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

EDITOR.—During November 1994 following the Joint Committee on Vaccination and Immunisations recommendations a widespread school based immunisation programme was set up for measles and rubella. The objectives were to negate the need for a single antigen rubella vaccine to be given to 11-year-old girls and to promote herd immunity to measles.

We describe two 13-year-old children who developed optic neuritis 2–3 weeks after measles/rubella vaccination.

CASE 1
A 13-year-old boy of Asian origin was seen on the 23 December 1994 with a 2–3 week history of deteriorating vision. Initially this began in the left eye but was bilateral within a few days and was associated with photophobia and pain on eye movements. Three weeks before the symptoms appeared he had received a measles/rubella vaccination at school. There was no family history of Leber's optic neuropathy, multiple sclerosis, or other neurological disease.

General and neurological examination excluding the ocular findings was normal. Visual acuities were corrected to right eye 1/60, N14, and left eye 6/36, N8. Ishihara plates for colour vision were right eye 1/17 and left eye 4/17. Visual fields demonstrated bilateral central scotomas. Funduscopy revealed mild bilateral optic disc hyperaemia with a single flame-shaped peripapillary haemorrhage on the left. The peripheral retina, macula, vitreous anterior segments, and extraocular movements were normal for each eye.

Investigations revealed normal full blood count, biochemistry profile, clotting studies, erythrocyte sedimentation rate, viral B12, and serum angiotensin converting enzyme. Autoantibodies, the VDRL test, and heavy metal screen were negative. Magnetic resonance imaging (MRI) (axial and coronal) revealed normal T2 weighted axial and T1 weighted coronal images. The optic nerves and chiasm were normal. 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 revealed 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.

COMMENT
Neurological complications following rubella or measles vaccination are rare. Rubella has been associated with carpal tunnel syndrome, paraparesis, myelitis, and myeloradiculitis. Measles vaccination has been linked to cases of encephalitis, encephalopathy, febrile convulsions, and encephalopathy, 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 0.16 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. 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, inflammatory exudation, 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 inflammation and demyelination. 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.

Optic neuritis has been reported as a complication with the use of several vaccines including rubella, 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 Kazar and Gager in 1978, 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., reported a 31-year-old woman who developed BSON 1 day after intramuscular rubella vaccination. A third patient, mentioned by Riikonen, 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, has an excellent prognosis. However, 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.

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 atypical 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 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.
Letters

Retinal arterial occlusion associated with resistance to activated protein C

EDITORS,—Resistance to activated protein C (APC) was described in 1994 as a thrombophilic factor responsible for deep venous thrombosis and pulmonary embolism.1 It represents a functional cause of thrombophilic disorder in the normal population (5%). APC is an important component of the physiological anticoagulant system that inhibits factors Va and VIIIa. The resistance to APC is related to a single mutation in the factor V gene which causes the switch from arginine to glutamine at position 506. This mutation of factor V blocks the site of cleavage by APC.2 Reported thrombophilic manifestations include venous thromboembolism and type of central retinal vein thrombosis.3 Arterial occlusion is not clearly associated with resistance to APC. Ischaemic stroke was recently reported in three patients with resistance to APC.4 We described a case of branchial retinal artery occlusion associated with resistance to APC.

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 20/30 in the left. A superotemporal branched retinal artery occlusion was noted in the left eye with an oedematous, whitish, retinal 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 but no papilloedema or optic disc abnormality. Cardiac rhythm 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, and antithrombin III, fibrinogen, plasminogen, 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. Heterozygous factor V Leiden mutation was disclosed by molecular analysis.

COMMENT

Occlusion of the retinal artery is more rarely encountered in younger than in older patients.5 Multiple causes of arterial occlusion in the retina were described. In a recent report, the causes of retinal arterial occlusions in 21 young adults were analysed.6 Emboli were identified in 33% of the patients. Cardiac valvular disease, including atrial myxoma, bacterial endocarditis, and mitral valve vegetation due to lupus anticoagulant, was the mainly recognised condition 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 Behçet’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.7 Protein S deficiency was associated with a case of bilateral branch retinal artery occlusion.8 This biological abnormality was detected in only one young woman with diabetes mellitus and pregnancy in the series of Greven et al.9 Antiphospholipid antibody syndromes are thrombophilic factors that occur in patients with either lupus anticoagulants or antibodies to cardiolipin or dissociated phospholipid serology. Antiphospholipid antibodies can lead to recurrent arterial and/or venous thrombosis.10 APC resistance is clearly related to venous thromboembolism.2 A recent report suggests the possible role of APC resistance in arterial thrombosis.11 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 heterozygous 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.

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Recurrent septic retinal emboli following dental surgery

EDITORS,—Metastatic bacterial endophthalmitis following head and neck surgery is rare.1,2 To our knowledge, no case of recurrent septic retinal emboli with a presumed dental source has been described before.

CASE REPORT
A healthy 36-year-old white man presented to a dental surgeon with a localised periapical abscess at his right upper first molar, which was confirmed by dental x ray. A volume of 0.2 ml of pus was drained after local periaural infiltration with 2% lidocaine with adrenaline 1:80 000 and postoperative irrigation with 0.01% dexamethasone solution. He was prescribed oral amoxycillin/clavulanic acid 375 mg three times daily but did not start antibiotics until 12 hours after the procedure. Three days later, the patient noted sudden blurring of vision and floaters in his right eye but was systematically well.

There was no previous ocular history and the ocular examination was normal. The symptoms were thought to be due to intravenous drug use, rheumatic fever, or other cardiac disease. He had no risk factors to suggest systemic immunosuppression. Systemic examination was unremarkable. He had no sweats, fatigue, or weight loss. Ophthalmological examination revealed a right relative afferent field defect of the central visual field. There was no optic disc swelling or superior retinal stigmata with inferonasal pallor. Fundoscopy revealed a circumscribed whitish retinal infarction involving the temporal macular area and the fovea. The patient was considered to have a recurrent endophthalmitis. The patient consented to a vitrectomy with removal of the septic emboli.

A posterior vitreous face detachment was noted with retinal blood vessels intact. Multiple white opacities were present within the vitreous. The white opacities were observed to float freely within the vitreous, associated with the choroid. The retinal surface was free of new vessels or other evidence of inflammation. Three small septic emboli were removed from the vitreous cavity. The vitreous sample was sent for a bacterial and fungal culture. The result of the bacterial and fungal culture was negative.

A week later, the patient was asymptomatic and the visual acuity was 20/20. The retina was normal, but residual mild macular oedema was present. According to the patient, the emboli were painless, not felt, and did not affect vision. The patient was discharged with no systemic or ocular treatment and was seen 1 month later without any symptoms of recurrence.

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1 Accepted on April 4, 2022 by guest. Protected by copyright. 2 Doi: 10.1136/bjo.2012.201110 on 1 December 1996.

Figure 1 Superotemporal branched retinal artery occlusion.