Benign Intracranial Hypertension in Infants due to Tetracycline

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Introduction

SIDE EFFECTS associated with tetracycline therapy are well known (Pflug, 1963). The commonest are gastro-intestinal effects such as nausea, vomiting and diarrhoea. Others include photosensitive skin rashes, fatty "degeneration" of the liver, especially in the pregnant woman, renal effects such as a high blood urea due to a negative nitrogen balance, and a transient renal tubular disorder mimicking the Fanconi syndrome. The last has been attributed to the effect of outdated tetracycline.

In addition, there are a number of side effects peculiar to the neonate and infant. Amongst the better known of these are the yellow-green pigmentation of decidous teeth seen in infants given tetracycline (Davies et al., 1962) and the inhibition of normal skeletal growth of the premature infant during tetracycline administration (Cohlan et al., 1963). It is less well known that benign intracranial hypertension occasionally occurs. This is indicated by a bulging anterior fontanelle in an infant receiving tetracycline therapy (Millichap 1959, Fields, 1961). Although benign in itself, these infants should all be admitted to hospital in order to exclude a more serious cause of the bulging fontanelle.

The following case is reported as an example of this complication.

Case Report

The patient, a 7 month old, Indian female infant was well till eight days prior to admission when she developed a fever, cough and coryza. She was seen by a general practitioner who commenced a course of oral tetracycline (dose not known). The fever and cough subsided but five days after tetracycline had been commenced the anterior fontanelle was noticed to be bulging. On admission to hospital the child was active and fed well. Her temperature, pulse and respirations were normal. The head circumference was 42 cm. (normal for her age). The anterior fontanelle was bulging but not tense. There was no nuchal rigidity and muscle tone and deep tendon reflexes were normal. The pupils were equal and reacted to light and the fundi were normal as was the remainder of the physical examination.

Investigations

Blood count and an X-ray of the skull showed no abnormalities. A lumbar puncture was unsuccessful but a ventricular tap showed a pressure of 100 mm and clear CSF with 2 RBC, 2 WBC, sugar of 80 mg% and protein of 10 mg%. No organisms were detected and culture showed no growth. Subdural taps were dry on both sides.

Following the ventricular tap, the anterior fontanelle was less full but it was another twenty-four hours before it returned to normal. No therapy was given and on discharge three days after admission, the infants's general condition was satisfactory. At follow-up 2 months and 4 months later there were no neurological deficits and the baby appeared to be developing normally.

Discussion

The history of tetracycline therapy followed by a bulging fontanelle in an otherwise well baby

suggested that the raised intracranial tension was due to tetracycline. However the possibility of an acute meningitis, a partially treated meningitis or a subdural effusion could not be excluded clinically.

Other causes of a bulging anterior fontanelle in a newborn or infant include, Nalidixic acid (Boreus and Sundstrom, 1967, Deonna and Guignard, 1974), Corticosteroids, particularly when reduced or withdrawn (Greer, 1963, Neville and Wilson, 1970), Vitamin A in excess, (Marie and See, 1954) and also in deficiency, (Keating and Feigin, 1970) and otitis media, (Symonds 1952, Greer 1962).

Our patient had received none of the above drugs and showed no evidence of otitis media, hypocalcaemia or avitaminosis. The anterior fontanelle returned to normal following cessation of tetracycline therapy.

The pathogenesis of benign intracranial hypertension due to tetracycline is uncertain but is probably due to a number of factors. Sereni et al., (1965) were able to show that an analogue of tetracycline, namely tetracycline-1-methylene-lysine is excreted more slowly by the human newborn baby than by an older infant, and that the plasma concentrations 6 and 12 hours after oral administration of a single dose (12 mg/kg) of the tetracycline analogue were always significantly higher in newborn babies than in infants more than 2 months old. It was concluded that this was because of the lower glomerular filtration rate of the neonate. The same paper also reported that the brain tissue concentration of the tetracycline analogue in newborn rabbits was approximately ten times higher than that in 2 month old rabbits given the same dose weight for weight. Among the tissues examined only the brain showed a marked accumulation of the analogue in the newborn rabbit. It is postulated that similar results would probably be found with tetracycline.

In the case reported here, the dose of tetracycline given was not known but signs of a raised intracranial pressure were only noticed on the fifth day of administration. It is possible that the accumulated doses of tetracycline given to this infant produced a high plasma tetracycline concentration. If the brain of the newborn infant also shows preferential concentration of tetracycline, the bulging fontanelle might have been the result of a local reaction to this unusually high concentration.

Although not a common side effect of tetracycline therapy, the possible development of intracranial hypertension following its use is a further reason for avoiding this drug in the treatment of infections in infants and young children.

Summary

An infant was given tetracycline for a febrile illness. Five days later she developed a bulging anterior fontanelle which subsided on cessation of tetracycline therapy.

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