LEUCOPENIA IN PNEUMOCOCCAL PERITONITIS TREATED BY SODIUM PENTOSE NUCLEOTIDE

BY

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The exceptionally high mortality rate of primary pneumococcal peritonitis (Rischbieth, 1910-11, 90 per cent.; McCartney and Fraser, 1921-2, 65 per cent.) justifies the evaluation of any ancillary methods of treatment used in surviving cases. There appears to be a general consensus of opinion to-day in favour of delaying operation until there are signs of localization of the abdominal exudate—that is, about the end of the second week of the disease in surviving cases. Horine (1935), quoting Continental surgeons, gives a 75 to 95 per cent. mortality rate in cases treated by early operation, compared with up to 25 per cent. in cases treated by simple drainage in the stage of localization. From time to time, however, a case occurs where the diagnosis is uncertain, and the surgeon, feeling that he may be overlooking peritonitis of appendicular origin and lacking the courage to temporize, decides to explore the right iliac fossa. In the diagnosis of such cases of peritonitis of doubtful origin much importance has been attached to the leucocyte count as indicating the type of infection present (Budde, 1933; Gibson, 1930). It is considered that an unusually high leucocyte count with a high percentage of polymorphonuclear cells is distinctive of pneumococcal peritonitis.

The case about to be described, in which the initial leucocytosis was slight, presented difficulties in diagnosis so far as the origin of the peritonitis was concerned, and the history of the administration of an aperient soon after the onset of the attack was the deciding factor in favour of immediate operation.

At operation the true state of affairs—namely, an “idiopathic” general peritonitis—was disclosed; this was found to be pneumococcal. The subsequent course of the disease, which responded to treatment in a remarkable manner despite the later complication of double basal pneumonia, leads me to publish this case, in the hope that the measures adopted may be useful to surgeons faced with a similar condition. For a few days, however, the case appeared to be hopeless, both clinically and especially so far as prognosis could be based on the blood picture.

Case History

A British girl aged 10 years, in good health, was seized with acute generalized abdominal pain on the night of May 22, 1937. This became progressively worse during the following morning, when she vomited several times. Her mother, attributing her symptoms to overindulgence at a recent party, administered a dose of salts. The child's condition became worse during the afternoon, when her temperature rose to 102°. Several loose motions were passed, and the abdominal pain appeared to be very severe.

I first saw the child at 6.30 p.m. on May 23, and it was obvious that there was general peritonitis. Her pulse was 120, her temperature 102.8°, and respirations 24 per minute. Abdominal distension was present, and she was in considerable distress from pain, most severe over the lower abdomen, which was held almost immobile during respiration. A vivid malar flush was evident. On palpation marked

rigidity of the lower abdomen was felt, and although tenderness was general it appeared to be most definite over the right iliac fossa. The patient stated that her pain was worse in that region when the right thigh was fully extended. On rectal examination general tenderness was elicited, but no localized swelling was palpable. There was no history of any vaginal discharge. Examination showed no abnormal signs in the heart or lungs, and urinalysis was normal. A blood count resulted as follows: Red blood cells, 4,980,000 per c.mm.; white blood cells, 10,600 per c.mm.; haemoglobin, 80 per cent.; colour index, 0.81. The differential count read: Polymorphonuclears, 80 per cent.; large lymphocytes, 2 per cent.; small lymphocytes, 17 per cent.; hyalines, 1 per cent.; eosinophils, nil. Owing to the extremely acute nature of the child's symptoms, and the history of the aperient, a diagnosis of acute peritonitis of appendicular origin was made and immediate operation advised. This was performed under ether anaesthesia at 7.45 p.m. on May 23, approximately twenty-two hours after the onset of the patient's symptoms.

The abdomen was opened by Battle's incision, and a small quantity of greenish-yellow seropurulent fluid escaped on incising the peritoneum. Smears and cultures were taken for examination. The coils of small intestine were intensely congested and dark red in colour, with numerous flakes of fibrinous lymph adhering to the serous coat. The appendix was red and congested, as were the pelvic organs, and some purulent fluid was present in Douglas's pouch. Apart from sharing in the general inflammation the tubes did not appear to be particularly inflamed. The case suggested an early streptococcal peritonitis; appendicectomy was performed, the fluid exudate completely removed by suction, and the abdomen closed without drainage. The patient was returned to bed and nursed in the Fowler position, a continuous rectal drip saline with 5 per cent. glucose being administered. Later the laboratory reported that the smears contained numerous pus cells with Gram-positive diplococci, showing evidence of a capsule. On the following day the cultures yielded a pure growth of pneumococci: the patient had therefore been operated on in the early phase of pneumococcal peritonitis. Unfortunately type sera were not available for the treatment of the case. Blood transfusions did not appear to be indicated.

On the day following operation (May 24) the patient's condition was fair: the pulse was 128, temperature 102°, and respirations 26. Abdominal distension was considerable, although the passage of the rectal tube resulted in the evacuation of fluid faeces and gas. Morphine was administered hypodermically in 1/12-grain doses whenever the patient became restless, and large hot fomentations were applied, covering the whole abdomen and flanks. The rectal drip was continued at intervals throughout, and only sips of water were given by the mouth.

Next day the patient's general condition was much worse, with a great deal of abdominal pain and distension, and several fluid motions were passed. The pulse was now 135, the temperature 103.5°, and the respirations 32. A blood count at this stage showed a sharp drop in leucocytes to the extent of a marked leucopenia, and the presence of numerous immature forms: Red blood cells, 4,850,000 per c.mm.; white blood cells, 2,600 per c.mm.; haemoglobin, 80 per cent.; colour index, 0.83. The differential count gave: Polymorphonuclears, 81 per cent.; large lymphocytes, 5 per cent.; small lymphocytes, 12 per cent.; hyalines, 2 per cent.; eosinophils, nil. The Schilling-Torgau ratio of immature to mature forms of polymorphonuclears was 6:5. From the general and haematological standpoints the prognosis appeared hopeless.

Dr. J. B. Robinson, who confirmed the blood findings with Dr. T. J. Hua, saw the patient in consultation that day, and suggested immediate treatment with a pentonucleotide preparation so as to try to induce leucocytosis. The preparation “sodium pentose nucleotide” (Evans Sons Lescher and Webb) was available, and treatment was at once started, giving 2 c.cm. intramuscularly twice daily. This dose was gradually increased during the following days until 5 c.cm.

was being given twice daily by May 30. The white cell counts during this period were as follows: May 27, 3,400; May 28, 6,600; May 29, 15,700; May 30, 23,700.

On June 1, as the patient's abdominal condition was assuming a more chronic character, a further rise in temperature, with dyspnoea and severe cyanosis, heralded the onset of pneumonic consolidation in the lower lobes of both lungs (pulse 140, temperature 104° , respirations 42). At this time the leucocytes numbered 27,000, but the Schilling-Torgau count gave a 3:6 ratio. During the next week the clinical picture was one of typical pneumonia, and the child's condition became very critical. Routine treatment and careful nursing, with intranasal oxygen when cyanosis was severe, tided her over until resolution by lysis started on June 6. The temperature now began to remit, and increasing lower abdominal distension suggested localization of the abdominal exudate. On June 10 several ounces of thick yellow pus were discharged from the wound, yielding on culture a pure growth of pneumococci. On June 12, under light ether anaesthesia, a suprapubic incision was made, and 14 oz. of thick odourless yellow pus was evacuated with masses of fibrin. A large drain was left in.

The patient thereafter proceeded to a prolonged but steady convalescence. Pockets of pus higher in the abdomen discharged along the drainage track at intervals. Some delay in complete resolution of the pneumonic consolidation at the left base occurred, but the right lung cleared up rapidly. She was discharged from hospital on July 20, and subsequently left for England with her family. She had lost 12 lb. in weight during her illness, but, apart from emaciation, was convalescing rapidly and had developed a voracious appetite. Dr. Hector Cameron, to whom the child was referred, wrote in October, 1937, that she had made great progress, had put on weight, and had regained the look of health.

Graph showing Fall in Leucocytes after Operation and the Development of Leucocytosis following Pentose Nucleotide Injections

Commentary

Fraser (1931) has suggested that the peritoneal area, as representing a mesothelial space, has peculiar properties of reaction in response to general infection. From observation of cases of so-called idiopathic peritonitis—that is, cases in which no obvious source of intraperitoneal infec-

tion can be demonstrated—he believes that the peritonitis is in some respects a salutary feature affording possibilities of an immunity influence. On such a basis pneumococcal peritonitis is explained as a local reaction secondary to pneumococcal septicaemia—a condition that was undoubtedly present in this case, as proved by the subsequent development of bilateral basal pneumonia.

Recovery from primary pneumococcal peritonitis is not unusual, though the mortality rate is high, but recovery in any case of peritonitis where leucopenia and a "shift to the left" mark the immediate post-operative course must be very rare. Piney (1926-7), in his Arris and Gale lectures on the importance of haematology in surgery, points out that recovery rarely occurs in infective processes where there is a progressive fall in the total number of leucocytes with an extreme degree of shift to the left, total absence of eosinophils, and well-marked lymphopenia.

In discussing cell counts in the different types of pneumonia, however, Fleming (1936) has stated that in Type I infection—the usual one in pneumococcal peritonitis according to Bréchet and Nové-Josserand (1931)—although high leucocyte counts are common, low leucocyte counts are found in many patients who recover despite a grave condition at the onset of the disease. He also points out that in young patients recovery may occur with moderately low counts. The remarkable response in the blood picture of this case during the course of sodium pentose nucleotide injections, however, coincided too closely with clinical improvement to be merely accidental.

Wilkie (1931) has advocated the pre-operative injection of *B. coli* and streptococcal vaccine, combined with sodium nucleate, as a useful prophylactic against peritonitis in abdominal operations where there is a risk of serious infection. While the pentose nucleotide preparations have been of special value in the treatment of agranulocytic anginas, they would appear to have also a definite place in the treatment of acute surgical infections in which neutropenia results from the effect of the circulating toxins on the bone-marrow.

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H. Brücke (*Zbl. Chir.*, February 12, 1938, p. 349) states that congenital local giantism in which both skeletal and soft parts are concerned may affect from one to four or various combinations of limbs, or small zones such as the finger, toe, ear, or nose. Macroductyly is not very rare. The distal is more commonly affected than the proximal part of limbs, and the right more often than the left side; a familial occurrence is very uncommon. The parts concerned are specially liable to be the site of pigmented naevi, lymphangiomas, lipomas, and fibromata. The case is recorded of a man, aged 21, mentally subnormal, in whom the whole of the left leg was enlarged; the shin and calf showed a large capillary-venous naevus and trophic ulceration. Surgical measures—for example, osteotomy to shorten the femur and improve secondary static defects such as scoliosis—are, it is said, unlikely to be successful, for the giant parts have generally an inferior functional capacity and regenerative power. This patient's trophic ulceration dated from attempts to cure by sclerosing injections the varicose portions of the naevus.