against any tentorial herniation as a cause of the oculomotor palsy.

Wilson et al. recently described three patients with internal carotid artery occlusions who also had transient ocular motor palsies, generally recovering within hours. However, pupil dilatation and ptosis were observed for up to three weeks. The most likely mechanism was transient impairment of the nutrient circulation of the ocular motor nerves. For example, the oculomotor nerve receives its blood supply from an anastomotic plexus of small arteries which in turn is supplied from branches of the internal carotid artery within the cavernous sinus, from multiple branches of the maxillary artery, as well as from the ophthalmic artery anteriorly, and from the posterior cerebral and basilar arteries posteriorly. This rich blood supply from multiple sources could explain why oculomotor palsy is so unusual, even transiently, after carotid occlusions or carotid ligations for the treatment of aneurysms, since occlusion of several components of the nerve's nutrient supply is probably required to produce significant ischemia. Thus in the oculomotor palsy in diabetes mellitus there are diffuse small vessel abnormalities in the vasa nervorum. Similarly, flow was absent in the ophthalmic and internal carotid arteries in our case and in those of Wilson et al. Whether the resulting oculomotor palsy is transient or permanent may perhaps depend on the adequacy of the collateral blood supply from the posterior circulation, or on the extent of segmental occlusion of the plexus of small vessels along the nerves themselves.

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 had to give up her housework. There was a similar familial 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 minute and regular, and blood pressure was 115/60. There was a mid and late systolic murmur loudest at the left sternal edge. Higher functions were intact, but her manner was disinhibited. Visual acuity was 6/9 on the right and 6/6 on the left. A red-free (546 nm) retinal examination showed normal optic disks. Slit lamp examination showed Kayser-Fleischer rings. The other cranial nerves were normal. She had titubation, tremor of the upper limbs, worse on the right and agranular and cogwheel rigidity of both wrists. Reflexes, power and sensation were normal.

Serum copper was 7.6 micromol/l (Normal: 12-26 micromol/l), caeruloplasmin 70 mg/l (Normal: 190-450 mg/l) and 24 hour urinary copper was 5.1 micromol/24 hours (Normal <0.8 micromol/24 hours). Biochemical screen, plasma glucose, and chest and skull radiographs were all normal. Haemoglobin was 119 to 136 g/l, white blood count 2.2 to 3.9 x 10^9/l with polymorphs 1.0 to 2.3 x 10^9/l and platelets 85 to 116 x 10^9/l. The bone marrow was mildly hypocellular, with reduced numbers of erythropoietin, myeloid cells and megakaryocytes. A CT brain scan showed low densities in the thalamus and cerebral peduncles. Echocardiography showed mild left ventricular hypertrophy.

A diagnosis of Wilson's disease was made and D-penicillamine 50 mg three times a day was started.

Three weeks after starting penicillamine the patient complained with failing vision. Three weeks after stopping treatment she had developed a "red light" in the centre of both visual fields and then progressive blurring of vision. On examination both optic discs were pale and both pupils reacted sluggishly to light. Corrected visual acuity was 6/24 on the right and 6/18 on the left. Near vision was N18 bilaterally. Visual evoked potentials (VEP) showed latencies of 102 ms on the right and 112 ms on the left (Normal <115 ms). Brainstem auditory (BAEP) and somatosensory evoked potentials (SSEP) were bilaterally delayed. The wave form of the BAEPs was small. Electroretinogram and autoimmune profile were normal.

Penicillamine was stopped and pyridoxine 50 mg twice a day was started. Nine days later near vision was 6/18 and 6/9. Visual evoked potentials (VEP) showed latencies of 90 ms on the right and 96 ms on the left (Normal <95 ms). Brainstem auditory (BAEP) and somatosensory evoked potentials (SSEP) were normally delayed. The wave form of the BAEPs was normal. Corrected visual acuity was 6/24 on the right and 6/18 on the left. Near vision was N18 bilaterally. Visual evoked potentials (VEP) showed normal amplitudes, 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 treatment the vision had 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 not been described. 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 pyrrolidonyl pyridoxine. In all cases there was no improvement with the Wilson's disease treated with penicillamine, despite 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 factor 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 autoimmuné 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. A raised level 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. This treatment has not been associated with neurological deterioration. Neuro-ophthal mic 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. Although copper is a normal complication, physicians should regularly assess the visual acuity of their patients on penicillamine, particularly when starting treatment or increasing the dose.

AHM LEON NW LAWTON Wessex Neurological Centre, Southampton General Hospital, Southampton, UK

Correspondence to: AHS Lee, Neurpathology Department, Level E, South Block, Southampton General Hospital, Southampton SO9 4XY, UK

5 Fall HS, Williams AC, Blake DR. Deterioration of Wilson's disease following the start of penicillamine therapy. Arch Neurol 1989;46:359-60.

Serum erythropoietin levels in von Hippel-Lindau syndrome

No serum marker exists in von Hippel-Lindau syndrome (HLS), an autosomal-dominant inherited cancer-prone disorder
Penicillamine treatment of Wilson's disease and optic neuropathy.

A H Lee and N F Lawton

*J Neurol Neurosurg Psychiatry* 1991 54: 746

doi: 10.1136/jnnp.54.8.746

Updated information and services can be found at:
http://jnnp.bmj.com/content/54/8/746.1.citation

**Email alerting service**

These include:

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/