UKALL III schedule and special vigilance is needed at that time.

Summary

A child with acute lymphoblastic leukaemia complicated by prolonged gastrointestinal and skin haemorrhages due to profound thrombocytopenia finally died of thrombotic occlusions of major cerebral arteries due to mucormycosis. Biopsy of any suspect lesion is needed urgently before prolonged therapy with amphotericin B is started. So far there have been no cures in childhood.

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References


D. G. SIMS,* D. J. SCOTT, and T. C. NOBLE
Departments of Child Health and Pathology, Newcastle General Hospital, Newcastle upon Tyne NE4 6BE.

*Correspondence to Dr. D. G. Sims.

Congenital rubella associated with hypsarrhythmia

Hypsarrhythmia, or infantile spasms, falls into two broad groups when considered on an aetiological basis. In one-third of cases there is no known predisposing factor, while in the other two-thirds a history of cerebral insult is a possible causative factor.

Some factors implicated in causing hypsarrhythmia have included cerebral birth injury, toxoplasmosis, postnatal head injury, meningitis, encephalitis, tubercous sclerosis, phenylketonuria, pyridoxine deficiency (Millichap et al., 1962), and infection with cytomegalovirus (Stern, Latham, and Tizard 1968). To our knowledge congenital rubella infection has never been implicated as a contributing factor.

Case report

In the 16th week of gestation the mother was infected with rubella. Diagnosis was confirmed by a rise in rubella antibody titre from 1:16 at the time of exposure to 1:2048 two weeks later. At 37 weeks' gestation a male infant was born after a 5½-hour labour. No resuscitation was required and physical examination showed no abnormality. Birthweight was 3.35 kg.

On the fifth day right-sided twitching, which later became generalized, was noted but was easily controlled with anticonvulsants. Examination of cerebrospinal fluid, blood culture, serum calcium, and blood glucose, was normal. Platelet count was not depressed and x-rays of the long bones were normal. Rubella virus was not grown from urine and nasopharyngeal secretions. Blood taken on the 6th day of life showed rubella HA test titre of 1:2048 and a rubella specific IgM titre of 1:40.

The patient was hypotonic and lethargic for the next 3 days but by the 11th day of life physical examination was normal, and he was discharged with no medication. He was next seen at 6 weeks of age, was smiling and physical examination was again normal. At 5 months he began to have episodes of quickly raising both arms and shuddering for 2 or 3 seconds. Infantile spasms were suspected and confirmed by electroencephalogram (EEG), which showed the widespread slow activity with numerous high voltage spike waves typical of hypsarrhythmia (Fig.). Physical examination, serum chemistry, and cerebrospinal fluid were normal.

A course of ACTH (20 IU twice daily) was started 2 weeks after the spasms were first noticed by his mother. EEG 10 days after ACTH was started showed low voltage with irregular theta rhythm and some delta activity in all leads, no longer the pattern of hypsarrhythmia. After 6 weeks the ACTH dose was reduced in steps and was completely withdrawn 3 weeks later. At 9 months of age his EEG was normal.

Monthly assessments since birth showed that development was normal up to the onset of hypsarrhythmia. Development then began to lag. By 10 months he was functioning at a 5-month level using the Stycar tests (Sheridan, 1968). A review at 25 months showed normal hearing and no evidence of cataracts or retinopathy. A Griffiths assessment (Griffiths, 1954) showed delay in all areas. Delays were most marked in language development (9-month level) and hand-eye co-ordination (12-month level).

Discussion

There is no doubt that this child was exposed to rubella at 16 weeks' gestation as shown by his mother's antibody response. The rubella specific IgM titre of 1:40 on the 6th day of life is not particu-
larly high but it has been shown that milder forms of congenital rubella are not frequently associated with raised IgM levels at birth (McCracken, et al., 1968).

A Medlars search of the world medical literature over the past 10 years did not show any reported association between congenital rubella and infantile spasms. This case suggests that congenital rubella should be added to the long list of factors contributing to this condition.

The treatment of infantile spasms has included conventional anticonvulsants, chlortetracycline, pyridoxine, ketogenic diet, L-glutamine, chlordiazepoxide, and clonazepam. In 1958, Sorel and Dusaucy-Bauloye reported that in 6 of 7 patients with infantile spasms, corticotrophin therapy controlled the seizures and modified the EEG. Since then ACTH or corticosteroids have been the most common treatment for infantile spasms, but though they may control the spasms and improve the EEG, their role in preventing intellectual impairment is not as well established.

Friedman and Pampiglione (1971), in a review of 105 infants with hypsarrhythmia, showed that the prognosis for normal intelligence was better in a group given steroids. This study did not compare results in patients divided into symptomatic and cryptogenic groups as described by Jeavons and Bower (1964), and did not mention how soon after the onset of spasms steroids were started. These factors seem to have some predictive value. If patients are put into either a cryptogenic group, where the aetiology is unknown, or a symptomatic group where there is known cerebral insult, the cryptogenic cases and those which follow pertussis immunization have a better prognosis (Jeavons, Harper, and Bower, 1970).

Improved prognosis with early steroid treatment was first reported by Sorel and Dusaucy-Bauloye (1958). A child from the symptomatic group who

**FIG.—Electroencephalogram showing hypsarrhythmia before ACTH therapy.**
made a full recovery when treatment was started 5 days after the onset of the spasms has also been reported (Oates and Stapleton, 1971). Because of delays in the diagnosis of hypsarrhythmia early treatment usually implies that it was started within 6 weeks of the onset of spasms (Chevrie, Aicardi, and Thieffrey, 1968).

A review of 150 cases (Jeavons, Bower, and Dimitrakoudi, 1973) showed no difference in long-term prognosis when steroids were used. This review showed that factors associated with a good prognosis were normal development before the onset of the spasms, a short period of spasms, and early steroid therapy in the cryptogenic group. 37% of children in the cryptogenic and immunization groups made a full recovery, the prognosis being much worse in the symptomatic group.

Summary
A child exposed to rubella at 16 weeks' gestation developed hypsarrhythmia at 5 months of age. Treatment with ACTH quickly improved the electroencephalogram and controlled the seizures, but at 2 years of age development was delayed. Hypsarrhythmia has not previously been described in association with congenital rubella infection.

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R. K. OATES* and DAVID HARVEY
St. Charles's Hospital and Queen Charlotte's Hospital for Women, London.

*Correspondence to Dr. R. K. Oates, Dept. of Medicine, Royal Alexandra Hospital for Children, Campedown, N.S.W., 2050, Australia.

Long-term results of surgical treatment for pulmonary valve stenosis

Since the introduction of surgical treatment for congenital pulmonary stenosis (Brock, 1948), the procedure has become well established with a low mortality (Nadas and Fyler, 1972). In reporting a series of 117 children who underwent pulmonary valvotomy or valve excision, we particularly refer to the progress of the 109 patients who survived.

Patients and indications for operation

All 117 patients had pulmonary valve stenosis with an intact ventricular septum, and underwent operation during the period 1956–1973. There were 60 boys and 57 girls, ranging in age from 1 to 14 years (mean 4·5 years). The indication for investigation was the clinical picture of substantial pulmonary stenosis, supported in most instances by characteristic x-ray signs and, in 41 patients (35%), by ECG evidence of right ventricular hypertrophy. 26 (22%) were investigated under the age of 4 years because of the onset of cardiac failure (4) or ECG evidence of severe right ventricular hypertrophy. Symptoms were present in a total of 12 patients (10%).

Investigations, which included cardiac catheterization and selective angiography, were completed in 102 patients (58%) just before school entry. The systolic pressure gradient across the pulmonary valve ranged from 40–250 mmHg (mean 108).

Operation. Operation was performed in 102 patients with cardiopulmonary bypass support, but in 15 patients early in the series moderate hypothermia at 30°C was used. Using the transarterial approach, mobilization of the fused commissures from the pulmonary arterial wall followed by commissurotomy was sufficient to relieve the obstruction in 91, but valve excision was necessary in 26 either because of an underdeveloped valve ring or because the severity of the obstruction made commissurotomy inadequate. Furthermore, 12 patients required infundibulotomy. Even so, in 43 patients right ventricular hypertension had not been abolished at this stage. 8 patients died at operation or within 72 hours; 4 had undergone commissurotomy and 4 valve excision. 6 (75%) deaths were in patients with a valve gradient exceeding 150 mmHg.