GANGRENE ASSOCIATED WITH THROMBO-PHLEBITIS

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That gangrene can result from venous obstruction, although rare, is not widely realized. A preliminary and brief examination of its genesis is worth while. As Learmonth (1950) pointed out, among other factors, the viability of tissue depends on an adequate rate of blood flow through the capillaries. Interference with the blood flow may be caused by a lesion in (1) the efferent vessel or artery, (2) the capillary itself, (3) the afferent vessel or vein, (4) some combination of the preceding.

Cessation or marked slowing of capillary blood flow sufficient to cause gangrene can result from venous blockage. This was shown experimentally by Fontaine and De S. Pereira (1937) and later by Veal et al. (1951). By different animal experiments they showed that gangrene of tissue could and did arise from complete venous occlusion unassociated with any active interference in the arterial blood supply.

In clinical practice venous obstruction is usually produced by thrombo-phlebitis preceded by a stage of phlebo-thrombosis. In phlebo-thrombosis, a length of thrombus, anchored only at its distal end, floats upwards in the blood stream. Obstruction to blood flow only becomes marked and clinically obvious when the floating thrombus becomes adherent to the vein wall by a chemical inflammation, i.e. thrombo-phlebitis is established.

Because of the massive venous collateral pathways it is seldom, in cases of thrombo-phlebitis, that the capillary blood flow can be stopped or slowed sufficiently to cause gangrene, but a combination of certain factors may alter this. These are (1) very widespread thrombo-phlebitis, (2) a very rapidly spreading thrombo-phlebitis whereby the rate of establishment of venous obstruction outpaces the rate of establishment of an adequate collateral circulation, (3) anatomical variations in the venous pattern which may be significant in certain circumstances.

It is also recognized in clinical practice that thrombo-phlebitis may be responsible for the production of arterial spasm. This may be brought about reflexly through the sympathetic nervous system (Oschner, 1947) or by direct involvement of the artery wall in peri-phlebitis (Haemovicci, 1950). It would seem, therefore, that a combination of marked venous obstruction with varying degrees of arterial spasm produce the tissue anoxia and resultant gangrene which is seen in clinical practice.

Case Report

Mrs. M. S., aged 33, on December 5, 1956, had a normal spontaneous delivery of her third child. She was subsequently discharged on December 16, 1956, apyrexial and apparently quite well.

After arriving home she suddenly developed pain in the chest. This was followed in the next day or two by a non-productive cough and elevation of her temperature. She was treated by her practitioner with oral penicillin.

On December 19, 1956, she was admitted to the North-Western Branch of the Royal Free Hospital as a case of puerperal pyrexia.

On admission she was noted to have slight dyspnoea with diminished air entry at both bases and a friction rub could be heard at the left base. Her temperature was 100° F., pulse 100/min., and respiration rate 22/min. No pain, tenderness, or swelling was found in the calf or thigh of either lower limb. No other abnormal clinical signs were found.

Investigations showed: (1) The sputum to be slightly blood-tinged and later a growth of staphylococcus viridans was obtained on culture. No acid alcohol-fast bacilli were seen on Z.N. staining; no tubercle bacilli grew on culture. (2) W.B.C. was 18,800 per c.mm., polymorphs 78 per cent., lymphocytes 22 per cent. (3) Catheter specimen of urine showed no abnormality. (4) Culture from a cervical swab failed to grow any pathogens. (5) X-ray of chest was reported as showing 'shadowing of the left base and the possibility of an infarct cannot be excluded.'

A course of injections of soluble penicillin 250,000 units six-hourly into each thigh, combined with an oral course of sulphatriad 1.5 g.
six-hourly, was given for eight days (December 19–27, 1956).

During the few days after admission the signs in the chest diminished and the temperature settled to normal.

On December 23, 1956, four days after admission, the patient again experienced sudden pain in the chest, this time on the right side and again associated with a friction rub. The sputum was on this occasion heavily stained with blood clots. With a diagnosis of pulmonary embolism a course of anticoagulants was started: 35,000 units of heparin in four doses was given intravenously for the first 24 hours, and a course of dindevan with a loading dose of 100 mg. b.d. initiated. The prothrombin levels in the four subsequent days are shown in the following table. The course eventually being terminated after 25 days on January 17, 1957.

<table>
<thead>
<tr>
<th>Date in Dec. 1956</th>
<th>Prothrombin Time in sec. and %</th>
<th>Control in sec.</th>
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<tbody>
<tr>
<td>24</td>
<td>22</td>
<td>15</td>
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<td>25</td>
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<td>26</td>
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<td>27</td>
<td>45</td>
<td>13</td>
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On December 24, 1956, five days after admission, swelling of the whole lower limb was noted for the first time, a difference in circumference of 1 inch was noted in comparing both thigh and calf with the right side. Two days later, December 26, 1956, a rapid increase in the swelling of the left limb was noted and several small ecchymoses appeared over the anterolateral aspect of the left thigh. These soon fused into one large ecchymosis about 12 inches by 4 inches with vesication of the skin overlying the discoloration. A difference in circumference of 3½ inches was subsequently noted on measuring the left and right calves. No tenderness was elicited in the left calf. After a further ten days it was obvious that the skin overlying the area of ecchymosis was gangrenous and a line of separation from the normal skin was apparent.

On January 22, 1957, when the signs in the chest had cleared, the affected area of skin was excised and split skin grafts applied. It was noted that the subcutaneous fat underlying the black skin was brownish yellow in appearance and no bleeding was encountered till the depth of the ilio-tibial tract and the fascia covering the thigh muscles was reached. At this level small arteries which bled were noted perforating the deep fascia at irregular intervals of 2 to 3 inches from above down, accompanied by small veins.

Recovery from the operation was interrupted by a further attack of pain in the chest six days post-operative and a second course of anticoagulants was given. Thereafter no further complications were encountered.

**Discussion**

The possible causes of the gangrene in this case appear to be: (1) Pressure necrosis of the skin by a haematoma induced by injections of penicillin in the presence of a prothrombin concentration of 12 to 15 per cent. No haematoma was found at operation only slightly brownish-stained avascular fat underlying the dead skin. (2) A necrotizing infection of the skin as described by Meleney. The only inflammatory reaction associated with the area of gangrene was the appearance of the line of separation ten days after the onset of ecchymosis. (3) Venous occlusion due to thrombo-phlebitis causing gangrene. The simultaneous appearance of marked swelling of the whole limb and ecchymoses with vesication of a limited area of the thigh would indicate that they are both due to rapid venous occlusion. It will be recollected that this occurred 48 to 72 hours after starting a course of anti-coagulants and at a prothrombin level of 12 to 15 per cent. Presumably a widespread phlebo-thrombosis was already existent before an adequate response to anti-coagulants was obtained, and it was the adherence of the free floating thrombus to the vein wall which precipitated the marked swelling.

Unfortunately no record of the peripheral pulses in the affected limb was made during this early phase, but subsequently they have all been noted to be present and apparently equal to those in the right limb.

The venous drainage of the affected area is in the nature of a watershed lying between the long saphenous and gluteal system of veins. There is some evidence to suggest that this was an ili-femoral thrombosis of proximal origin, viz. the absence of calf tenderness and the early swelling of the thigh as well as the calf occurring in a post-partum case. If that is so, then the thrombo-phlebitis will be more widespread in the proximal veins and I would suggest that the three factors originally postulated as being likely to cause gangrene of venous type are present in the case at that particular site, namely:

(1) Widespread thrombo-phlebitis in the proximal veins of the limb.
(2) Rapid spread of thrombo-phlebitis with venous blockage as evidence by rapid swelling, ecchymoses and vesication in the thigh.
(3) Anatomically an area of less rich venous drainage. A localized area of insufficient venous drainage followed by gangrene is produced.

In 1950 Haemovici reported 27 cases of gan-
Gangrene associated with thrombo-phlebitis. These were mainly collected from the literature.

In almost 80 per cent. of his cases the lower limb, usually the left, was affected and the upper limb in the rest. In 2 of the 27 the condition was bilateral and 8 had areas of thrombo-phlebitis other than in the affected limb.

The factors associated with the thrombo-phlebitis were post-operative 5, post-partum 4, post-traumatic 6, visceral malignancies 2, miscellaneous (pulmonary tuberculosis, post-I.V. transfusion, etc.) 6, unknown 4.

The average age of the cases was 41.4 years and the sex incidence almost equal.

Clinically 56 per cent. of his series of cases presented initially as a phlegmasia caerulea dolens (blue phlebitis or blue leg) and 44 per cent. as a phlegmasia alba dolens (white or milk leg) which progressed to the blue state. In two-thirds of the cases the peripheral pulses of the affected limb could not be felt. In the absence of peripheral pulses patency of the arterial tree was proved by pathological examination of the amputated specimens in association with free arterial bleeding from the proximal end of the main artery at operation or by arteriogram.

Gangrene, in this series, followed usually four to eight days after the onset of the blue state. In contrast to the case described above, the gangrene was of the distal type affecting toes or the distal part of the foot. As emphasized by Haemovici, the gangrene predominantly affects the superficial tissues so that a conservative attitude with later excision of necrotic skin and grafting avoids unnecessary amputation.

Pathological examination of amputation specimens in this series confirmed widespread thrombo-phlebitis of superficial and deep veins with a patent arterial tree.

The mortality in this series of 27 was almost 40 per cent., but is naturally affected by the factors underlying the thrombo-phlebitis.

Summary

1. Experimentally complete venous obstruction to a part produces gangrene. In clinical practice thrombo-phlebitis with some element of arterial spasm may be responsible.

2. A case of gangrene of skin of thigh is described and an attempt made to prove it was of venous type.

Acknowledgments

I beg to acknowledge the permission, encouragement, and advice of Mrs. D. Barclay, M.S., F.R.C.S., Consultant Surgeon, Royal Free Hospital, in publishing this case, and to thank Dr. A. M. Ramsay for the use of the case notes.

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