

Familial benign intracranial hypertension

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SYNOPSIS Three sisters with benign intracranial hypertension are reported. This is the first documentation of benign intracranial hypertension in three family members. Obesity is a striking feature in these patients as well as five of the six previously reported patients with familial benign intracranial hypertension. Pregnancy and chronic dysfunctional uterine bleeding, well known predisposing factors in this syndrome when it occurs sporadically, were present in two of the sisters. A familial metabolic defect may be responsible for the intracranial hypertension in these patients.

Pseudotumor cerebri, or benign intracranial hypertension, is a syndrome defined as increased intracranial pressure with no evidence of nervous system dysfunction other than that caused by the intracranial hypertension itself—that is, transient visual obscurations, enlarged blindspots, headache, sixth nerve palsy, papilloedema, and secondary optic atrophy (Johnston and Paterson, 1974). Some patients with benign intracranial hypertension have no clear accompanying cause but demonstrate abnormalities or alteration in endocrinological or metabolic function. These patients are, typically, young females who are obese and may be pregnant or suffering from chronic dysfunctional uterine bleeding (Greer, 1968).

The purpose of this paper is to report the occurrence of benign intracranial hypertension in three sisters who demonstrate these alterations in metabolic function.

CASE REPORTS

CASE 1

A 41 year old lady has suffered from obesity and idiopathic dysfunctional uterine bleeding for most of

her adult life. She has a history of bilateral corneal dystrophy beginning in 1955 and requiring several corneal transplantations over the next few years. Her first complaint of chronic headache and transient visual obscurations was in October 1963, at which time her vision was finger counting in the right eye and 20/60 in the left eye. Visual field examination by finger confrontation was normal. This reduction in visual acuity was thought to be consistent with the corneal dystrophy present. In April 1964, definite papilloedema was observed in the left eye. The right fundus could not be visualized adequately. Skull radiographs were negative. The patient was lost to follow-up until July 1965 when she was hospitalized for another keratoplasty and the left fundus was reported as normal. Headaches persisted, however. In April 1966 she again complained of transient darkening of vision but also of progressive visual loss. Finally, in July 1966, papilloedema was again noted in the left eye. Visual acuity was reduced to hand movements in the right and 20/100 in the left eye. The progressive visual loss could not be explained on the basis of corneal disease. She was admitted to the neurological service at Jackson Memorial Hospital in July 1966, at which time her weight was 100 kg (220 pounds) and the chief complaint was transient three to four second episodes of darkening vision and chronic bifrontal headache. The patient had paleness of the left optic disc with swelling and loss of disc margins consistent with chronic papilloedema. The right disc could not be seen. Lumbar puncture revealed an opening pressure of 530 mm H₂O with clear, colourless fluid, containing one mononuclear cell per mm³ and total protein of 0.22 g/l. Skull radiographs revealed mild enlargement

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of the sella turcica, thinning of the dorsum sellae, and increased convolitional markings consistent with chronic intracranial hypertension. Brain scan, pneumoencephalogram, and right carotid arteriogram were normal. The patient was discharged on acetazolamide and prednisone. She received weekly lumbar punctures for two months, with the opening pressure consistently above 400 mmH₂O. She developed worsening optic atrophy and was noted to have vision to hand movements four months after discharge. At present, the patient is blind and is otherwise well except for obesity and intermittent headache.

CASE 2

A 22 year old woman was admitted to Jackson Memorial Hospital on 14 January 1974 with a chief complaint of transient episodes of blurring and darkening of vision, headache, and horizontal diplopia upon right gaze for several weeks before admission. She was in the fourth month of pregnancy and was ingesting one tablet of multivitamins per day as prescribed by her obstetrician. She had taken birth control pills for one year but had stopped 14 months before admission. She has been obese all her life but denied menstrual disturbance or other drug ingestion. The physical examination revealed a lady weighing 88.6 kg (195 pounds) with a normal blood

pressure and pulse rate. She was bright and alert and in no acute distress. The abnormal findings included marked papilloedema bilaterally without haemorrhages (Fig. 1). There was bilateral lateral rectus paresis, more marked on the right. Visual field examination showed enlargement of the blind spots. Visual acuity was 20/20 bilaterally. Lumbar puncture revealed an opening pressure of 540 mmH₂O with clear colourless fluid containing no cells and a total protein of 0.14 g/l. The plasma cortisol was 717.6 nmol/l which is the upper normal limit. The 24 hour urine hydroxy- and ketosteroid outputs were normal and thyroid function tests were normal. Skull and chest radiographs, EEG, and echoencephalogram were normal. No further diagnostic studies were performed. The patient was given acetazolamide, 500 mg per day. Cessation of diplopia and transient obscurations of vision, and marked diminution of headache occurred after the lumbar puncture. Neurological, fundusoscopic and visual field examinations were normal three and 14 months after discharge (Fig. 2).

CASE 3

A 28 year old woman developed headache and transient obscuration of vision for three weeks before her admission to the hospital. She had mild bifrontal headache as well. The physical examination was

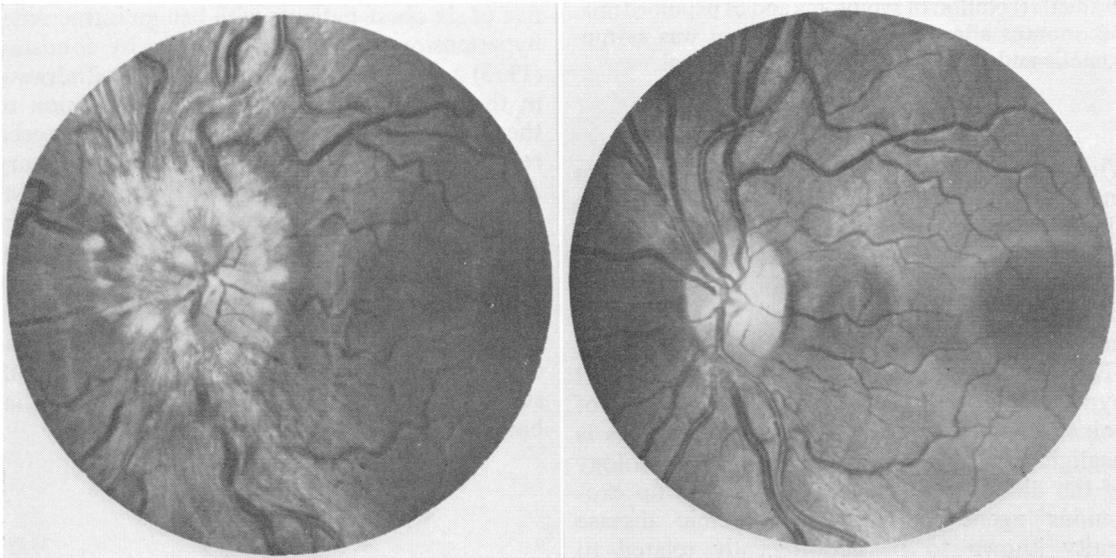


FIG. 1 (left) Case 2. Left fundus during hospitalization showing papilloedema. FIG. 2 (right) Case 2. Normal left fundus 14 months after discharge from hospital.

TABLE
THREE SISTERS WITH BENIGN INTRACRANIAL HYPERTENSION

Patient	Age at onset (yr)	Weight (kg)	Predisposing factors	CSF pressure (mmH ₂ O)	Special studies	Follow-up
1 M.H.	30	100.0	Obesity, menstrual irregularity	530	Brain scan Pneumoencephalogram Bilateral carotid arteriograms Electroencephalograms	Optic atrophy Blindness (9 yr)
2 H.C.	22	88.6	Obesity, pregnancy	540	Brain scan Echoencephalogram Electroencephalogram	Asymptomatic (14 m)
3 T.W.	28	97.7	Obesity	—	Brain scan Bilateral carotid arteriograms Electroencephalogram	Asymptomatic (6 m)

normal except for the weight of 97.7 kg (215 pounds) and the presence of 4+ papilloedema without haemorrhages bilaterally. The visual acuity and visual fields were normal except for enlarged blind spots. There was no history of any predisposing factor of pseudotumor cerebri. Routine blood studies were normal. Chest and skull radiographs, bilateral carotid arteriograms, and brain scan were normal. The patient was given methylprednisolone, 32 mg per day, for one month followed by tapering dosage to a maintenance of prednisone 5 mg/day. The medication was stopped four months after discharge. Several examinations during this time revealed gradual resolution of symptoms and of papilloedema. Six months after discharge the patient was asymptomatic and the optic discs appeared normal.

DISCUSSION

Three previous reports have described benign intracranial hypertension in family members (Bucheit *et al.*, 1969; Howe *et al.*, 1973; Rothner and Burst, 1974). Two female siblings were affected in two reports and a mother and son in the third. The present report is the first documentation of this illness in three family members (Table). The prevalence of benign intracranial hypertension is unknown but the probability of coincidental occurrence in these three sisters is negligible. A genetic defect is a likely aetiology of the disorder in these patients, since no exogenous agent or common systemic disease entity known to be aetiologically related to benign intracranial hypertension was present.

Obesity is a common abnormality in the reported patients with familial benign intra-

cranial hypertension. It was present in five of the six reported familial patients and is a striking feature in the three sisters reported here. Severe chronic dysfunctional uterine bleeding and pregnancy present in two siblings just described were not noted in the previous cases. Searches for a definite aetiological link between obesity and benign intracranial hypertension have been unsuccessful. Two separate reports suggest such a link but require confirmation. Oldstone (1966) used the metapyrone test to demonstrate a deficiency of anterior pituitary ACTH reserve in five of six obese patients with benign intracranial hypertension. More recent studies by Johnston (1973) have shown that acute steroid withdrawal in the rat, producing persistent suppression of the pituitary ACTH reserve, results in increased resistance to CSF outflow. Defective pituitary ACTH reserve with subsequent increased resistance to CSF absorption and intracranial hypertension has been hypothesized as the pathophysiological mechanism in these patients (Johnston, 1973).

Study of future cases of familial benign intracranial hypertension may be particularly fruitful, since a metabolic defect may occur on a familial basis in these patients.

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