STAPHYLOCOCCAL SEPTICAEMIA TREATED WITH SULPHADIAZINE

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The chemotherapy of staphylococcal septicaemia by means of drugs of the sulphonamide group has been disappointing. In a study of the efficacy of the newer derivatives of this group Kolmer and Brown (1942) conclude that the chemotherapy of staphylococcal infections is unsatisfactory and is certainly inferior to similar therapy applied to haemolytic streptococcal and pneumococcal infections. Reimann (1942), after an exhaustive review of published cases, is of the same opinion. The treatment of choice for these infections is by means of penicillin. Unfortunately penicillin is not yet available for general use, and until supplies are forthcoming the sulphonamides remain the most hopeful therapeutic agents.

In the case here recorded sulphadiazine showed itself to be remarkably efficacious. Finland, Peterson, and Goodwin (1942), who have compared the efficacy of various preparations of sulphonamides, treated five cases of staphylococcal septicaemia with sulphadiazine. The average total dose given was 147 g. They claim a good therapeutic response in one case and a doubtful response or good initial response with relapse in the other four. It should be noted that, of these four, one was complicated by pyonephrosis and three by osteomyelitis. There were no deaths, but the cases complicated by bone involvement needed surgical drainage before chemotherapy was effective. These authors conclude that the efficacy of sulphadiazine is probably similar to that of sulphathiazole, but its lower toxicity makes it the drug of choice, particularly when prolonged therapy is desirable. In the present case sulphadiazine was not used until sulphathiazole had proved to be ineffective.

Case History

The patient, a soldier 32 years of age, was admitted to a military hospital on Feb. 23, 1943, complaining of aching in the limbs and malaise for one week. His health previously had been good, but a fortnight before the onset of his illness he had had a boil on the back of his neck which had been treated with hot fomentations and vigorous expression of pus. During several days before admission he had felt unwell and feverish, and was thought to have an influenzal attack. There had been some cough with blood-stained sputum, and heavy night sweats had been troublesome. The bowels had been constipated. He complained also of a tender lump over the left scapular angle that was painful when he sat back against his pillows. There had been no known contact with any infectious disease.

On examination the temperature was 101° F. and pulse rate 115. There was no evident anaemia, but the lips had a cyanotic tinge. The throat and teeth were in good order. The lungs showed no obvious abnormality. The cardiovascular system was normal and the blood pressure 130/95. The spleen could not be felt. No abnormality was found in the central nervous system. There were tender nodules at the angle of the left scapula, in the right lumbar region, in the groins, on the abdominal wall, in the right thigh, and on the inner aspect of the left knee. Some of these were acutely tender, and over several the skin was reddened. The urine was acid in reaction, with no sugar or albumin, and the deposit contained a few leucocytes and epithelial cells. The blood count on admission was: haemoglobin, 84%; red blood cells, 4,690,000 per c.mm.; colour index, 0.91; white blood cells, 14,000. The sputum contained no tubercle bacilli, but was blood-stained.

The patient was put on full doses of sulphathiazole. On March 2 a fresh crop of nodules appeared, a hectic temperature persisted, and his general condition was very poor. A differential white cell count gave a total of 20,700, with 78% polymorphonuclear cells. Blood culture proved sterile, but pus from a fluctuant nodule on the left arm was reported on as follows: "Smears: Large numbers of pus cells and clusters of Gram-positive cocci, morphologically staphylococci. Culture: Profuse growth of *Staph. aureus*." X-ray examination of the chest showed a "right basal pneumonitis."

By March 9 the patient's condition had still further deteriorated. There was no abatement in the fever and he had developed an ulcer on the right cornea. Several of the abscesses were fluctuant, and from two of them a small amount of thick pus was aspirated. A few petechial spots were noted on the trunk. A large, deep, and very tender abscess developed in the muscles of the right thigh, and

there was acute pain with local tenderness in the region of the left elbow; but radiographs of the joint and of the right femur were negative. The white blood cell count was 16,690.

On the following day a shower of emboli occurred over the lower extremities, giving the picture of an extensive macular rash. The temperature was at this time 103.5° F. and the pulse rate 145. On March 13 sulphathiazole was stopped, a course of 60 g. having been completed without obvious benefit. The administration of sulphadiazine was then begun. After 48 hours the temperature was normal, and the patient's comment was: "I feel quite different. I did not expect to feel as I do now in six months' time." A blood count showed: haemoglobin, 82%; red blood cells, 4,600,000 per c.mm.; colour index, 0.9; white blood cells, 22,000, 77% being polymorphonuclears.

The temperature did not settle altogether, and a slight evening rise persisted, but the general improvement in well-being was maintained and there were no further embolic phenomena. The white cell count on March 17 was 11,600, and on March 25 14,200. At this time sulphadiazine was stopped after a total dosage of 100 g. The patient's general condition was now fairly satisfactory. Pathological examination of the urine had been repeatedly negative. The haemoglobin was 82% and the leucocyte count on April 1 was 13,600. A large indurated swelling of the right thigh was still present, causing much pain and discomfort. A further radiograph of the right femur was negative. By April 13 this swelling had become more localized, with a suggestion of central fluctuation. The haemoglobin and white cell count were unaltered. There was no further rise of temperature. On April 20, in view of the prolonged septic infection and moderate degree of anaemia, one pint of fresh compatible blood was given by intravenous transfusion. Haemoglobin was 96% after transfusion. On May 4 the abscess in the right thigh was aspirated, 30 c.cm. of blood-stained serous fluid being withdrawn: this was sterile on culture. Convalescence thereafter was uneventful.

Summary

A case of staphylococcal septicaemia is recorded in which a dramatic response was obtained with sulphadiazine after sulphathiazole had proved ineffective. Since penicillin, the drug of choice, is not generally available, optimum use must be made of the sulphonamides in treating this condition. Sulphadiazine is the preferable derivative of this group because of its low toxicity and its apparent greater efficacy.

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SPONTANEOUS RUPTURE OF ABNORMALLY MOBILE SPLEEN

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Spontaneous rupture of the spleen in non-tropical countries is a very rare condition, and is known to occur occasionally in patients suffering from malaria or typhoid; a few cases of rupture of leukaemic spleens have been recorded. Zuckerman and Jacobi (1937) reviewed 28 cases of rupture of the normal spleen, but considered that only 21 of these could be accepted. In the case now reported a spontaneous rupture of the spleen occurred while the patient was in bed in hospital suffering from acute axillary lymphadenitis; subsequent examination showed only inflammatory changes in the spleen.

Case Report

A soldier aged 35 was admitted to the Borough General Hospital, Ipswich, on Sept. 13, 1942, suffering from pain in the left axilla of 24 hours' duration. On the evening before his admission he complained of aches and pains all over the body and had vomited once. On admission the temperature was 101.6° F., pulse rate 95, and respiration rate 22. A few enlarged tender glands were felt in the left axilla, but no primary cause for this adenitis was found. He had been given 7 g. of sulphapyridine during the previous

day in a camp reception station. After admission he was given sulphathiazole by mouth and local treatment by short-wave therapy.

On Sept. 15 the patient suddenly collapsed. It was apparent that a severe intraperitoneal haemorrhage had occurred; a blood count was carried out and blood transfusion was given. The count showed: red cells, 3,800,000 per c.mm.; Hb, 60% (Sahli—standard 100% = 15.5 g.); white cells, 36,370 per c.mm.: myelocytes 3,700, metamyelocytes 6,600, neutrophil polymorphs 22,000, lymphocytes 2,590, eosinophils 370, mononuclears 1,110 per c.mm. There were no nucleated red cells: this was taken to be a response to severe haemorrhage. A pre-operative diagnosis was made of rupture of the spleen or of an intraperitoneal aneurysm, probably of the splenic artery.

At operation the peritoneal cavity was full of blood, five and a quarter pints being measured. The spleen was ruptured transversely at its convex border. Splenectomy was easily performed, as there were no adhesions and the splenic pedicle was unusually long. The patient collapsed during closure of the abdomen and died in spite of the usual resuscitation methods.

Post-mortem Findings.—The stomach contained a fair quantity of undigested food and some bright blood. The mucosa showed minute erosions, but no chronic ulceration. The sternal bone marrow was greyish red and hyperplastic. No other pathological lesions were found.

Histological Examinations.—Spleen:—No definite pathological change was noted in the sections, apart from evidence of acute inflammation. Sections were sent to Dr. A. H. T. Robb-Smith for his opinion. His report is as follows: "The spleen has the appearances, apart from actual trauma, of those found in a reaction to an acute inflammation, and it is likely to be an example of an acute inflammatory condition with an acute splenic tumour which has ruptured spontaneously." The weight was 280 g. Axillary lymph glands showed microscopical evidence of subacute lymphadenitis; this finding was confirmed by Dr. Robb-Smith. Bone-marrow films (taken immediately after death) revealed marked myeloid reaction, presumably due to inflammatory changes. The liver showed no abnormal changes.

Past History.—Steps were taken to trace the previous medical history of the patient. His Army record sheet showed that he had never been abroad. There was no history from the patient or from his unit of any injury within recent months. Apart from bronchitis he had had no other illnesses.

Discussion

Zuckerman and Jacobi (1937) consider that minor degrees of torsion or of angulation of the splenic pedicle are sufficient to slow the circulation and to cause congestion of the spleen, resulting in rupture. They also consider that minor gastro-intestinal disorders may initiate the torsion or angulation and thereby cause the congestion and rupture. They found that the phrenico-splenic ligament is absent in about 2% of individuals; absence of this ligament is one of the causes of undue mobility of the spleen.

In the present case the serious condition of the patient prevented accurate anatomical investigation, but it was remarked at the time of the operation that the spleen was excessively mobile and thus splenectomy was a most simple procedure. It is therefore probable that the phrenico-splenic ligament was absent, and no restricting peritoneal bands were encountered. The patient had vomited before admission: this and the finding of food residue in the stomach, long after solid food had been taken, suggest that a gastro-intestinal disorder had developed. The presence of blood in the stomach may be attributable to obstruction of the vasa brevia by the same angulation or torsion that contributed to the rupture of the spleen. The presence of blood in the stomach and intestines has been reported in conditions of shock. The spleen in our case was not grossly enlarged; the structural changes were those representing the normal response of the spleen to a toxæmia and, as such, are to be expected in any acute inflammatory process. The rupture must therefore be regarded as being due to a mechanical process rather than to a pathological condition.

Ledderhose (1890) and Foucault (1925) considered that spontaneous rupture could occur only in a diseased spleen. Zuckerman and Jacobi have reviewed 28 cases of rupture of the alleged normal spleen, but accepted only 21 cases as genuinely normal. None of these was associated with acute inflammation. In their series spontaneous rupture occurred in 16 males and 12 females. The age incidence was: under 20 years, 2 cases; 20–30, 7 cases; 30–40, 6 cases; 40–50, 7 cases; 50–60, 5 cases. In 5 cases there was a history of epigastric distress related to meals, and in 5 cases the onset of

rupture was just after eating or drinking. Shock was noted in only 15 cases. Pain in the left shoulder was present in 3 cases and in the right shoulder in 1 case. Halliwell (1933) reported a case of spontaneous rupture of a normal spleen in which there was a long splenic pedicle. In Stretton's case (1926) rupture occurred in a female patient after coitus. In Susman's case (1927) the rupture occurred after the patient had bent down to lift a heavy object, and it was suggested that the contraction of the abdominal wall caused the rupture. Bohler (1933) reported a similar case occurring after the patient had bent to lift a heavy object. Abell (1933) recorded a case of rupture of a wandering spleen with torsion of its pedicle. In the cases described by Smith, Morrison, and Sladden (1933) and by Burnett and McMenemy (1935) splenomegaly was solely due to congestion, and in the former case pregnancy was thought to be a contributory factor.

In our own case the spleen was excessively mobile and rupture occurred at rest in bed. No gross pathological changes were discovered in the spleen beyond simple inflammatory processes such as must exist in most septic conditions. Some gastro-intestinal disorder was indicated by the vomiting before admission and also by the post-mortem finding of undigested food residue in the stomach many hours after the preceding meal.

Summary

A case of spontaneous rupture of an abnormally mobile spleen is described in which the rupture occurred while the patient was at rest in bed and in which there was no preceding accident.

A discussion of the causes of spontaneous rupture of the spleen and a review of the literature suggest that excessive mobility may subject the spleen to congestion by angulation or torsion of its pedicle sufficient to result in spontaneous rupture.

Our sincere thanks are due to Dr. Robb-Smith for reporting on the sections and for helpful criticisms.

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Medical Memoranda

Achrestic Anaemia with Achlorhydria

Achrestic anaemia as first described by Israëls and Wilkinson is characterized by: (1) the findings of a macrocytic anaemia; (2) free HCl in the stomach contents; (3) a prolonged course which fails to respond to efficient anti-pernicious-anaemia therapy; (4) megaloblastic hyperplasia of the bone marrow; (5) the recovery of adequate amounts of the anti-anaemic principle from the liver. The aetiology is the failure to utilize the anti-anaemic principle or to mobilize it from the tissue stores.

Recently I have had under my care a case of achrestic anaemia differing a little from the above outline in that there was achlorhydria. Such a condition must be very rare.

CASE HISTORY

A widow aged 56 was admitted to hospital, having complained for six months of dyspnoea, faintness, weakness of the arms and legs, extreme exhaustion, nausea, and vomiting. The symptoms were gradually getting more pronounced. Her appetite had been poor, but her weight was steady. She had received no previous treatment.

Examination revealed a pale woman who looked older than her years but showed no signs of wasting. The pulse was 100 and regular. The face was puffy and the teeth were carious. There were purpuric spots on the arms, chest, and abdomen, with oedema of the hands and feet. The tip of the spleen was just palpable, and the liver was enlarged 2 in. There were no enlarged lymph glands, and no other abnormality in the heart, lungs, C.N.S., or urine was detected. The blood count was: red cells, 715,000; white cells, 4,000; haemoglobin, 20%; colour index, 1.4. The film showed definite macrocytosis. Fractional test meals even with histamine revealed achlorhydria, with excess of mucus. The stools were always negative for occult blood.