one magnetic resonance imaging of the brain was normal. She refused spinal fluid examination. Standard electroencephalogram (EEG) was normal and EEG recordings during tremor showed no time-locked cortical potentials (myoclonus). Masseter reflex latencies and amplitudes, blink reflex studies and facial nerves compound muscle action potential amplitudes and latencies were normal. Facial, tongue and masseters electromyograms (EMG) were normal. Synchronous 5–6 Hz tremor with burst duration of 75 to 125 ms and 600–800 μV amplitude was recorded from risori muscles with concentric needle electrodes (TECA CF 25, 26 gauge; TD 20 EMG recording system). Tremor appeared on moderate contraction effort (fig A) and was suppressed by maximal contraction of the muscles (fig C). Unilateral contraction induced ipsilateral tremor (fig B). Right arm median sensory potential was normal. The patient greatly improved with oral propranolol 80 mg a day.

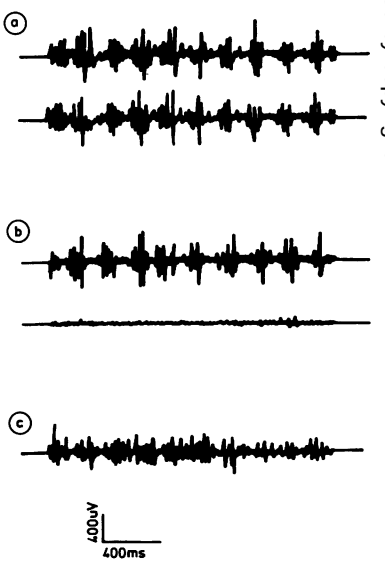

Fig *Tremor recorded with concentric needle electrodes. (A) 5–6 Hz synchronous tremor of risori muscles on moderate effort of contraction. (B) Unilateral tremor of risorius induced by ipsilateral moderate effort contraction. (C) Tremor is suppressed by maximum effort of contraction of risori muscles (only one side shown in the figure).*