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Pseudotumour cerebri with amiodarone

Sir: Amiodarone is a relatively safe antiarrhythmic agent, but is also has some extracardiac side effects, which may involve the cornea, the skin, the thyroid, the lungs, the gut and the nervous system. The neurological side effects include tremor, sleep disturbances, headaches[1] amd, less commonly, peripheral neuropathy,[2] proximal weakness and cerebellar dysfunction.[3] We report a case of pseudotumour cerebri (PTC) as another possible side effect of amiodarone.

A 58-year-old man had been treated for 6 months with amiodarone (400 mg/day) for supraventricular arrhythmias on exercise. He had also received pindolol (5 mg/day), allopurinol (100 mg/day) and clofibrate (500 mg/day) for several months prior to amiodarone. He was referred to us after he developed acute blurring of vision in the right eye. The general examination was normal except for a moderate obesity (81 kg, height 162 cm). The blood pressure was 180/90 mm Hg and the ECG was normal. The neurological examination showed bilateral papilloedema, which predominated in the right eye, with normal visual acuity (1·0 in both eyes). A partial inferior field defect was present in the right eye. The CSF pressure was 300 mm H_2O with normal protein (305 mg/l), leucocytes ($2{\cdot}8.10^6$/l) and glucose (5·0 mmol/l). A brain CT scan, including a survey of the pituitary and orbital regions, was entirely normal. Standard blood and urine tests were normal. A diagnosis of pseudotumour cerebri was made. Acetazolamide (3 × 250 mg/day) was administered for 5 months and prednisone (60 mg/day) for 1 month, but both were discontinued in the absence of improvement. The CSF pressure also remained elevated (range 270 to 300 mm H_2O) on follow up 2, 5 and 12 months later. At 12 months, neurological examination still showed bilateral papilloedema with developing disc atrophy. Visual acuity was 1·25 (OD) and 0·8 (OS). Corneal deposits typical of amiodarone were present. Serum levels of amiodarone were determined by HPLC and were within the optimal range,[4] that is 1·5 mg/l for the parent drug ($n = 1{\cdot}93 \pm 0{\cdot}80$) and 0·9 mg/l for its major metabolite, desethylamiodarone. Because of the possible side effects, amiodarone as well as any other medication were withdrawn. Sequential spinal taps after 4 and 7 days showed a decrease in CSF pressure (180 and 80 mm H_2O). During the following months the visual acuity improved (1·5 (OD) and 1·0 (OS)) with disappearance of the papilloedema. Some degree of optic disc atrophy persisted bilaterally. A partial field defect also remained in the inferior nasal quadrant of the right eye.

This observation suggests that pseudotumour cerebri was induced by amiodarone because it developed shortly after amiodarone was administered and resolved after the drug was discontinued. The other drugs had been administered previously for a much longer time. The role of amiodarone in the pathogenesis of pseudotumour cerebri is also suggested by the fact that the toxicity of this drug is similar to that of perhexiline, which indeed may produce pseudotumour cerebri.[5,6] The same types of keratopathy[1,5] and peripheral neuropathy with lysosomal inclusions[2,7] have also been reported as side effects of both drugs. This is possibly due to the fact that these drugs are amphiphilic.[8] A rise in venous pressure or an impairment in CSF outflow have been proposed to explain the elevation of intracranial pressure in pseudotumour cerebri.[9] In the cases of pseudotumour cerebri associated with perhexiline and in our patient the exact mechanism remains unsettled.

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Adult onset spinal muscular atrophy with atrophic testes: report of two cases

Sir: Adult onset progressive spinal muscular atrophy is often considered to represent a variant of amyotrophic lateral sclerosis[1] or, less commonly, a heredofamilial entity.[2–5] Here we report two sporadic cases of severe adult onset progressive spinal muscular atrophy associated with testicular atrophy and normal hormone levels.

Patient 1, a 31-year-old male native of the Ivory Coast, presented with a 2 year history

of progressive asymmetric weakness and atrophy of the upper extremities with more recent and milder involvement of the lower extremities, tongue, and respiratory muscles. Early in the course of his illness he had noted aching discomfort in the shoulder regions, but had not been aware of paraesthesias or diminished sensation. Between the ages of 19 and 29 yr he had experienced multiple febrile episodes which had been diagnosed as malaria and had been treated with frequent courses of chloroquine. His father died at age 50 yr of unknown cause. His mother was alive and well and he had twelve healthy siblings. His only child, a son, died 8 years earlier in the Ivory Coast at age 9 months with severe muscle weakness.

On examination there was asymmetrical weakness and atrophy involving all four extremities, most marked proximally. Fasciculations were seen in the tongue and the extremities. Deep tendon reflexes were absent in the right upper extremity, diminished in the left upper extremity, and normal in the lower extremities. Plantar responses were flexor. Superficial abdominal reflexes were present only in the left lower quadrant. The neurological examination was otherwise normal. The testes were small (1·5 cm in long axis), non-tender, and somewhat softer than normal. The epididymis was moderately atrophic bilaterally, the prostate was normal to palpation, and the prostatic fluid was clear on microscopic examination. There was no gynaecomastia. Electromyography demonstrated widespread denervation, large motor unit potentials, and normal sensory potentials. Myelogram and CSF examination were unremarkable. CK was consistently in the 1,000–2,000 range (100% MM) with mild elevations of aldolase, SGOT, and LDH. Muscle biopsy revealed neurogenic atrophy. Serum testosterone, LH, and FSH, as well as urine 17-ketosteroids and 17-ketogenic steroids, were normal. The sperm count was 15 million per ml; only 10% were motile and the quality of motility was poor. Seminal viscosity was increased. The following additional laboratory studies were normal: CBC, differential, sedimentation rate, VDRL, thyroid function studies, serum protein electrophoresis, routine chemistry screen, antinuclear antibodies, rheumatoid agglutinins, karyotypic analysis, urine heavy metals, and titres for antibodies against Epstein-Barr virus, cytomegalovirus, and poliovirus.

Patient 2, a 47-year-old male, developed progressive bilateral lower extremity weakness over a period of one year. Subsequently he noted an aching discomfort and weakness in the arms, without paraesthesias or sensory loss. He had been deaf in the left ear since childhood, and had noted his left side to be smaller than the right since an early age. Over the previous year he had been aware of progressive testicular atrophy, although his libido and ability to maintain an erection and to ejaculate were unimpaired. There was no family history of neuromuscular disease nor any history of toxic exposure.

On examination there was severe muscle weakness and atrophy in the legs, with moderate proximal and mild distal weakness in the upper extremities. The left extremities were smaller than the right. Fasciculations were present in all four extremities. Deep tendon reflexes were mildly exaggerated in the arms and markedly reduced in the legs. Sensory examination was normal and the plantar responses were silent. The right testis was 1·0 cm in long axis and of normal consistency; the left testis was small and soft. LH, FSH, testosterone, and prolactin levels were normal. Electromyography revealed evidence of denervation (increased insertional activity, fibrillation potentials, sharp waves, and polyphasic potentials) in all four extremities. Motor and sensory nerve conduction velocities were normal. Muscle biopsy revealed neurogenic atrophy with small groups of atrophic fibres and many target fibres.

Although in most instances of adult onset motor neuron disease no aetiology is found, sporadic cases may be attributable to heavy metal intoxication (lead, mercury),[6] remote effects of carcinoma,[7] or syphilis.[1] Hereditary forms of adult onset spinal muscular atrophy have been described,[2-5] and, at times, subjects who have stabilised or recovered from an episode of infectious poliomyelitis at a young age subsequently develop progressive anterior horn cell dysfunction.[8]

Both of our subjects demonstrated clinical and laboratory evidence of spinal muscular atrophy. Neither exhibited evidence of heavy metal intoxication, carcinoma, or lues. Patient 1 had fathered a son who died of apparent neuromuscular disease, thus raising the possibility of a heredofamilial disorder. At least three families have been described with adult onset sex-linked spinal muscular atrophy associated with arrest of spermatogenesis.[9] Unlike our two patients, however, those subjects demonstrated gynaecomastia and elevated FSH levels, and gross testicular atrophy was not present. Of pertinent interest is a recent report of chronic asymmetric spinal muscular atrophy in eighteen patients, two of whom had positive family histories for Werdnig-Hoffman disease.[10]

Case 1 was further distinguished by frequent bouts of a malaria-like illness between the ages of 19 and 29 yr. During this period he received large dosages of anti-malarial medication. Although chloroquine may be associated with a toxic vacuolar myopathy, we are not aware that this agent has been implicated in the pathogenesis of anterior horn cell disease.

In summary, two unrelated patients are described who share the clinical pattern of severe adult onset spinal muscular atrophy, both with aching discomfort in the proximal upper extremities early in the course of their illnesses, each demonstrating weakness which tended to be more marked proximally, and both with associated testicular atrophy without demonstrable alterations in serum hormone levels. The similarities of their neurological illnesses and the associated testicular changes suggest a possible common aetiologic mechanism. In light of the burgeoning literature describing peptide hormones of central nervous system origin, it is tempting to speculate that these patients may lack a neuroendocrine factor which also possesses trophic activity for the anterior horn cell.

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Book reviews

The Psychology of Schizophrenia. By John Cutting. (Pp 457; £40·00.) Edinburgh: Churchill Livingstone, 1985.

"When I first read Eugen Bleuler's account of schizophrenia I was enthralled". This splendid opening sentence sets the tone for what is essentially an account of John Cutting's personal odyssey through the literature on the psychology and the pathogenesis of schizophrenia. He covers a great deal of ground and cites some 1300 references, many of them *verbatim* and a high proportion from before 1950. He also writes very clearly, with frequent summary restatements of his argument and numerous cross references. Essentially his thesis is this: that Jaspers and the phenomenologists described the subjective phenomena of schizophrenia comprehensively and brilliantly, and were convinced that they were "understandable", only to be explained as a secondary consequence of brain disease. Unfortunately, the phenomena in question (delusional perception, delusions of control, incongruity and flattening of affect and so on) were wholly different from those associated with all the forms of brain disease known at that time (general paralysis, Korsakoff's psychosis, senile dementia and delirium). There was therefore an impasse; and this led to a long series of attempts, some crude and ingenuous, others elaborate and ingenious, but all ultimately futile, to account for schizophrenia in existential, psychodynamic or social terms. Only now that the subtle psychological deficits associated with section of the corpus callosum or of selective damage to one or other cerebral hemisphere are being revealed do we begin to possess a convincing brain disease model for schizophrenia. Whatever the cause or causes of this disorder, Cutting argues, they must be capable of producing localised brain damage, and he commits himself to the idea that selective damage to the right hemisphere is probably of central importance.

It is an interesting and intelligent book. It contains the best and the most comprehensive English language account of the attempts of pre-war European psychiatry to comprehend schizophrenia, and the central thesis is well argued. But is has two important shortcomings. Like most of the rest of us Dr Cutting does not speak German and so can only read texts that have been translated. There is therefore no mention of Janzarik's concept of "dynamic insufficiency", only a brief passing comment on Huber's "uncharacteristic" or "basic" symptoms, and the prognosis of schizophrenia is discussed without reference to Ciompi and Muller's 37 year follow up of nearly 300 patients. Nor can his right hemisphere hypothesis be regarded as much more than a hunch. As yet, he can produce no convincing neuropathlogical or neuroradiological evidence in support, and as good a case could probably be made for the left hemisphere, the temporal lobes or even the diencephalon.

RE KENDELL.

Neuroscience. Edited by Philip H Abelson, Eleanore Butz and Solomon H Snyder. (Pp 460; $29.95 h/back; $14.95 p/back.) Washington DC: AAAS (American Association for the Advancement of Science), 1985.

Duplicate publication is widely regarded as sinful, and here we have a flagrant example. This volume reproduces 27 articles on neurobiological topics that have recently appeared in *Science*. Nevertheless it is warmly welcome. Of course most keen students have access to library copies of *Science* and most serious neuroscientists are members of AAAS and receive their own copy. The advantages of this publication are two-fold. Firstly is the format. It is pleasant to carry and to read, and is substantially cheaper than xerox copies. Secondly, it provides editorial supervision that guides the reader into topics that may be unfamiliar.

What are these editorial choices? Principally the emphasis is on molecular biology. Not only is one of the four sections headed "Molecular Biology" but in the others ("Neuroplasticity" "Synaptic Transmission", and "Behavior") there is a very strong emphasis on molecular aspects.

Thus two chapters propose molecular mechanisms for learning, one involving cyclic AMP and protein kinases (Kandel and Schwartz) and one involving calcium activated proteinases and glutamate receptors (Lynch and Baudry). Clinicians who feel dispirited when higher cerebral functions are described in terms of synaptic changes observed in aplysia will be comforted by Roger Sperry's 1982 Nobel oration on cerebral hemisphere disconnection, and will also appreciate the chapters on Alzheimer's disease (by Coyle, Price and Delong) and on DNA markers for nervous system disorders (by Gusella and colleagues).

In terms of its key objective which is presumably to provide the young neuroscientist