Benign Intracranial Hypertension after Antibiotic Therapy

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Benign intracranial hypertension or pseudotumour cerebri is a syndrome of increased intracranial pressure and bilateral papilloedema in a patient with normal or small ventricular systems in the absence of space-occupying lesions. No intracranial infection, hypertensive encephalopathy, or hypercapnic respiratory failure is found, and the cerebrospinal fluid content is normal. It has been described in the past in association with hypervitaminosis A, hypovitaminosis A, hypoparathyroidism, prolonged corticosteroid therapy, chronic adrenal insufficiency, severe hypochromic microcytic anaemia, and pregnancy (Koch-Weser and Gilmore, 1967).

Clinical uses of tetracycline have become associated with a number of unusual complications, one of which is benign intracranial hypertension described in infants as the "bulging fontanelle syndrome" (Gellis, 1956-7; Fields, 1961; O'Doherty, 1965; Folsom, 1966; Krevsky, 1968). There is only one recorded case of benign intracranial hypertension secondary to tetracycline therapy in an adult (Koch-Weser and Gilmore, 1967). The present report concerns a patient who received ampicillin and tetracycline sequentially and who was admitted to hospital with evidence of benign intracranial hypertension.

Case Report

The patient, a Caucasian man aged 54, was admitted to hospital on 7 January 1972. He had no relevant past history of ill health and had never received antibiotics. About four weeks previously he had experienced vague pain across the lower anterior chest area not related to respiration but associated with a feeling of "chill." His general practitioner prescribed ampicillin capsules 250 mg six-hourly for what he thought to be an episode of pleurisy, but about two hours after the first dose he developed constant frontoparietal headache lasting for two hours. After this he awoke each morning with a severe headache in the same area lasting one to two hours, passing off slowly, exacerbated by coughing and straining, and associated with "heaviness" in the eyes.

The chest pain cleared in three days but the practitioner was not satisfied with the clinical progress, and after seven days of ampicillin therapy he substituted capsules of tetracycline 500 mg six-hourly. This immediately led to an increase in the severity and duration of the morning headaches. Medication continued for 16 days, the patient having consumed an oral dose of 32 g of tetracycline. The patient then discontinued the therapy voluntarily and symptoms were less severe at the time of admission two days later. On the morning of admission he experienced tingling in the right half of the body and became dazed for about an hour.

On examination no abnormality was found in his higher mental functions. Systemic examinations showed nothing abnormal except for the presence of bilateral papilloedema (three dioptries). Fortu-

nately a consultant ophthalmologist had seen the patient on many occasions in the past because of his refraction errors and confirmed the appearance of papilloedema. There was no tenderness over the sinuses or any obvious morbidity in the ears.

Haemoglobin was 14.6 g/100 ml, W.B.C. 6,000/mm³, and E.S.R. 18 mm/hr (Westergren). The blood urea was 29 mg/100 ml, with serum sodium 139 mEq/l. and serum potassium 4.0 mEq/l. The electrocardiogram and chest x-ray film showed no abnormality. Midstream urine analysis was normal, as were x-ray pictures of the skull and cervical spine. Electroencephalogram taken 13 days after admission was normal. A technetium brain scan showed a normal uptake.

The headache, which was improving before admission, disappeared in about two hours after admission. The patient remained well and asymptomatic. Papilloedema cleared in 12 days.

Comment

Benign intracranial hypertension developing as an unusual complication of tetracycline was apparently not recognized until Gellis (1956-7) mentioned it in an editorial comment. Since 1961 many cases have been reported in infants in whom administration of tetracycline resulted in the bulging fontanelle syndrome, which subsided within a few hours to three days after discontinuance of the drug. Though the complication may appear five hours to four days after tetracycline therapy there is no definite relation between the occurrence of benign intracranial hypertension and the tetracycline dosage or length of therapy (Koch-Weser and Gilmore, 1967).

In the present case ampicillin seemed to be the prime offender because headache was provoked a few hours after the first dose of the drug. This was made worse and perpetuated by tetracycline therapy. Prompt spontaneous progressive diminution and disappearance of headache within two days after discontinuance of tetracycline therapy suggests a cause-and-effect relationship. Papilloedema cleared in 12 days whereas in the only other case in an adult reported by Koch-Weser and Gilmore (1967) it took four weeks for papilloedema to subside. All previous reported cases of benign intracranial hypertension after tetracycline therapy resolved completely with no sequelae, as did the present case in which the patient remained well 28 days after admission.

The mechanism of benign intracranial hypertension after tetracycline therapy remains obscure though hypersensitivity has been suggested.

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