Optic neuritis following measles/rubella vaccination in two 13-year-old children

CASE 2
A 13-year-old girl received the measles/rubella vaccination in December 1994. Eighteen days later she developed, over a 24–48 hour period, blurring of vision with associated pain on ocular movement in the left eye. There were no other neurological symptoms and no family history of neurological or ocular disease.

General examination was normal. Visual acuities were corrected to right eye 6/6, N4.5, and left eye 1/60. Ishihara plates for colour vision were right eye 17/17 and left eye 0/17. There was a relative afferent pupillary defect on the left. Visual fields demonstrated normal fields on the right but a large central scotoma on the left. Funduscopy revealed a hyperaemic and swollen optic disc. The peripheries, retina, macula, vitreous anterior segments, and extracocular movements were normal in each eye. Investigations revealed a normal full blood count, biochemistry profile, and erythrocyte sedimentation rate. The serum angiotensin converting enzyme was mildly elevated at 68 (reference range 16–53), serum calcium and chest x ray were normal. The autoantibodies and VDRL tests were negative. MRI (T2 weighted axial and T1 weighted coronals, no contrast) showed mild asymmetry of the optic nerves only. There were no white matter lesions in the brain. CSF examination revealed normal constituents; the oligoclonal bands were positive. Virology 6 weeks after the measles/rubella vaccination showed no detectable measles or rubella IgM but a serum measles IgG titre of 1:160.

The patient was treated with intravenous methylprednisolone and made some recovery. On review 2 months later, visual acuities were right eye 6/6 and left eye 6/12. Ishihara plates were right eye 17/17 and left eye 2/17. Funduscopy revealed left optic atrophy.

COMMENT
Neurological complications following rubella or measles vaccination are rare. Rubella has been associated with carpal tunnel syndrome, paraesthesia, myelitis, and myeloradiculitis. Measles vaccination has been linked to cases of encephalitis, encephalopathy, febrile convulsions, and encephalomalacia but these are extremely rare. It must be remembered that the risk of encephalitis following measles infection is one per 1000 cases and the incidence of all reported neurological disorders following measles vaccination is only 1.16 per million doses. This compares with the background incidence of encephalitis not related to immunisation of 2 to 3 per million children of similar age.11 There is certainly no doubt that the risks of serious neurological disorders are much greater with the natural disease than after the vaccination and widespread immunisation programmes are justified by the available evidence.

The onset of symptoms is usually 1–3 weeks after vaccination, the period when virus replication is maximal and when viraemia is expected to occur. The mechanism is thought to be due to immune complex mediated vascular injury causing alterations in vascular permeability, cellular infiltration, and consequent blood–brain barrier impairment. This may allow lymphocytes committed to specific viral antibody synthesis outside the brain compartment to enter the brain producing neurological symptoms.24 It has been suggested that viral infection or vaccination with live or inactivated viruses are often preceding events in optic neuritis; however, population based studies have shown no such association for influenza vaccines.3

Optic neuritis has been reported as a complication with the use of several vaccines including rubies, smallpox, swine flu, diphtheria, tetanus, and BCG, although it is extremely rare. There have only been three cases of optic neuritis following immunisation against rubella or measles reported to date. The first was by Kazarian and Gager in 1976,5 who described a 6-year-old boy developing bilateral simultaneous optic neuritis (BSON) 18 days after measles/mumps/rubella vaccination; the second, by Kline et al,9 reported a 31-year-old woman who developed BSON 3 months after measles/mumps/rubella vaccination. A third patient, mentioned by Riikonen,6 developed unilateral optic neuritis, and later multiple sclerosis, 4 weeks after rubella vaccination.

In the first two reported cases visual recovery was good, in contrast with our patient with BSON who is now registered partially sighted. Optic neuritis in childhood, which is usually bilateral and often associated with a febrile illness, is an excellent possibility. Visual acuities often returning to normal within 4–6 weeks of onset, making our first case unusual. The frequency of later development of multiple sclerosis after optic neuritis in childhood appears to be low and after BSON is extremely rare.10

The differential diagnosis in our first patient must include LHON despite the early age of onset, the eyes being affected simultaneously, and the negative family history. Many typical cases of LHON are now recognised and the phenotype is expanding as a consequence of mitochondrial DNA mutation testing; however, our patient is negative for the described DNA mutations. The presence of positive oligoclonal bands in the second case is indicative of local synthesis of IgG typical of demyelination but is also seen as a response to the presence of viral antigens.

The association between immunisation and optic neuritis has now been described on several occasions and there is certainly biological plausibility in the suggested pathogenesis. However, the number of reported cases are too small for a definite causal relation to be defined at present.11

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Retinal arterial occlusion associated with resistance to activated protein C

COMMENT

Oclusion of the retinal artery is more rarely encountered in younger than in older patients. Multiple causes of arterial occlusion in the retinas were described. In a recent report, the causes of retinal arterial occlusions in 21 young adults were analysed. Emboli were identified in 33% of the patients. Cardiac valvular disease, including aortic myxoma, bacterial endocarditis, and mitral valve vegetation due to lupus anticoagulant, was the main recognised cause and was present in 19% of the patients. Other associated risk factors for cerebrovascular occlusion such as cigarette smoking, oral contraceptive use, obesity, pregnancy, and Behcet's disease were found. In 91% of the patients, Antithrombin III, protein S, or protein C deficiencies are hypercoagulable conditions that can lead to recurrent venous or arterial thrombotic events. Protein S deficiency was associated with a case of bilateral retinal branch artery occlusion. This biological abnormality was detected in only one young woman with diabetes mellitus and pregnancy in the series of Greven et al. Antiphospholipid antibody syndromes are thrombophilic disorders that occur in patients with either lupus anticoagulants or antibodies to antiphospholipid or dissociated syphilis serology. Antiphospholipid antibodies can lead to recurrent arterial and/or venous thrombosis. APC resistance is clearly related to venous thromboembolism. A recent report suggests the possible role of APC resistance in arterial thrombosis. APC resistance was not searched for as a thrombophilic factor in retinal arterial occlusions in young adults. In our case, the cause of retinal arterial occlusion could be attributed to the hypercoagulable mutation of factor V. Owing to the severity of retinal arterial occlusion, long-term oral anticoagulant treatment was proposed in our patient for secondary prevention of thrombosis. APC resistance should be considered in patients with retinal arterial occlusion when the usual embolic or thrombotic diseases are ruled out.

CASE REPORT

A 35-year-old non-smoking man was referred for a sudden decrease of visual acuity in the left eye. He had no familial or personal history of thrombophilic disorders. At examination, his best corrected visual acuity was 20/20 in the right eye and 20/20 in the left. A superotemporal branched retinal artery occlusion was noted in the left eye with an oedema, vitreous, intraretinal infarction in the affected vessel. A fluorescein angiogram confirmed the branched retinal artery occlusion (Fig. 1). After 2 months, visual acuity improved to 20/25 in the left eye. He had a permanent visual field defect in the area of damaged retina. Goldmann perimetry showed no abnormalities. Heart rate was regular; transthoracic echocardiography, and carotid Doppler studies showed no abnormalities. Red blood cell, white cell, platelet counts, and erythrocyte sedimentation rate were all normal. Platelet aggregation was normal. A search for antinuclear and anticardiolipin antibodies was negative. Prothrombin time and activated partial thromboplastin time (APTT) were normal. Plasma levels of protein C, S, antithrombin III, fibrinogen, plasminogen, and plasminogen activator inhibitor were within normal ranges. APC resistance was determined by evaluating the anticoagulant response of plasma samples to APC with an APTT-based assay. Results were expressed as the following APC sensitivity ratio (APTT + APC)/(APTT – APC). The cut off value was 2.2. In our patient, the APC sensitivity ratio was 2.1. Hypercoagulable V Leiden mutation was disclosed by molecular analysis.
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