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 work on the line. There was no past or 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 was heard in the past.

On examination her pulse was 80/min and regular, and blood pressure was 115/60. There was a mid and late systolic murmur and loudest at the left sternal edge. Higher functions were intact, but her memory was disoriented. Visual acuity was 6/9 on the right and 6/6 on the left, with normal fields and normal optic discs. 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 aggragation of grip and weakness in the right leg, with hyporeflexia of both wrists. Reflexes, power and sensation were normal.

Penicillamine was stopped and pyridoxine 50 mg twice a day was started. Nine days later she had visual blurring with vision of left eye. Trientine 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 SSEP 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 penicillamine 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 prophylactic pyridoxine. In all cases there was an improvement of the Wilson's disease with penicillamine treatment, 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 chorea in a patient with titre of 1:520 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 autoimmune 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. The development 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-ophtalmic 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 idiopathic hypersensitivity reaction. Although in the presence of neurological complication, physicians should regularly assess the visual acuity of their patients on penicillamine, particularly when starting treatment or increasing the dose.

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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.