Visual field changes following hepatic transplantation in a patient with primary biliary cirrhosis

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Abstract
A case of severe visual field restriction complicating primary biliary cirrhosis is described. The clinical features demonstrated vitamin A deficiency which did not respond to oral supplements of vitamin A. Hepatic transplantation restored the visual fields to near normal.

A 51-year-old woman was referred to the Bristol Eye Hospital by her general practitioner. She was known to be suffering from primary biliary cirrhosis for five years and was persistently jaundiced. For several months prior to her referral she had been aware of gradual deterioration of vision in her left eye. She had no relevant past ophthalmic history. She was on treatment for biliary cirrhosis and was receiving intramuscular vitamin A, D, and K replacement. She was also taking oral loperamide, spironolactone, terfenadine, and cholestyramine.

Ocular examination showed her visual acuities were 6/9, N 8, in the right eye and 6/18, N 10 in the left eye. The anterior segments were normal, but both fundi showed small discrete retinal pigment epithelial lesions extending from the posterior pole to the equator. Some spots were intensely white and well demarcated, whereas others, particularly those in the periphery, were paler with soft edges (Figs 1A, B). The peripheral visual fields were markedly constricted to less than 10° bilaterally (Fig 2A). 100-Hue testing showed error of scores of 71 in the right eye and 237 in the left eye, with a tritan axis in each eye.

Fluorescin angiography showed slight masking of the background choroidal fluorescence by the pigment epithelial spots in the early stages of the run, progressing to slight

![Figure 1A](image1)

![Figure 1B](image2)

Figure 1 A and B Preoperative appearance with multiple white punctate lesions of variable density throughout the fundi of both eyes.

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<th>Table 1 Electrophysiological, colour vision, and serological data</th>
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ERG and VEP latencies all normal. (a)=a wave. (b)=b wave. DA=dark adaptation. R=right eye. L=left eye.
staining of lesions from the late venous phase onwards. A few spots showed intense staining (Figs 3A, B).

Electrophysiological studies showed delayed dark adaptation. The B wave of the electroretinogram (ERG) to blue flashes of light was reduced in the early stages but reached normal levels after 30 minutes. The ERG to white light and the electro-oculogram (EOG) were normal. The methods used for electrophysiological testing have been described in detail. The EOG was recorded after a 10-minute period of dark...
adaptation followed by exposure to bright light (3000 cd/m²). The ERG was measured with skin electrodes and stroboscopic flashes at 1-second intervals 30 cm in front of the patient. Initially patients were light adapted in normal room illumination for 15 minutes, following which the lights were extinguished. Recordings were taken immediately and at 5 minutes for white light and at 7 and 30 minutes for blue light (stimulus reduced by 2 log units by the filter).

The fundus changes were consistent with vitamin A deficiency. Serum vitamin A was measured and found to be 0·8 mmol/l (normal 1·1 to 3·5). The vitamin A dosage was increased from 300 000 units monthly to 300 000 units weekly and the serum vitamin A level increased to 1·8 mmol/l. Subjectively her vision improved. Her visual acuities in February 1988 were 6/9 right and left, but her visual fields remained essentially unchanged at approximately 10° (Fig 2B).

The patient’s general condition deteriorated, with increased jaundice, anorexia, and weight loss, and hepatic function became grossly abnormal (Table 1). In April 1988 she underwent hepatic transplantation, which produced rapid improvement in her general health and restoration of normal hepatic function. Reassessment of her visual function six months later showed considerable improvement in her visual fields (Fig 2C) and 100–hue tests, with reduction of the tritan axis. However, her fundal appearances showed that the white lesions had persisted but were fainter (Fig 4). The blue flash ERG remained unchanged with delayed dark adaptation. At follow-up 18 months after transplantation her visual acuities and fields remained stable.

Discussion
Primary biliary cirrhosis is thought to be an autoimmune disease causing destruction of the small intrahepatic bile ducts. There is an association with other autoimmune diseases, and frequently a high serum IgM and circulating immune complexes are found. Antimitochondrial antibodies are seen in over 90% of cases. The patients are usually female and aged 40–60 years, and the disease produces pruritus, steatorrhoea, weight loss, and hepatosplenomegaly. The development of jaundice is considered a poor sign for survival, indicating progressive liver failure. Vitamin deficiencies are well recognised, particularly of vitamins D and K, but approximately a quarter of patients have a low serum vitamin A level. The patient under discussion showed all the typical findings.

Chronic liver disease may produce sufficient vitamin A deficiency to induce ocular complications: nystagmus, peripheral visual field restriction, white punctate retinal pigments, loss of dark adaptation, and reduction in the values of the EOG and scotopic ERG have been described. The mechanism of these effects is presumed to be poor absorption through the gut. Reduced bile acids in the intestinal tract impair absorption of lipids and fat soluble vitamins, including vitamin A. Chronic liver disease may also decrease the production of retinol binding protein and pre-albumin, which are necessary for vitamin A transport to the retinal pigment epithelium. Plasma proteins were normal in this patient, though retinol binding protein was not measured specifically.

Previous reports have suggested that intramuscular vitamin A supplements reverse the visual field and electrophysiological changes, though the fundus appearance remains abnormal. Walt et al recommended that in primary biliary cirrhosis vitamin A is more effective by mouth than by intramuscular injection. Parenteral administration bypasses the normal hepatic delivery and esterification of vitamin A following gut absorption, and it may therefore reduce its efficacy. In the present case injections of vitamin A did not produce significant functional improvement in spite of several weeks of normal plasma vitamin A levels, whereas hepatic transplantation caused a rapid restoration of peripheral field. The outcome in this patient would support this theory.

Functional amblyopia was considered unlikely in view of her precise consistency on repeated field testing, physical changes in the pigment epithelium, and abnormal electrophysiological findings.

Colour vision abnormalities have not been described before in primary biliary cirrhosis, and though not severe in this patient there was a notable change after transplantation. This may suggest that photopic photochemistry, like scotopic photochemistry, has some degree of dependency on liver metabolism.

ERG or EOG abnormalities have been described as the first indication of abnormal retinal function in vitamin A deficiency, but the electrophysiological changes in this case were remarkably small compared with the functional field deficit and fundus appearances. It is also interesting that the mild delay in dark adaptation persisted along with the fundus abnormalities in spite of the improvement in visual fields after transplantation. Prolonged hypovitaminosis has the capacity to induce some degree of permanent structural and functional damage to the photoreceptor-pigment epithelial complex, but treatment leads to considerable improvement.

My thanks are expressed to Dr D Papakostopoulos for performing the electrophysiological tests, Mrs Gill Bennerson for photographic help, and Mrs Linda Clayton for typing the manuscript.
FIFTY YEARS AGO

Mustard gas and its implications

DEAR SIRS,—In reply to Messrs. John Eyre and Frank W Law may I state that I have seen one drop of 4 per cent solution of hyd. perchlor. in glycerine accidentally fall on the cornea and in a few seconds which elapsed before washing out the conjunctival sac, severe and lengthy, but not permanent damage was inflicted on almost the whole of the corneal epithelium. Here there was no question of absorption. I quite agree with them that in the field of biology there is nothing more misleading than the argument from analogy, which indeed led eminent men to assume and publish results on the assumption that because man could accommodate the mammals could also.

But the argument from analogy hardly applies in this instance just quoted.

As regards the late effects of mustard gas on the cornea, the few cases I have seen showed deep seated infiltration rather than ulceration and there was very little clear cornea left anywhere. So that I doubt whether either diathermy or contact glasses would have assisted. If such cases, which I am glad to say are rare, present themselves, the method suggested will be borne in mind. It is true that these conditions do recur without obvious cause. No one will be more grateful than myself if the writers have devised an effective treatment of mustard gas in the field, and will look forward to their publication of their experimental results. But the practical use of any remedy of the kind in advanced positions of any army is very difficult but not insuperable.

Some idea of the difficulty of acting efficiently in advanced stations may be learnt from the Palestine campaign, where towards the end men with high temperature were given quinine at once, no matter what seemed to be the cause of the temperature. If the medical officers had waited until they could be sure that malaria was the cause it would at times have been too late. To neutralise the effects of mustard on the eyes, special instruction for the forward units will be a necessity. —Letter from James W Barrett.
