CLINICAL ASPECTS OF CONGENITAL TUBERCULOSIS

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(RECEIVED FOR PUBLICATION DECEMBER 5, 1955)

Congenital transmission of tuberculosis is rare. In the past the diagnosis has usually been made in the post-mortem room and the condition has interested the pathologist more than the clinician. In the majority of published cases the nature of the illness has been apparent soon after birth. In others, however, the symptoms have not appeared for several weeks or months and it is not easy to accept all of these as true examples of congenital transmission of the infection, even though they fulfil all the criteria detailed by Beitzke (1935), for it is well known that a very brief exposure to an adult with phthisis may be sufficient to infect an infant.

Since streptomycin became available about a dozen cases have been diagnosed early, treated and apparently cured. In this paper another successful case is recorded and the symptoms, diagnosis and management are discussed.

Case Report

A female infant was born in Walton Hospital on November 2, 1953, three weeks before the expected date and weighing 5 lb. 12 oz. (2,632 g.). Her mother had developed pleurisy with effusion when five months pregnant. She had responded well to treatment without antibiotics and was afebrile for several weeks before going into labour. A week after parturition her temperature again rose, but a radiograph of the chest showed thickening of the basal pleura only. Two weeks later another radiograph showed miliary tuberculosis. She was treated with streptomycin and isoniazid and she made a good recovery.

The infant was segregated from her mother immediately after birth and did not come into contact with any other case of tuberculosis. She was vaccinated with B.C.G. (0.1 ml.) in the left arm on the second day of life. Her progress was uneventful until the eighteenth day when she lost 2 oz. (57 g.) and seemed lethargic. The next day a respiratory infection was suspected and chloramphenicol prescribed. Three days later her condition had deteriorated and there were signs of consolidation in both lungs. Material aspirated from the stomach the same morning (the nineteenth day of life) contained many acid-fast bacilli, and a radiograph taken the day previously showed generalized bronchopneu-

monia. Treatment with streptomycin and isoniazid was started forthwith. She was nursed in an 'oxygenaire' incubator with a high humidity and occasional periods of oxygen administration. During the next three or four weeks she remained very ill. She fed badly, vomited at times and had severe dyspnoea with inspiratory recession of the lower chest. The spleen became palpable and almost reached the level of the iliac crest. Eventually there was considerable improvement in the chest signs and radiological appearances, but she did not gain weight. Chemotherapy was stopped after three months. Her weight was then 6 lb. (2,736 g.). In the next two months she gained 1½ lb. (694 g.), but at the age of 6 months there was clinical and radiological deterioration. A second course of treatment with streptomycin and isoniazid lasted three months. During this period she gained 4 lb. (1,816 g.) in weight and the clinical signs in the chest improved considerably. On her first birthday she weighed 17 lb. 6 oz. (7,925 g.). She was then able to sit without support, could almost stand and took a lively interest in her toys and surroundings. A radiograph of the chest showed basal congestion in the lung fields and some increase in the mediastinal shadow. The B.S.R. was 9 mm. in one hour (Westergren) and haemoglobin 12 g. %. At the age of 18 months she still appeared very well and weighed 20 lb. 3 oz. (9,205 g.).

During the first course of treatment she developed a purulent discharge from the right ear and this continued intermittently for about one month. Tubercle bacilli were not isolated from this discharge and there has been no recurrence. During the second course of treatment a fluctuant swelling developed in the right groin. This was incised and caseous material was expressed from which tubercle bacilli were cultured. The lesion soon healed and has not given further trouble. There were never any meningeal signs and the C.S.F. was not examined. The eyes were examined frequently but no choroidal tubercles were seen.

There was very little local reaction to the B.C.G. vaccination. Though potent testing material was used the Mantoux reaction remained negative until the seventh month of life.

Tubercle bacilli were cultured from stomach washings obtained on the nineteenth day of life and again in April, 1954, and in February, 1955. None were found in samples taken in July, 1954. Bacilli cultured from the inguinal lesion in August, 1954, were fully sensitive to streptomycin, isoniazid and P.A.S.

Discussion

The Clinical Picture. Much of the literature about congenital tuberculosis deals with the pathological aspects of the disease and only the more recent reports give many clinical details.

Usually the symptoms start during the first month of life and are those common to any infection in the newborn period. The infant refuses some feeds, vomits a little and loses weight. The temperature may be raised. The spleen is often enlarged and sometimes the liver. A cough and physical signs of bronchitis or pulmonary consolidation have been recorded on some occasions, but there have also been instances of extensive lung involvement with few clinical indications of its presence. In more than half of the reported cases the infant has died within three or four weeks of the first sign of illness, and the diagnosis has been made at necropsy.

The shortest history was recorded by Horley (1952). Apparently well during the first week of life, the infant had a cyanotic attack on the eighth day and died 24 hours later. Post-mortem examination revealed miliary tuberculosis.

Hughesdon (1946) records the longest survival without treatment. This infant suffered from frequent attacks of bronchitis and otitis media and latterly symptoms suggesting pink disease. She was not taken to hospital until the age of 27 months when her weight was 21 lb. (9,575 g.). Tuberculous meningitis was diagnosed a few days after admission and she died two weeks later. At necropsy a primary focus was found in the liver and this was held to confirm congenital transmission of the infection. Amick, Alden and Sweet (1950) reported two cases where the presenting sign was enlargement of the cervical glands. In one infant this was noticed at the age of 56 days. The chest radiograph was then clear but two weeks later showed miliary tuberculosis, and the gastric washings contained tubercle bacilli. The other infant had fever and enlarged neck glands at 49 days, followed by right otorrhoea and right facial paralysis. Material obtained from the mastoid bone and biopsy of a lymph node showed tuberculous lesions. Surprisingly the chest radiographs of this baby remained clear throughout the illness. Both were considered to be undoubted cases of intra-uterine infection and both recovered after streptomycin therapy.

Obstructive jaundice was a prominent feature in four cases (Hughesdon, 1946; Debré, Furiat-Laforet and Royer, 1948; Ballabriga Aguado, 1950). One infant developed deep jaundice and pale stools at the age of 1 month then recovered and lived for nearly a year before dying from miliary disease. A focus assumed to be the primary infection was found in

the liver. Another infant became acutely ill at 14 days with vomiting, abdominal distension and jaundice. Tubercle bacilli were found in the gastric washings. The biliary obstruction in these cases was presumably caused by enlarged portal glands.

Tuberculous meningitis has not been common in cases of congenital infection, possibly because early death has precluded the development of a Rich focus. Siegel (1934) found only three examples in 38 case reports. A more recent case in which the meninges were involved was recorded by Lesné, Cayla, Roche and Allard (1949).

The mother of this infant developed miliary tuberculosis and meningitis in June, 1948. She received a total of 60 g. of streptomycin in the four weeks preceding parturition. The placenta was examined for tuberculous lesions and acid-fast bacilli, but none were found. The infant weighed 2,360 g. at birth and appeared normal. When he was 5 weeks old streptomycin treatment was started because a radiograph of the chest 'montrait une image granulique'. Two weeks later (the infant being only 54 days old) increased tension was noticed in the anterior fontanelle and so lumbar puncture was performed. The cell count and protein content of the cerebrospinal fluid were increased but Koch's bacilli were not found on direct examination. Another specimen obtained later caused tuberculosis when inoculated into a guinea-pig. Treatment with streptomycin was continued for nine months after which the cerebrospinal fluid was normal. When 1 year old the child weighed 8 kg. and appeared well.

Diagnosis. Of what value are the usual aids to diagnosis when applied to tuberculous infection of congenital origin, and does the condition of the mother and examination of the placenta help in predicting the likelihood of the disease?

THE INFANT. Experience with B.C.G. vaccination has shown that the young infant is capable of producing a positive tuberculin skin reaction.

In many case reports of congenital tuberculosis the Mantoux reaction is not mentioned. In my patient it did not become positive until the infant was 7 months old in spite of the added stimulus of B.C.G. vaccination. A positive response to intradermal P.P.D. has, however, been found as early as the twenty-first day of life, and in this case (Amick *et al.*, 1950) it preceded all symptoms of illness. An intradermal tuberculin test may be helpful in diagnosis, but its value will be diminished by the increasing use of B.C.G. for newborn infants.

Siegel (1934), reviewing the pathological findings in 38 cases, found the lungs to be involved in 37 and

the liver in only 31. As lung infection is common and usually extensive, examination of the fasting stomach contents for tubercle bacilli is likely to give a positive result. This was so in my patient and in a number of others in the literature. It is probably the quickest and most helpful way to establish the diagnosis. The value of the chest radiograph needs no emphasis.

Confirmation of the diagnosis during life has been made by histological examination of material from an infected mastoid, a cervical lymph node and tibial bone marrow (Amick *et al.*, 1950).

THE MOTHER. In some reports of congenital tuberculosis the mother's lesion has been recorded as 'slight' or 'mildly active', and her progress has been good. More commonly she has had a severe generalized infection, and in more than half the reported cases has died within a few weeks of parturition. On the other hand, there are many records of women with severe miliary tuberculosis giving birth to healthy infants.

In five cases the mother has shown no evidence of tuberculosis at the time of delivery (Straus, 1895; Morley, 1929; Söderström, 1932; Pagel and Hall, 1946 and 1948; Hughesdon, 1946). In one (Pagel and Hall) the mother developed widespread and fatal tuberculosis 12 months later, but in Hughesdon's report she was still alive and apparently healthy two years later.

When the mother has tuberculosis of the pelvic organs the infant may aspirate infected material from the liquor amnii or the birth canal. Undoubted cases of transmission of the disease by this route are rare. In 1939 Reichle and Wheelock found only eight acceptable cases of this nature in the literature. In all of these the infant quickly succumbed to severe tuberculous bronchopneumonia.

To keep this problem in perspective it is good to recall Debré's study of 1,369 infants born to tuberculous mothers. None showed evidence of congenital infection over a period of four years (Rich, 1944).

THE PLACENTA. The foetus of a tuberculous woman escapes infection far more often than does the placenta. Schmorl and Geipel (1904) examined 20 placentae from tuberculous mothers and found microscopical lesions in nine, though the infants remained healthy. Pathologists engaged on routine hospital work will note with interest that these workers examined 2,000 sections from one case before demonstrating the disease. Inspection and microscopy of the placenta are not therefore of practical help in finding cases of congenital tuberculosis. In view of the frequency of placental

infection, however, there is much to be said for the recommendation of McIntyre, Drimmie and Gordon (1953) that milking the cord and delay in its ligation should not be practised when the mother has tuberculosis.

Management. Congenital tuberculosis is rare and in the past has often proved rapidly fatal. The likelihood that it will occur in any particular case cannot be predicted by consideration of the mother's lesion, nor by the presence of foci in the placenta. All infants born to tuberculous mothers (whether 'active' or not) should therefore be kept under close observation, particularly during the first two months of life. If there is any departure from normal health, samples of the gastric content should be examined for tubercle bacilli by direct microscopy, as well as by culture and guinea-pig inoculation. Radiographs of the chest taken at the age of 2, 4, 6 and 8 weeks may also be helpful. There is no need to perform a Mantoux test before giving B.C.G. vaccination as was advocated by Mason (1954). This would cause unnecessary delay, for the vast majority of infants are not infected, and it might be negative in the presence of infection. The danger of provoking Koch's phenomenon by vaccinating an infant during the early stage of infection is probably very slight, if indeed it exists at all. This problem was fully discussed at the Conference on European B.C.G. Programmes and in its report Dr. H. J. Ustvedt (1951) writes 'there is very little evidence to indicate that tuberculous disease occurring in individuals vaccinated with B.C.G. in the pre-allergic phase is more serious than where no B.C.G. has been given'.

As soon as it is likely that an infant is infected, treatment with streptomycin and isoniazid should be started without delay and continued for six months. P.A.S. may cause severe digestive upsets in the newborn (Delthil, Péretti de la Rocca and Thévenier, 1952) and is probably unnecessary.

Summary

A case of congenital tuberculosis is recorded. The infant received B.C.G. vaccine before symptoms developed and responded to treatment with streptomycin and isoniazid. The symptomatology, diagnosis and treatment are discussed. Direct examination of the gastric contents for acid-fast bacilli is probably the most rapid way of confirming the diagnosis.

I wish to thank Dr. O. F. Thomas for giving me clinical details of the patient's mother.

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