Hemispheric infarction after herpes zoster ophthalmicus

Sir: Cases of CT-documented internal capsule infaracts following herpes zoster ophthalmicus have been reported recently.1-3 It has been suggested that a viral-induced granulomatous angiitis of the ipsilateral middle cerebral artery may produce infarction and thus account for the syndrome of contralateral hemiparesis following herpes zoster ophthalmicus. We recently cared for a patient with this syndrome who later developed additional neurological sequelae and was also discovered to have coincident pulmonary sarcoidosis.

A 47-year-old right-handed male was well until 16 June 1982 when he developed a painful, erythematous, vesicular rash on his right forehead and about his right eye. The diagnosis of herpes zoster ophthalmicus with nasociliary involvement was made. He was treated with topical steroids and mydriatics with gradual clearing of his symptoms. Sharp burning pains over his right forehead and scalp continued for a number of weeks. On 15 July 1982 he experienced a sudden stabbing, right frontal pain resembling an attack of trigeminal neuralgia. On admission to hospital, he was alert, rational and orientated, and had stable vital signs. Neurological examination confirmed a mild left hemiparesis with increased tone and reflexes and an extensor left plantar response. There was marked incoordination of the left limbs. Visual fields were full to confrontation. Cerebrospinal fluid contained 35 lymphocytes/min, protein 0-77 g/l and glucose 3-1 mM with a blood glucose of 4-3 mM. Electrolytes, liver and renal function were all normal. A CT head scan (fig A) showed a haemorrhagic infarct in the right internal capsule and a small area of hypodensity in the right occipital pole. Six weeks later, the patient was able to return to work despite a continued hemiparesis. On 25 September 1982 he woke with urinary incontinence and fell repeatedly to the left. He was re-admitted to hospital alert, but disorientated and dysarthric. His spastic left hemiparesis was more marked. He now had left homonymous hemianopia and marked sensory extinction to light touch and pin prick on the left. Varicella-zoster antibody titres were 1:32 in the serum and negative in the CSF. CSF contained 8 lymphocytes/min and protein 0-77 g/l. A CT scan showed a large hypodense area involving the right occipital lobe in the distribution of the posterior cerebral artery (fig B) in addition to a small hypodense area in the region of the previous haemorrhagic capsular infarct. Burr hole biopsy of the right occipital lobe demonstrated no abnormality. Routine chest radiographs and subsequent CT of the chest showed a right hilar density with multi-nodular infiltrates bilaterally. Open lung biopsy demonstrated a non-caseating granulomatous pattern involving parenchyma as well as blood vessels consistent with sarcoid granulomatosis. Serum calcium and angiotensin-converting enzyme levels were normal. Despite radiological abnormality and reduction in vital capacity the patient had no respiratory complaints. Repeat CT scans two weeks after admission demonstrated a new hypodense area in the parasaggital region of the right parietal lobe (fig C) without obvious change in the patient’s condition. He was treated with a five day course of intravenous acyclovir (500 mg 8 hourly) and a six week course of prednisone 30 mg/day with no change in clinical examination, chest radiographs or head CT scan after three and six weeks.

This patient has evidence of multiple areas of infarction involving the ipsilateral cerebral hemisphere following herpes zoster ophthalmicus. In addition to the previously documented pattern of post-zoster capsular infarction, this patient subsequently developed clinical and radiographic findings indicative of parietal and occipital lobe infarcts. There was no central nervous system tissue diagnosis; however, the pattern of involvement was more consistent with vasculitis following herpes zoster ophthalmicus than with neurosarcoidosis. Previous studies have provided radiographic4,5-6 and pathologic3-7 evidence of post-zoster middle cerebral artery angiitis. Basilar artery involvement following herpes zoster ophthalmicus has also been documented.8 An unusual feature of the present case is the co-existence of pulmonary sarcoidosis. There were no chest radiographs prior to the current illness and thus it is not possible to ascertain whether this sarcoid preceded or followed the herpes zoster ophthalmicus. It is well established that patients with sarcoidosis have diminished T cell function9 and such
immunocompromise may confer susceptibility to varicella-zoster infection.10

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References

Discordant HLA haplotype segregation in a family with progressive extrinsic ophthalmoplegia and ragged red fibres.

Sir: “Ophthalmoplegia plus” or “Oculocraniosomatic neuromuscular disease” is a complex syndrome that includes a great variety of clinical and pathological manifestations, with characteristic mitochondrial abnormality in muscular tissue.1,2 Familial cases are very few and a wide spectrum of clinical patterns has been observed in a single family, suggesting that various clinical manifestations must be considered as a different expression of a single genetic defect, but no unequivocal transmission pattern has been found.3,7

We have seen a family with five members affected by “ophthalmoplegia plus”. The pedigree of this family is shown in fig 1. Patients MA, GT, GL and BS developed the disease in their 3rd decade of life, with similar symptoms: bilateral progressive ptosis and short stature. Muscular strength was normal as well as serum muscular enzymes and EMG. Muscle biopsy performed in patient BS showed the presence of numerous ragged red fibres. Patient BL developed at age of 26 years a severe bilateral ptosis, ophthalmoplegia and signs of severe, generalised muscular weakness. Laboratory and clinical investigations revealed: (a) increased levels of serum lactate and pyruvic acid (both at rest and after ischaemic exercise test); (b) diabetes mellitus; (c) sensory neural hypo-acusia; (d) partial conduction heart block; (e) slight truncal ataxia and cerebellar atrophy on CT scan. Muscle biopsy showed the presence of numerous ragged red fibres. No information was obtained about subject GE. All the other members listed in fig 1 apparently were healthy. In this pedigree, “ophthalmoplegia plus” appears to be an autosomal dominant trait: no generation was skipped, no member of the family was affected without having a parent affected, males and females were equally affected. Indeed, the high frequency of disease in children of affected parents (50%) is a criterion for dominant inheritance as opposed to a chance finding.

To investigate the mechanism of inheritance of the disease, we investigated the HLA haplotype segregation of this family. If a gene predisposing to disease, but distinct from the HLA genes, is located in close proximity to the Major Histocompatibility Complex (MHC) within a particular family pedigree, the susceptibility to the disease preferentially segregates with a particular HLA haplotype. This would be true even in the absence of an association between the disease susceptibility and a given HLA antigen. Subjects were typed for HLA-A, B, C, DR specificities by means of the standard cytotoxicity techniques.8 HLA haplotypes within the family are reported in fig 1. These data do not support an HLA linkage for “ophthalmoplegia plus” in this family, since the segregation of HLA haplotypes is clearly discordant with the disease segregation. Indeed, HLA types in this pedigree showed an unexpected and puzzling concentration of HLA-B5 cross-reacting group antigens (that is B51+, B51-, B52)9-11 This finding could suggest an interaction between environmental factors with a particular genome, and may explain the different clinical patterns observed in a same family with a common “disease susceptibility” load. From this, interest rises in HLA typing of both familial and sporadic cases of the disease. The suggestion to go further and to look for a population associated as well as to extend linkage analysis of affected families is only apparently contradictory with the present observation. Clear examples exist in which HLA-population association with a disease suggests tight linkage,12 but the family studies are conflicting13 and do not support any linkage.14 Several explanations can be advanced which might partly account for population-family discrepancy: genetic heterogeneity between familial and non-familial cases of the disease, heterogeneity of aetiology, epistatic

Fig 1 The family pedigree

![Pedigree](image-url)