plasmatic organelles between the various axons. In some axons the mitochondria were arranged peripherally around a core of filaments and microtubules, whereas in others the entire axonal profile was stuffed with mitochondria, dense bodies and filaments. These differences have been reported in lamellated sensory corpuscles in the oral mucosa of the adult cat and miniature pig, and have been correlated with terminal and ultraterminal segments of the central axons respectively. The aggregate was loosely encapsulated by fibroblast-like cells, similar to those that have been described forming a "pseudocapsule" around coiled simple corpuscles in primate skin. This finding appeared to be incidental to the clinical presentation which was that of a multiple mononeuropathy associated with sarcoidosis. We have not encountered similar structures in any of over 100 other sural nerve biopsies. However, Pacinian corpuscles have been described within the connective tissue associated with human peripheral nerve fibres (Hall, Hughes and Atkinson, unpublished observations). Timofeev's corpuscles, encapsulated sensory receptors similar to, but smaller than, Pacinian corpuscles, have been described as transient structures which occur in close relation to pelvic autonomic nerves and ganglia in late fetal and early post-natal life: their function is unknown. Presumably the corpuscles that we have described are mechanosensitive: their situation within a relatively mobile section of peripheral nerve may therefore be significant.

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Figure 2 Axon (a) exhibits stubby side arm (arrow) and accumulations of mitochondria. Note concentric layers of pale-staining lamellar cells (1). Scale bar 10 µm.

Figure 1 A) Axon (a) exhibits stubby side arm (arrow) and accumulations of mitochondria. Note concentric layers of pale-staining lamellar cells (1). Scale bar 10 µm.

Permanent oculomotor palsy with occlusion of the internal carotid artery

Transient palsies of the third, fourth and sixth cranial nerves, as well as retinal ischaemia, have recently been described ipsilateral to occlusion of the internal carotid artery. We report a case of permanent oculomotor palsy occurring in this situation. A 77 year old right handed white woman had admitted having developed sudden left sided weakness two weeks previously. Two days before admission she experienced supraorbital pain with visual loss in the right eye and abnormal eye movements.

Four months earlier she had developed left hemianesthesia, weakness and dysarthria in a stepwise manner over two weeks. There was occasional jerking of the left hand, she had a homonymous left hemianopia and left sided pyramidal signs. The fundi were normal. Carotid doppler ultrasound was normal. The CT brain scan showed patchy gyral enhancement in the right frontal and parietal lobes, and a diagnosis of ischaemia in the right internal carotid artery territory was made. Over the next three months her neurological disability improved.

There was also a past history of ischaemic heart disease (treated with verapamil, aspirin and dipyridamole) and a five year history of chronic myelomonocytic leukaemia. Occasional myelosuppression was treated with etoposide the last treatment being given two months previously. The anticoagulant factor was known to be weakly positive (spackled) with negative DNA and ENA antibodies. There were no cryoglobulins and circulating immune complexes. Serum complement levels were normal.

On examination the blood pressure was 150/90, and both carotid arteries were palpable with no bruits. The mental state was normal. Vision was NPL on the right and 6/6 on the left with a left hemianopia. The right globe was mildly injected, there was a complete ptosis on the right, and adduction, up and downgaze were absent, with intortion on attempted downgaze. Abduction, and movements of the left eye, were normal. The right pupil was dilated and fixed, the left pupil reacting briskly to direct light and to accommodation. The retina was normal on the left but on the right it had the appearance of a central retinal artery occlusion with diffuse retinal oedema sparing the macula, and attenuated vessels. No haemorrhages or emboli were visible and the optic disc was normal. There was also weakness of the lower face on the left, and in the limbs tone was normal but there was no movement of the left arm or leg, together with left hyperreflexia and an extensor plantar response. Finally, there was sensory inattention on the left.

As before, the blood count and film, erythrocyte sedimentation rate and routine biochemistry were normal. The CT scan (fig A) now showed a large infarct involving the whole of the right middle cerebral and part of the anterior cerebral territory, with swelling of the hemisphere but no abnormal enhancement. In a selective right carotid angiogram (fig B), the right internal carotid artery was occluded 2 cm from its origin. There was no filling of the ophthalmic artery, nor any intracranial filling from the external carotid circulation. Flow through the ophthalmic veins, and the cavernous sinus itself, were normal.

There was no recovery in the ocular findings during a further month in hospital, although motor function improved slowly.

Thus the patient presented with occlusion of the right internal carotid artery, ischaemic visual loss in the right eye, and contralateral hemiparesis. The close temporal association of a complete right oculomotor palsy with these latter deficits suggests that it too was caused by ischaemia following the carotid occlusion. Indeed, there were no signs of brainstem ischaemia, nor indications of active vasculitis clinically or in laboratory tests. Her chronic leukaemia remained in remission, and the CT and angiographic studies showed no cavernous sinus lesion. Finally, the conscious level was not depressed at any stage, there were no ipsilateral motor deficits, and the vital signs remained stable, arguing

References


Penicillamine treatment of Wilson's disease and optic neuropathy

We report a case of optic neuropathy associated with penicillamine treatment of Wilson's disease.

A twenty six year old woman presented with a one year history of progressive shaking of her hands and four months of shaking of her head. As a result she had to give up her job. There was a strong family history of neurological or liver disease. She had a history of tachycardia and had taken disopyramide 100 mg three times a day for three years. A mitral regurgitation murmur had been noted in the past.

On examination her pulse was 80/min and regular, and blood pressure was 115/60. There was a mild and late systolic murmur.

Penicillamine was stopped and pyridoxine 50 mg twice a day was started. Nine days later near vision was 6/18. Serum copper was 10 μg/dl (Normal <15). Penicillamine dihydrochloride 600 mg three times a day was started. Three weeks after stopping penicillamine colour vision had returned to normal. A week later pupillary reactions were improved and near vision was N6 (right) and N4 (left). The VEPs showed improved amplitude, but the latencies were unchanged.

Three months after stopping penicillamine the VEP latency on the left had improved to 99 ms and on the right was 106 ms. The BAEPs and SSEPs were unchanged. After seven months the visual acuity was 6/12 on the right and 6/9 on the left. After a year of therapy the vision had been greatly improved. She has since returned to work and her manner appears normal.

No case of untreated Wilson’s disease with optic neuropathy has been described. BAEPs are commonly delayed in Wilson’s disease, but delayed VEPs have been found in only a minority of cases with neurological involvement. Recovery of VEP latency with treatment has been seen in one study. The abnormal VEPs may be related to cerebral hemisphere involvement.

Optic neuropathy in Wilson’s disease treated with D-penicillamine and D-penicillamine has been attributed to penicillamine induced pyridoxine deficiency: in two cases the optic neuropathy developed only after months at higher doses of penicillamine and improved with pyridoxine. Against this theory is a third case, which developed while on pyrithionyl pyridoxine. In all cases there was an improvement of the Wilson’s disease patients treated with penicillamine, making the Wilson’s disease itself unlikely to be the cause of the optic neuropathy.

Optic neuropathy has been described in association with D-penicillamine treatment of chronic active hepatitis for two months and rheumatoid arthritis for six months and for a year. The last was associated with development of antinuclear antibody titre of 1/320 and improved with steroids. This case differs from the others described as the duration of treatment before the development of optic neuropathy is much shorter. Pyridoxine deficiency is unlikely, because of the low dose and short duration of treatment. The short history and negative autoimmunity profile make autoimmune disease unlikely. Neurological deterioration in the first month of penicillamine treatment of Wilson’s disease has been recognised recently and the time course in this case would be consistent although optic neuropathy has not been described in this situation. Presence of extrapyramidal signs is often seen in this syndrome, but was absent in this case. The neurological deterioration may be due to redistribution of copper. Trientine therapy has not been associated with neurological deterioration. Neuro-opthalmic complications of desferrioxamine, including one case with optic neuropathy, have been associated with raised cerebrospinal fluid copper levels and attributed to redistribution of copper.

Another explanation of the optic neuropathy in this case consistent with the short history would be an idiosyncratic hypersensitivity reaction to the drug associated with copper accumulation. Physicians should regularly assess the visual acuity of their patients on penicillamine, particularly when starting treatment or increasing the dose.

Selenium erythropoietic levels in von Hippel-Lindau syndrome

No serum marker exists in von Hippel-Lindau syndrome (HLS), an autosomal-dominant inherited cancer-prone disorder.