CASE REPORT

COMBINED FORMS OF MENINGITIS:

MIXED INFECTION OF THE MENINGES BY THE TUBERCLE BACILLUS AND MENINGOCOCCUS

BY

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It is rare to find two different causative organisms in a case of meningitis and of extreme rarity when one of these organisms is the tubercle bacillus.

Neal (1924) reported her analysis of 1535 cases of meningitis, in which only six (0.32 per cent.) were due to mixed organisms. All six cases were in children and included such organisms as the meningococcus, staphylococcus, *b. paratyphosus* B., haemolytic and non-haemolytic streptococcus, pneumococcus, and organisms of the *b. coli* group, but not the tubercle bacillus. An interesting case of mixed meningitis was described by Ravitch and Washington (1937) in a child whose blood culture grew meningococci and salmonella *suipestifer*. Both organisms were also cultured from the cerebrospinal fluid, but it was believed that the salmonella *suipestifer* had been introduced by blood contamination of the cerebrospinal fluid during lumbar puncture. Ashmun (1933) had five cases of mixed meningitis with pneumococci and streptococci present in the cerebrospinal fluid of all cases. In two cases the diplococcus *catarrhalis* was also present.

The source of the infection was significant in a case reported by Knights (1937). A boy was admitted to hospital with meningococcal meningitis and had a relapse in three weeks. Both haemolytic streptococci and meningococci were cultured from the cerebrospinal fluid and from his throat. Many cases are of otitic origin, and such a case was described by Huenekens and Stoesser (1927) in a child who had both haemolytic streptococci and pneumococci in the cerebrospinal fluid and who recovered after a bilateral mastoidectomy. The case of a baby whose cerebrospinal fluid grew on culture both pneumococci and bacillus *influenzae* was reported by Gaffney (1940), and an account of successful chemotherapy of haemolytic streptococcal meningitis and pneumococcal meningitis in the same patient is given by Reid (1940), but here the infections did not occur simultaneously.

The only reported case I could find of the tubercle bacillus being present with other organisms affecting the meninges was that of Moritz (1936). This patient died after both the tubercle bacillus and Friedlander's bacillus had been found in the cerebrospinal fluid. Griffith (1937) has described the case of a girl with tuberculous meningitis in which the organisms were mixed bovine and human tubercle bacilli, and refers to several similar cases.

Case report

The patient was a female child aged fourteen months, weighing 19 lb. 4 oz. She was a full-time baby, born by normal delivery, and weighed $9\frac{1}{2}$ lb. at birth. She had been breast fed till twelve months of age and then had a good mixed diet. Her mother and father were alive and well and she had one healthy sister aged six years. The maternal grandfather had pulmonary tuberculosis and the patient had frequently been taken to visit him.

She had been quite well till six weeks before admission, and then she became fretful, 'off colour,' and slowly lost weight. Three weeks ago she had 'gone off her legs,' although she had begun to walk when aged nine months. For the last seven days she had refused all solid food and vomited nearly all fluids. During that week she had only one constipated stool with the help of an enema. Her mother had noticed that while lying in bed she would suddenly scream, and this screaming was followed by prolonged crying. She had had no rash, no convulsions, no aural symptoms or disturbance of micturition and no cough. The mother did not think she had been feverish but she had become more and more fretful and miserable.

On examination the infant was pale, flabby, wasted and very unhappy. The temperature was normal. The anterior fontanelle was closed. There were no abnormal physical signs. Miliary tuberculosis with tuberculous meningitis was suspected, and an x-ray of the chest showed a small opacity at the left apex. The case was therefore diagnosed as one of tuberculous meningitis with the primary focus in the apex of the left lung.

Lumbar puncture gave a turbid, yellow fluid under considerable pressure and the laboratory gave the following report on the cerebrospinal fluid :

PROTEIN. 240 mgm. per cent.

SUGAR. No reduction with Benedict's solution.

CHLORIDES. 705 mgm. per cent.

CELLS. 750 per c.mm.

Polymorphonuclears 55 per cent.

Lymphocytes 45 per cent.

FILM STAINED BY GRAM'S METHOD. A few extra-cellular meningococci seen. This was a surprising result, but the blood count also showed an excess of polymorphonuclears. The total white blood cells numbered 14,500 per c.mm., the polymorphonuclears 56.5 per cent., and the lymphocytes 39.5 per cent.

It was presumed that the case was one of missed meningococcal meningitis now in the chronic stage and that the x-ray appearance of the chest was a coincidence. The infant was given sulphapyridine by mouth slightly in excess of the dose given in the table by Hynes (1940). Next day the temperature had risen to 100° F., but the child had stopped vomiting and was taking solid food, although she was still miserable and there was a suspicion of neck rigidity. Lumbar puncture gave a fluid which was still turbid, and had a pressure of 170 mm., which rose to 240 mm. on crying. About 20 c.c. of this fluid was removed. There was no change on the third day and the slight stiffness of the neck persisted. A tuberculin patch test and a Mantoux 1 in 100 gave strongly positive results, but it was decided to investigate the chest more thoroughly after the meningitis had been treated.

On the fourth and fifth days the temperature remained raised but the infant was much brighter and taking notice. On the sixth and seventh days the temperature rose to 101.6° F., and she became drowsy, with definite neck stiffness. Her white count still showed an excess of polymorphonuclears. The total white blood cells numbered 13,730 per c.mm., the polymorphonuclears 60.5 per cent., and the lymphocytes 32.5 per cent. Lumbar puncture gave a turbid yellow fluid with a drip of normal speed containing :

PROTEIN. 750 mgm. per cent.

CELLS. 642 per c.mm.
 Polymorphonuclears 44 per cent.
 Lymphocytes 56 per cent.

FILM. No organisms seen.

The child was still having large doses of sulphapyridine, but as it did not seem to be efficacious she was also given 5 c.c. of anti-meningococcus serum intravenously. The temperature then fell to normal for two days, but she was still extremely drowsy and difficult to feed. She began to vomit for the first time since admission. Fluid from the lumbar puncture on the ninth day was not so turbid, but the pressure rose to overflow the manometer. 30 c.c. of the fluid were withdrawn and 10 c.c. of meningococcus antitoxin were injected intrathecally. The report on the cerebrospinal fluid was :

PROTEIN. 200 mgm. per cent.
 CELLS. 190 per c.mm.
 Polymorphonuclears 35 per cent.
 Lymphocytes 65 per cent.

The combination of chemotherapy and antitoxin appeared to be having some effect. The x-ray appearance of the chest had not changed.

On the following day the temperature rose again to 101° F. ; the child vomited and became more drowsy. In the evening she began to twitch down the left side, and this twitching was followed by a convulsion, after which the arms and hands were spastic. She had a bilateral positive Babinski's sign and went into opisthotonos for about thirty seconds. Her pupils, which had never been fully dilated, were now dilated with homatropine and the fundi examined. There was some fullness of both physiological cups and a large tubercle was seen just above the right disc. Later that evening her breathing became stertorous, and she had convulsions followed by opisthotonos every few minutes. Three-and-a-half hours after the onset of the twitching she went into a position of opisthotonos and remained in that position (fig. 1).

A lumbar puncture that evening produced an extremely turbid fluid, more turbid than at the time of admission, but no meningococci nor tubercle bacilli were found. The next day she remained in a state of extreme opisthotonos, with the head almost touching the buttocks when she was disturbed. She was unconscious, and it was impossible to feed her. The temperature remained above 101° F., with a pulse of 180 per minute. The following day, the twelfth after admission, the temperature rose to 105° F., the pulse to over 200, and she died, having been in opisthotonos for forty hours. Spasticity of the arms was persistent during this time but the legs only became spastic when she was disturbed.

Post-mortem examination. The body was that of a thin female infant. The brain was first examined and weighed 975 grammes. The external appearance was interesting, as two types of exudate were present in the meninges. On the ventral surface of the cerebellum and stretching forward to the pons was a thick, greenish-yellow, purulent exudate. Covering the mid-brain and crura cerebri, and running into the cerebral sulci, along the vessels, was a much thinner, whitish exudate containing many miliary tubercles, especially about the vessels of the Sylvian fissure. There was a great excess of cerebrospinal fluid in the ventricles. The brain was fixed, and when examined later both lateral ventricles were greatly dilated and many miliary tuberculomata were seen in their walls. In the left optic thalamus, at the level of the genu of the corpus callosum, a tuberculoma 1 mm. in diameter was found. Another minute one was present in the white matter of the second left frontal convolution. On the right side of the brain, a tuberculoma, identical in size and situation with that on the left side, was in the optic thalamus. A minute one was also present just above the middle of the body of the right lateral ventricle.

The surfaces of the lungs were free from miliary tubercles and the right lung was normal. The bifurcation and tracheobronchial glands were not enlarged. In the left lung a primary focus, measuring 2×1.5 cm. in diameter, was found bordering on the apex of the upper lobe, but no miliary tubercles were present. On the posterior surface of the left lung, attached to the pleura, was one caseous gland in the situation corresponding to that of the so-called ductus arteriosus gland. This was the only mediastinal gland affected by the tuberculous process.

The heart was normal. The liver showed fatty change but no tubercles were found on or in it. The spleen was covered with tiny miliary tubercles but none

FIG. 1.—Position of opisthotonos in which child remained for 40 hours. Taken 24 hours before death.

was seen in its substance. Two tiny tubercles were seen in the cortex of the left kidney. The right appeared normal, as were the suprarenals. The stomach was normal, but one small tuberculous ulcer, the size of a pin's head, was found in the terminal portion of the ileum. There was no enlargement of the mesenteric glands.

Discussion

This case was interesting both as a rarity and as an unusual problem in diagnosis. It was unfortunate that the original clinical diagnosis was discarded because of the indisputable pathological diagnosis, but the physician is trained to abhor the double diagnosis. The diagnosis of a combined form of meningitic infection might have been made sooner had the choroid tubercle been seen on admission. The treatment of the case, while believed to be

meningococcal meningitis, was orthodox in that large doses of sulphapyridine were given and lumbar punctures performed to note progress. Blood counts were done every few days to make sure that the sulphapyridine was not having a deleterious effect. Anti-meningococcus serum and antitoxin were given while the final diagnosis was still unmade.

The order in which the infections occurred can be surmised from the post-mortem examination. The primary tuberculous focus in the lung, which was fibrotic, was presumably acquired some months before, perhaps from the grandfather, and the onset of the tuberculous meningitis was, no doubt, six weeks before the child was seen at hospital when a change was first noticed. The intracranial tuberculosis must have been present for some time, judging by the tuberculomata in the substance of the brain and the many miliary tubercles on the surface. The child might have been a carrier of the meningococcus in the throat, and, presumably, this organism only became sufficiently virulent to cause meningitis about a week before the patient was admitted.

Two other unusual aspects of the case were, first, that the pus in the cerebrospinal fluid from the post-basic suppurative type of meningitis increased greatly just before death in spite of the fact that the sulphapyridine had not been withdrawn; and, second, that the opisthotonos, or 'gun-hammer' position, was of such severity and sustained for so long.

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