MINI REVIEW

Ophthalmic zoster

Ophthalmic herpes zoster is a disease varying in severity from devastating, threatening life and sight, to so mild that it may pass unnoticed. The ophthalmic division of V is involved in 7-17.5% of all herpes zoster patients, affecting many of the tissues of the globe and orbit by highly varied types of lesions.

The current theory of aetiology is that after an attack of chickenpox and its attendant viraemia some virus is retained in the dorsal root ganglion, perhaps reaching there by retrograde spread along the sensory nerves from the skin lesions. Later, under the influence of largely unknown trigger factors it reactivates replicates and migrates back down the sensory nerves to the skin and eye where it causes its characteristic lesions. Virus has been cultured from these sites in the acute stage of the disease.

Varicella zoster virus (VZV) or as it is now known human herpes virus 3 (HHV3) is a typical herpes virus containing DNA, an icosahedral nucleocapsid, and a glycoprotein containing outer cell membrane. It is indistinguishable by electron microscopy from other members of the herpes family. Recently several different strains of virus have been identified by means of restriction endonuclease analysis.¹ However, overall, scientific research into the virus has been sketchy due to difficulties in obtaining cell-free virus, in culturing it, and failure to find a satisfactory animal model.

Reactivation of latent virus is often stated to be associated with a temporary depression of immunity and there have been many studies attempting to confirm this. So far there is no information immediately prior to developing the disease. However, shortly after onset, there is a clear anamnestic rise in circulating antibody demonstrating that the virus has been encountered before and there is a consistent depression of cell-mediated immunity (this may be an artefact due to recruitment of immunologically competent cells into the affected tissues). There is also a reversal of T cell subsets²: the number of cytotoxic lymphocytes increases and these have the capacity to destroy the virus. Interestingly the disease is no worse in those with defects in circulating immunity but is undoubtedly more common and severe in those with established impairment of cell-mediated immunity such as AIDS and Hodgkin's disease. Nevertheless the vast majority of ophthalmologists' patients are previously healthy and the mechanism of reactivation remains unknown.

Epidemiology shows that there is no seasonal incidence but there is a steady increase in incidence with age. Second attacks occur in about 4% of patients.

Pathologically virus has been identified in the trigeminal ganglion very early on³ and is accompanied by a perineuritis and perivasculitis which lead to varying degrees of neuronal necrosis and fibrosis. The adjacent brain stem and carotid artery may be involved by the inflammatory process and encephalitis, isolated cranial palsies, and late hemiplegia may ensue. Severe skin lesions are characterised by haemorrhagic bullae probably caused by a dermal vasculitis. This too is followed by extensive necrosis and scarring. The globe shows marked cellular infiltration in the neurovascular bundles and frequently a perivasculitis in iris and ciliary body. Damage to the ocular tissues may be direct, as the result of the cellular infiltration, or indirect by denervation and the ischaemia induced by the vasculitis. These changes may be chronic and relapsing but in spite of it being assumed that they are due to

continuing virus replication there is no scientific evidence barring the recent discovery of viral DNA in old enucleated eyes and corneal buttons.⁴

The disease can be divided into three phases: an acute phase (within the first 4 weeks) which may totally resolve, a chronic phase (which may persist for years) and a relapsing phase where the acute or chronic lesions appear to have been controlled but break through again (even years later).

The commonest ocular lesions are conjunctivitis, punctate epithelial keratitis, episcleritis, iritis, and nummular keratitis, of which the first two are very transient and resolve quite rapidly without treatment. Many cases of episcleritis are indolent and seem to respond best to oral Froben (flurbiprofen) which is easily withdrawn. Nummular keratitis has a very variable course; some cases resolve without trace after a minimum of treatment, others become indolent with chronic cellular and lipid infiltration accompanied by faceting which may seriously interfere with vision. Unfortunately this tends to occur more in young people and therefore these lesions should be observed carefully and treated with low doses of topical steroid when active. Acute lesions giving rise to problems in management are hypertensive iritis, acute corneal oedema, disciform keratitis, sclerokeratitis, and neurotrophic ulcer. Both systemic and topical acyclovir (ACV) seem to have little effect on them and invariably potent topical steroids have to be used in all but the corneal ulcers. The disadvantage of this is the dependency on steroids that develops and the difficulty in weaning patients off the drug: it can take years. Chronic lesions which are troublesome are neurotrophic, mucous plaque (MPK), exposure and lipid keratitis. The first is best treated with taping the lids closed, botulinus toxin-induced ptosis, or a partial tarsorrhaphy. All too often a severe central scar ensues that is very unfavourable to keratoplasty. MPK has a tendency to recurrence, particularly in association with a glaucoma that is difficult to manage medically, but responds well to surgery. It may go onto a neurotrophic or exposure keratitis. Exposure keratitis is very difficult to manage; artificial tears and lid toilet are often disappointing. It may be necessary to carry out a tarsorrhaphy and a superficial keratectomy. Lipid keratopathy can be prevented by adequate suppression of inflammation but, if established and with good corneal sensitivity, does well with keratoplasty. All these lesions respond poorly to systemic and topical ACV.

Systemic treatment of zoster patients is controversial and largely ineffective. Steroid and ACV have been advocated in the very early stages.^{5,6} I feel the former should be used in immunocompetent patients with optic neuritis, haemorrhagic skin bullae, total external ophthalmoplegia with proptosis, and contralateral hemiplegias by means of a pulsed dose of 80 mg of prednisolone rapidly reduced over 1 week. ACV, on the other hand, should be used in the immunosuppressed but has a doubtful effectiveness in the immunocompetent with regard to the prevention of post-herpetic neuralgia and development of ocular complications.^{7,8}

A significant degree of post-herpetic neuralgia (PHN), defined as pain after the first 6 weeks, occurs in about 7% of patients and is notoriously difficult to treat. The list of cures is legion; presently fashionable are stellate ganglion block, cimetidine, transcutaneous electric nerve stimulation

(TENS), and acupuncture. It is probably best to try to treat the acute neuralgia fully with analgesics as there is some evidence that this may reduce the degree of PHN. There may be a severe accompanying depression compounding the problem and this responds well to amitriptyline.

Perhaps the most misleading complications are the recurrent lesions which may present years after the original disease. Therefore meticulous follow-up is needed in all complicated zoster. We are still very ignorant of the pathogenesis of the disease and the part, if any, the virus plays in chronic and relapsing lesions. The search must continue for a more effective antiviral drug but if viral replication is confined to the onset of the disease and if the later lesions are, as seems likely, due to immunologically mediated reactions not dependent on the presence of live virus (as we know it), the results will not prove useful unless the antiviral drug is

administered at the very onset of the disease. Thus anti-inflammatories, mainly in the form of topical steroids, remain the backbone of treatment for the severe ocular complications of zoster.

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