SUPPURATIVE THROMBOPHLEBITIS TREATED WITH AUREOMYCIN

BY

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Of the various types of thrombophlebitis, the infectious and suppurative cases form only 3% (Barker, 1934). They are often fatal, however, owing to the development of pyaemia and metastatic foci. The following case of ilio-femoral thrombophlebitis is of particular interest for three reasons: (1) the prognosis was made worse by the infecting organism being a penicillin-resistant *Staphylococcus aureus*, (2) a mistake was probably made in discontinuing the chemotherapy too early, and (3) a successful recovery was nevertheless obtained with "aureomycin" without vein ligation proximal to the thrombus.

Case Report

A boy aged 3 years fell into a bath of hot water and received scalds of his back, thighs, and left arm. The extent of the scalded area was 24% of the body surface, 2% being whole-skin loss.

On admission he was treated for shock with 850 ml. of plasma during the first 27 hours. The dressing was done seven hours after admission, and the bacteriological swabs from the scalded surface at that time grew micrococci only. Systemic penicillin was begun with an initial dose of 250,000 units, and then 30,000 units four-hourly. Further swabs on the fourth day showed the presence of *Staph. aureus* and *Pseudomonas pyocyanea*.

Temperature chart during the treatment of thrombophlebitis with aureomycin.

Onset of Thrombophlebitis.—On the sixth day the child's haemoglobin was 69%, and a bottle of blood was given after cutting down on the right great saphenous vein at the ankle. Four days later his temperature rose to 105° F. (40.6° C.) (see Chart) and the pulse to 160: the right calf was grossly swollen, hot, and tender, and the drip incision was inflamed. Systemic penicillin was increased to 150,000 units six-hourly, and a course of sulphadimidine was started (2.5 g. initially, then 0.5 g. four-hourly). On the following day (13th) a small abscess was incised over the upper end of the tibia, and from the pus a pure growth of penicillin-resistant *Staph. aureus* was grown. The local inflammatory lesion subsided during the next three days, but as the temperature remained at 102° F. (38.9° C.) and the pulse at 160, aureomycin was begun on the 16th day (375 mg. initially, then 125 mg. six-hourly). On the 19th day tender, indurated, thrombosed superficial veins appeared on the medial side of the right thigh, extending to within 2 in. (5 cm.) of the junction with the femoral vein, which was not palpable. The course of sulphadimidine was stopped after a total dosage of 21.5 g., the white cell count being 5,030 per c.mm.

Operation on the Femoral Vein.—On the 21st day it was decided to tie the right saphenous vein, since the local signs suggested involvement of the superficial veins only. At operation the saphenous vein and its tributaries were collapsed and empty, but the femoral vein was found to be thrombosed, though it had been impalpable. It was opened and some of the yellow thrombus smeared on a slide and taken for culture: the external iliac vein was not explored, and was too small for an attempt at sucking out the clot. The femoral vein was tied, but the thrombus was palpable at least $\frac{1}{2}$ in. (1.25 cm.) proximal to the ligation. The smear showed well-stained Gram-positive cocci, and the culture grew penicillin-resistant *Staph. aureus*.

Blood cultures taken on the day of operation and the next two days (21st, 22nd, and 23rd) were all sterile after 48 hours. An operation to tie the iliac vein above the thrombus was decided against because the child's condition was improving, the organism was known to be sensitive to aureomycin, blood cultures were negative, and there was no sign of metastatic spread. By the 24th day, eight days after aureomycin was started, his clinical condition was much better, and the *Staph. aureus* had entirely disappeared from the scald. On the 33rd day penicillin and aureomycin were stopped after total dosages of 24,160,000 units and 9,375 mg. respectively.

Skin-grafting Operations.—The granulating areas were covered with split skin grafts on the 27th and 39th days; and by the 48th day healing was complete and there was no oedema of the leg or any palpable veins.

First Recurrence of Pyrexia.—Three days later, however, the child became ill again with a temperature swinging between 99 and 103° F. (37.2 and 39.4° C.). Clinical examination and investigations revealed no cause, so that after three days a recurrence of the previous infection was presumed in spite of a sterile blood culture, and aureomycin was restarted. There was a rapid response, and the drug was discontinued after nine days (total 4,500 mg.).

Second Recurrence of Pyrexia.—After a further eight days the child's temperature again rose to 102.5° F. (39.15° C.), and again it was impossible to confirm the diagnosis. A further exacerbation of the thrombophlebitis was presumed, and a 28-day course of aureomycin was begun. The temperature became normal in a week and did not rise again. The boy was discharged at the end of this course (14,000 mg.) perfectly fit, and during the next 10 weeks showed no sign of further recurrence.

Comment

The three lines of treatment in general use for this condition are antibiotics, proximal ligation of the thrombosed vein, and anticoagulant therapy.

There is no controversy about the use of chemotherapy: the most powerful drug against the particular organism isolated should be given as soon as possible, in adequate dosage and for a sufficient period. The recurrence of the clinical picture of sepsis with too early cessation of the drug has often been noticed—for example, Hyman and Leiter, 1944. Lyons (1941) reported two consecutive cases of staphylococcal cavernous sinus thrombophlebitis treated with sulphathiazole and heparin, with recovery. Each of these cases had a bacteraemia which lasted six and eight days respectively, and he advised continuing the sulphathiazole for three months in a dosage sufficient to maintain the blood level at 5 mg. per 100 ml. Schall (1941) reported three further cases of staphylococcal cavernous sinus thrombophlebitis successfully treated with sulphathiazole and heparin. There is little doubt that if control of the pyaemia can be obtained by chemotherapy for a sufficient time, this is likely to be successful in curing the thrombophlebitis. For staphylococcal infections the antibiotic of choice is now aureomycin (Long, 1950), and Spink and Yow (1949) have reported five cases of staphylococcal bacteraemia treated with aureomycin, with four recoveries.

According to Van Duyn and Van Duyn (1940), the idea of trying to stop the spread of infection from a diseased vein into the general circulation originated with John Hunter in 1793, when he advised putting a compress on the vein just above the suppuration. Since then, and until the development of chemotherapy, the mortality of suppurative thrombophlebitis has been proportional to the inaccessibility of the septic focus and the difficulty of eradicating it (Rosenow and Brown, 1938). Before the advent of sulphonamides vein ligation was the only rational therapy, but the mortality was still high: septic thrombophlebitis of the neck, for example, had a mortality of 20–30% even with operation (Iglauer, 1942).

The present value of proximal ligation of the thrombosed vein is more debatable. Kern and Berman (1945) reported a case of ilio-femoral thrombophlebitis following pneumococcal lobar pneumonia, empyema, and septicaemia, which proved resistant to sulphonamides and dicoumarol; the patient was cured, however, after ligation of the inferior vena cava above the thrombus and a course of penicillin. Which one of these procedures played the major part in the patient's recovery it was impossible to say, but they felt justified in stating that the convalescence was very definitely shortened by the surgical intervention, and the danger of embolism, minor or fatal, was eliminated. In contrast, a case described by Kirk (1947) illustrates that proximal ligation without control of the pyaemia is likely to be fatal. His case of suppurative ilio-femoral thrombophlebitis due to *Aerobacter cloacae* was temporarily controlled with streptomycin, but drug resistance developed, and when infection spread to the opposite side the inferior vena cava was tied. In spite of this the patient developed septic meningitis on the sixth post-operative day and died two days later.

In practice few would doubt the wisdom of proximal ligation when the vein was easy of access, when there was a positive blood culture, and when the organism was resistant to the drugs available. Again, there is unlikely to be disagreement in adopting a conservative attitude if the site of the proximal end of the thrombus is inaccessible, if repeated blood cultures have been negative, if the organism is sensitive to the antibiotic, and

there is serious concomitant disease. Between these two extremes it may be difficult to come to a decision, but the chief indication for vein ligation is inability to control the bacteraemia with antibiotics.

Anticoagulant therapy is of less importance, but as it may prevent extension of the thrombus it should be given when possible. An open wound such as was present in the case described is of course an absolute contraindication. It is interesting that both cases described by Lyons (1941) developed pulmonary infarcts while receiving heparin.

Summary

A case of suppurative ilio-femoral thrombophlebitis arose from a transfusion incision infected with penicillin-resistant *Staph. aureus*, and this was treated with aureomycin. At operation the diagnosis was confirmed, but because of the organism's sensitivity to aureomycin, the repeated negative blood cultures, and the sustained clinical improvement proximal ligation was not performed. Failure to give the aureomycin for a sufficient period initially is believed to have resulted in two recurrences, but after 125 mg. had been given six-hourly for 28 days (total 14,000 mg.) the condition was finally cured. The treatment of suppurative thrombophlebitis has been considered briefly.

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Medical Memoranda

Case of Ovarian Pregnancy

The occurrence of an ovarian pregnancy is still rare enough to excite interest. It is estimated to occur in 0.7–1% of all ectopic pregnancies. In recent years the subject has often been reviewed (Isbell and Bacon, 1947; Bolton, 1949; Deweese, 1949), and the numbers of authentic cases have been variously calculated as approximately 60 (Curtis, 1941), 52 (Way, 1941), and 50 (Novak, 1947).

CASE REPORT

A woman aged 21, married for one month, was admitted to hospital on October 20, 1949, complaining of pain in the abdomen. Four months before admission (three months before marriage) she first had coitus. Her next menstrual period was 14 days late but otherwise normal. The following period, which occurred 28 days later, was normal. She then married and engaged in coitus, but the menstrual period which was imminent did not occur. Seven days after her marriage she suddenly collapsed in the street and complained of dizziness, low abdominal pain, and vomiting. There was no vaginal bleeding.

She was admitted to another hospital believed to be suffering from acute food-poisoning, but was discharged after three days, though still complaining of intermittent abdominal pain, and she stayed in bed at home.

A week later a profuse vaginal haemorrhage occurred associated with abdominal pain localized to the left side. Large clots were passed, and the bleeding lasted three days.