COMMUNICATIONS

UNUSUAL PRESENTATION OF BENIGN INTRACRANIAL HYPERTENSION*†

EARLY TREATMENT WITH ORAL GLYCEROL

BY

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INCREASED intracranial pressure in the absence of a space-occupying lesion or internal hydrocephalus was first described by Quincke (1893). The condition has since been variously described as serous meningitis (Quincke, 1897; Warrington, 1914; Sheldon, 1933), otitic hydrocephalus (Symonds, 1931), meningeal hydrops (Passot, 1913; Davidoff and Dyke, 1937), pseudotumour (Warrington, 1914), toxic hydrocephalus (McAlpine, 1937), and raised intracranial pressure without brain tumour (Dandy, 1937).

The subject has been greatly clarified by Foley (1955), who described 106 cases from the literature and sixty personal cases, dividing them into two main groups:

(1) Otitic hydrocephalus with preceding middle ear disease and thrombosis of the major lateral sinus, as suggested by Symonds (1931), and borne out by operative findings, and by sinography (Frenckner, 1937; Ray and Dunbar, 1951).

(2) Non-otitic cases, in which the condition was described as benign intracranial hypertension, and which fell into two sub-groups, one with a history of antecedent infection or mild head injury (young age group, with equal sex incidence), and the other with no history of infection, consisting predominantly of females aged 35 to 50, with either obesity or uterine dysfunction. Those cases following infection are also described by Foley as toxic hydrocephalus, although McAlpine (1937) applied this term to cases following nasopharyngeal infection, including cases of otitic hydrocephalus.

Bradshaw (1956), in an analysis of 42 cases, described very similar groups, and included them all under the heading of benign intracranial hypertension, a term also used by Davidoff (1956).

The essential diagnostic criteria are increased cerebrospinal fluid pressure, with accompanying papilloedema, and the presence of a normal ventricular system. Thus accurate diagnosis has only been possible with the advent of ventriculography (Dandy, 1937; Davidoff and Dyke, 1937), and the term hydrocephalus is inappropriate. There is no good evidence to warrant the name meningeal hydrops, the deep sub-arachnoid space found at craniotomy being an artefact (Foley, 1955).

The following case is unusual in that the patient presented with unilateral anterior and posterior uveitis accompanied by transient secondary glaucoma, and went on to develop typical benign intracranial hypertension.

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Case Report

A boy aged 7 was seen as an emergency at night with a 36-hour history of pain over the left eye, mistiness of vision, vomiting, and general malaise. He had had tonsillitis a few months previously.

Examination.—Right eye: normal, visual acuity 6/6.

Left eye: visual acuity 6/18. Ciliary injection, slight corneal oedema, pupil semi-dilated reacting sluggishly to light, aqueous flare with cells. Fundus showed peripheral patches of chorio-retinitis, swelling of the disc with dilated veins, peripapillary haemorrhages and soft white exudates, and macular oedema.

Intra-ocular pressure (Schiötz): Right eye 6·0/5·5 = 14·6 mm. Hg. Left eye 4·0/7·5 = 30·4 mm. Hg.

Treatment.—He was admitted to hospital and treatment was started with Diamox tablets 125 mg. stat. and twice daily; gutt. atropine 1 per cent. daily; gutt. betamethasone four times daily to left eye.

Subsequent Clinical Findings and Progress

(a) *General Condition.*—Irregular pyrexia up to 99·8°F. for 2 weeks, with initial drowsiness and cervical lymphadenopathy. Throat and ears normal. By the second day there was right as well as left papilloedema, and nystagmus on looking to the left with slight left facial weakness, lasting for 3 days.

INVESTIGATIONS: Erythrocyte sedimentation rate 7 mm. in 1st hr (Westergren). Hb 103 per cent. (15 g./100 ml.). White blood cells 9,000/mm³., normal film. Normal bleeding and clotting times. Wassermann reaction and gonococcal complement-fixation test negative. Toxoplasma dye test positive 1/256. Mantoux test negative at 1/1,000. X rays of chest, skull, and sinuses normal. Paul Bunnell test negative. No cytomegalic inclusion bodies in spun deposit of urine.

NEUROSURGICAL OPINION (Mr. Antony Jefferson): Papilloedema without tumour the most likely diagnosis. Treatment with oral glycerol 1 g./kg. three times a day started on fourth day, with fluid intake limited to 25–30 oz. daily. Diagnosis of benign intracranial hypertension confirmed by normal electro-encephalogram and echogram, and a normal air encephalogram (Mr. Antony Jefferson) with normal ventricular fluid. Discharged on oral glycerol 26 days after admission.

(b) *Optic Discs:* Left peripapillary exudates absorbed by the second day, but left disc remained

FIG. 1.—Appearance of optic discs after 6 days' glycerol therapy.

more swollen than right (Fig. 1).

After 18 weeks' glycerol therapy there was considerable reduction in papilloedema (Fig. 2, opposite), but cessation of therapy for three days caused an increase in papilloedema, shown by fundus photographs and size of blind spots.

FIG. 2.—Appearance of optic discs after 18 weeks' glycerol therapy.

(c) *Uveitis and Visual Acuity*: Right eye remained quiet, with 6/6 vision. Uveitis in the left eye became inactive after 3 weeks, with pigmentation of peripheral foci (Fig. 3); the visual acuity improved to 6/6 after 19 weeks.

FIG. 3.—One of the peripheral foci of chorio-retinitis in the left eye, 26 days after admission.

Toxoplasma dye test titre 1/256 on 1st day, 1/128 on 10th day, after topical betamethasone, 1/210 on 15th day (complement-fixation test negative), 1/65 on 22nd day after Tetracycline 250 mg. four times a day, 1/17 on 35th day after Daraprim 12.5 mg. daily, and 1/48 19 weeks after admission. (The mother's dye test was negative.)

Discussion

This patient fits into the group of non-otitic cases of benign intracranial hypertension associated with preceding infection.

Symptoms include vomiting and drowsiness, while headache is uncommon in children with this condition (Bradshaw, 1956).

Neurological signs include mild upper motor neurone lesions (facial weakness in this case), nystagmus in about one-sixth of all cases, and 6th nerve palsy in a quarter of the non-otitic cases (Foley, 1955; Bradshaw, 1956).

Electro-encephalogram is normal, with no slow activity associated with reduced cerebral blood flow in intracranial tumour.

Cerebrospinal fluid pressure is never as great as would be expected from the papilloedema, and was not markedly increased at ventriculography in this case owing to the full glycerol therapy.

Papilloedema, although invariably bilateral, may be unequal, as in this case and in those reported by Giller and Cogan (1952), Foley (1955), Bradshaw (1956), and Friedman (1957). Haemorrhages and exudates on or near the nerve head are common, as are macular oedema and exudates, and this retinopathy may be asymmetrical. The type of exudate is not always specified in the literature, but in the present case the exudates consisted of areas of massive retinal oedema round the disc, simulating juxta-papillary choroiditis, and disappearing without trace in 2 days, except for residual macular oedema.

Visual defects may appear early and be severe (in contrast to papilloedema with intracranial tumour), more especially in the non-otitic group (Turner, 1961; Foley, 1955), about half of which show some early failure, which may be unilateral. Approximately 10 per cent. of all patients may become blind or almost blind in one or both eyes, developing optic atrophy.

Of the field defects, apart from the enlarged blind spots initially, Cross (1948) found that the earliest defect was an arcuate scotoma arising from the blind spot, while central scotomata and homonymous quadrantic defects have also been described.

In this patient the visual acuity in the left eye returned to normal 4½ months after admission, and no central field defect was demonstrated other than the enlarged blind spots. (Campimetry was easy and reliable).

Pathogenesis of the Non-otitic Group

An undistorted ventricular system under increased pressure occurs in (i) obstruction to venous outflow, (ii) active dilatation of cerebral vessels, and (iii) swelling of brain tissue.

(i) There is no good clinical or radiological evidence for superior sagittal sinus thrombosis in the non-otitic group. Mural thrombosis of this sinus involving the arachnoid villi, thus reducing the absorption of cerebrospinal fluid, was suggested by Symonds (1932), but any resulting excess of fluid should cause ventricular dilatation. Similarly, overproduction of cerebrospinal fluid by the action of toxins (McAlpine, 1937) is unlikely.

(ii) Dandy (1937) observed that great fluctuations of the intracranial pressure occurred within a few minutes in these patients, and thought that changes in the cerebral vascular bed were responsible. Foley (1955) also believed that an increased cerebral blood flow existed.

(iii) Cerebral oedema probably plays a part in those female patients with hormonal dysfunction. Thus, Jefferson (1956) described cerebral oedema and papilloedema occurring in Addison's disease, and typical benign intracranial hypertension can be produced in patients (mostly children) receiving systemic steroids, usually when the dose is decreased. Cerebral oedema is a known factor in the otitic group of cases with lateral sinus thrombosis (Symonds, 1952), and it may well play a part in those non-otitic cases with preceding infection.

Role of Allergy.—Both cerebral vasodilatation and cerebral oedema might be expected to occur as a result of allergic phenomena, which are known on occasion to

produce cerebral and meningeal symptoms, with increased intracranial pressure, often accompanied by urticaria or angioneurotic oedema. Sheldon (1933) and McAlpine (1937), among others, described cases of benign intracranial hypertension in which there was a strong suggestion of bacterial allergy, and three cases with anterior (but not posterior) uveitis are recorded.

Role of Toxoplasmosis in This Case.—Three possibilities exist:

(i) The whole illness might represent an acute primary infection with *Toxoplasma gondii*. Although such an infection usually passes unnoticed, it can cause a febrile illness with adenopathy resembling glandular fever, as in this case. There may be ocular involvement and encephalitis, but this would have produced both a more serious illness and a very high and rising titre of dye test antibodies.

(ii) The febrile illness initiated both benign intracranial hypertension and a recrudescence of previous primary ocular toxoplasmosis, and the association of these two conditions in this case is a coincidence.

(iii) The uveitis and the intracranial hypertension have a common aetiology, namely the recrudescence of a primary toxoplasmosis, (neonatal here, since the mother's dye test was negative) precipitated by the stress of a febrile illness (Beverley, 1956).

The moderately high dye test titres are compatible with this, since only a low grade proliferation of organisms occurs, although there is a brisk delayed-type hypersensitivity reaction to cyst content (Beverley, 1958; Beattie, 1958).

The fall in titre from 1/256 to 1/65 over 3 weeks may be correlated with the use of potent topical steroids, reducing the release of local antibody from the eye. The further fall to 1/17 occurred after Daraprim treatment, "rebounding" to 1/48 after 13 weeks with no treatment.

Cerebral cysts have been demonstrated in tertiary toxoplasmosis, and François (1961) postulated the rupture of a cyst, with dissemination of proliferative organisms, to explain the occurrence of a late relapse in the contralateral (normal) eye. It is suggested that rupture of cerebral cysts occurred in the present case, either instead of or at the same time as the rupture of retinal cysts, and that the release of proliferative organisms and toxoplasma antigen into sensitized cerebral tissue produced a hypersensitivity reaction leading to cerebral vasodilatation, increased cerebral blood flow, and cerebral oedema, comparable to the reaction in the retina and choroid, and giving the picture of benign intracranial hypertension.

Treatment with Glycerol

The use of glycerol to reduce intracranial pressure was first suggested by Bovet, Cantore, Guidetti, and Virno (1961) and results were described by Cantore, Guidetti, and Virno (1963). The rapidly effective use of oral glycerol in two cases of benign intracranial hypertension was described by Buckell and Walsh (1964).

The reduction of pressure becomes essential when vision is threatened, and in the past repeated lumbar punctures or a decompression were required. The use of Diamox to reduce the production of cerebrospinal fluid is of little value (Turner, 1961) as might be expected from the discussion on the aetiology of the condition, while, conversely, the use of substances to raise the plasma osmolarity and thus shrink the brain by reduction of interstitial fluid is more successful. Of these agents, glycerol is better than urea, since it can be taken by mouth for long periods, is non-toxic, produces a greater rise in plasma osmolarity but a smaller diuresis, and

penetrates but little into the cerebrospinal fluid, thus causing no "rebound pressure" (Buckell and Walsh, 1964).

The value of the use of glycerol in this case is shown by the effect on the papilloedema of temporarily stopping treatment, and by the fact that there has been no permanent visual impairment or field defect.

Summary

A case is described of benign intracranial hypertension of the non-otitic type presenting in a boy aged 7 with a febrile illness and unilateral ocular toxoplasmosis accompanied by transitory secondary glaucoma. The condition is briefly reviewed and the diagnosis and clinical features in this patient are discussed.

The aetiology is considered, and reasons are advanced for believing that a recrudescence of primary toxoplasmosis could explain both the uveitis and the benign intracranial hypertension on the basis of a hypersensitivity reaction, producing in the brain vasodilatation, increased blood flow, and oedema, with consequent raised intracranial pressure.

The advantages of treatment with oral glycerol are discussed, and its beneficial effects in this case are described.

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