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A Case of Localised Traumatic Lymphoedema: Observations Concerning the Obstruction of Initial Lymphatics and Tissue Channels by Fibrin, and Menkin's Hypothesis

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Summary

A case of acute lymphoedema is described. It was caused by a sharply localised, nearly circular, trauma. While there was minimal bruising, the trauma broke enough blood vessels to cause the blockage, by fibrin, of the initial lymphatics and tissue channels. This encircled a region, superficial to the deep fascia, and significantly prevented both the tissue fluid reaching the lymphatics and transport via the system. In addition, there was a short-lived, generalised lymphoedema, presumably caused by damage to the saphenous collecting lymphatics.

I rarely approve of the publication of reports of single cases. Still less do I approve of those who afflict others with a long account of their own illnesses. I am therefore rather non-plussed that circumstances compel me to write a report about my own leg; nevertheless I think that it has something to offer of scientific value, and it is at least of some interest when a Lymphologist suffers from lymphoedema! In addition, the mode of injury, while a traditional one in the history of medicine, has lately (and regretably) become somewhat rare.

Recently, I was leading a horse to water just before dawn. The horse (a stallion) was understandably anxious to visit two neighbouring mares. I tripped over one of the many objects which are somewhat inconveniently strewn around the Great Australian Outback and fell under his hoofs. Two of them landed in almost identical positions on the medial aspect of my left leg, just below the knee.

Bruising was minimal, but for about two days one could see the almost superimposed bruises in the shape of the two horse-shoes, about 11 cm in diameter and 0.5 cm in width (from the inside to the outside). The injury was approximately circular and followed the line of the shoes exactly, with a 3 cm gap at the posterior – where there is a gap in the shoe over, the horse's heel. The saphenous vein and lymph vessels ran across the centre of the lesion.

Not only was the superficial bruising minimal, but in the days which followed there was only a slight discolouration of the foot from blood tracking down the fascial planes. Hence it appeared that the swelling which followed was not a haematoma, but was due to some other cause. Other reasons for considering it to be a lymphoedema are mentioned below.

The swelling developed gradually and was maximal after 48 hours. The whole leg was involved, especially the medial aspect, down to the ankle joint, but was less below it. The circumference of the leg was increased by 7 cms just below the knee, and 5 cms over all the rest of the leg, to the ankle. There was a loss of normal sensation over the whole leg, only deep-touch remaining. Sensation returned as the oedema disappeared, but after 21 days was fully restored, even over still oedematous regions.

After six days, most of the oedema had disappeared – with just a residual 1 cm difference in circumference over most of the lower leg. However, this disappearance of the generalised oedema revealed that there remained

a sharply localised area of oedema, just confined to the area inside the original marks from the horse-shoes (Figs. 1, 2). This persisted as a 10 cm diameter circle, with an elevation of about 2 cm above the rest of the leg. The extra volume was about 150 ml; aspiration of 35 ml of fluid was easily done, at 14 days, but no efforts were made to aspirate it all. This temporally reduced the swelling, but it returned to its original size after 48 hours (as would be expected with a lymphoedema). When 25 ml of the aspirated fluid was injected, subcutaneously, into the normal leg, it completely disappeared, clinically, in 20 minutes.

The aspirated fluid did not clot. It was a pale straw-colour, with a haematocrit of 0.1% and a protein concentration of 5.1 g/dl (plasma 8.3 g/dl). The A/G ratio was 1.7 (plasma 1.08) and the fibrinogen content was less than 10 mg/dl (plasma 190 mg/dl). These findings are also indicative of a lymphoedema, with the very low fibrinogen suggesting its deposition in the injury.

On the 13th. day, dye-lymphography (using Evan's blue) showed that indeed the lymphatic system in the dermis, both over the persisting oedema and to a lesser extent over the rest of the leg, had almost no transport capacity. During mild exercise, while the lymphatics on the normal leg formed streamers of dye within 5 minutes, dye injected on the affected leg remained stationary for some days. This was both over the localised lymph oedema and over the rest of the leg, where the lymphoedema had subsided. (It is of some interest that, in the normal leg, the streamers were longer and more numerous in a downwards direction; this was no doubt caused by a vertical stance, causing the lymph to flow downwards until it entered deeper collectors equipped with valves.)

The dye-lymphography was repeated on the 22nd. day, when the localised lymphoedema was also much reduced, but there was still almost no sign of dermal lymphatic transport.

On the 14th day, biopsies were taken from a region deep to where the horse-shoes had impacted and into the oedematous region, and

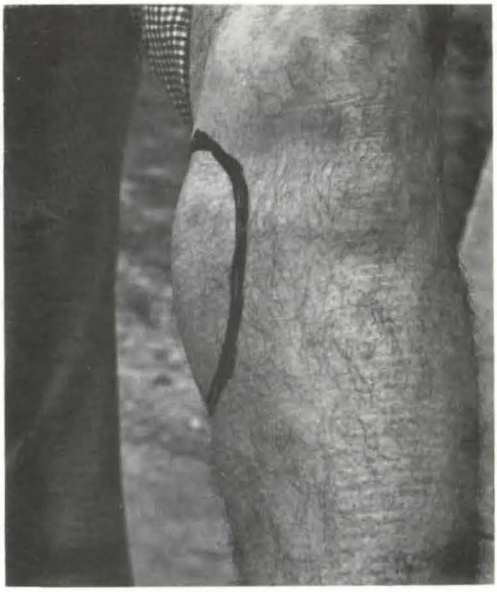

Fig. 1 A frontal view of the left leg, at 14 days; the region where the horse-shoes impacted is marked in black

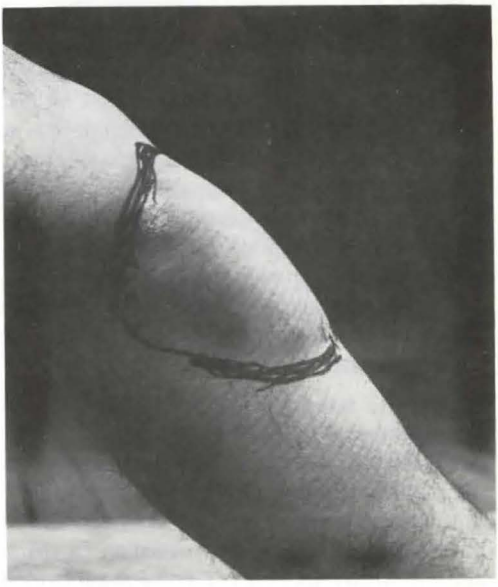

Fig. 2 As for Fig. 1; a posterior-medial view. The thin part of the black line is where the gap occurred in the bruise, corresponding to the gap in the horse-shoes

from the normal leg. (It is of interest that the incision in the normal leg healed in 7 days: that on the lymphoedematous leg took 18 days.) The biopsies were processed for electron microscopy by the usual methods, including the use of ferri-ferrocyanide to out line the tissue channels (counting 15 micrographs per region, at 26,500x, showing areas of 67 μm^2 each – Casley-Smith et al. 1979). In the region just under where the horse-shoes impacted, the initial lymphatics often had many open junctions, and were usually filled with a dense, proteinacious material – which often looked like deposits of fibrin (Figs. 3, 4). This also occupied much of the interstitial tissue, in which were many macro phages (Fig. 6). Many of the blood vessels contained thrombi.

The tissue channels of the normal leg (Fig. 5) had mean equivalent radii and numbers of: 41 nm [Standard Error of Mean, 7.1] and 0.21 μm^2 [0.012], respectively. In the region where the horse-shoes impacted (Fig. 6), these values were greatly reduced: 11 nm

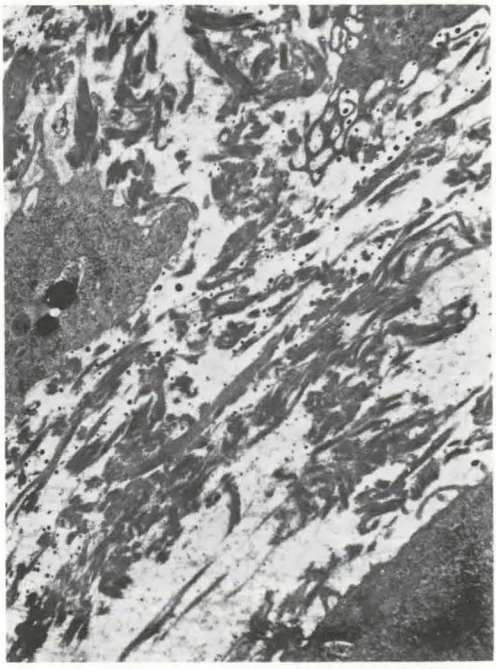

Fig. 4 A large collection of fibrin (as established by light microscopy of an adjacent region) in the lumen of an initial lymphatic. 5,000x

Fig. 3 An initial lymphatic, under the impact region. Its lumen contains a high concentration of plasma protein and some fibrin-like deposits. (Light microscopy established high concentrations of the latter in initial lymphatics in an adjacent region.) 5,000x

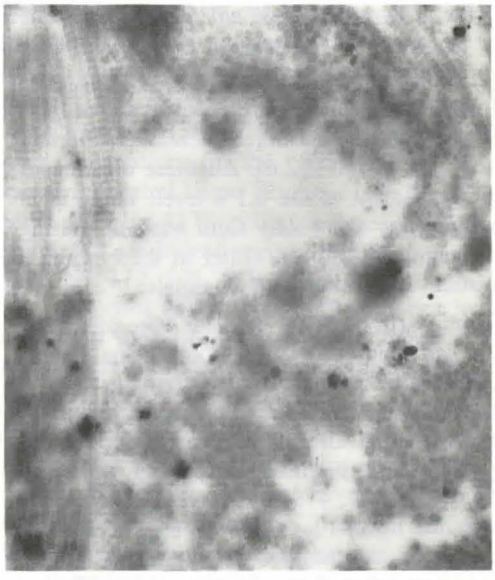

Fig. 5 Tissue channels, filled ferri-ferrocyanide (see text), in the interstitial tissue of the normal leg. 25,000x

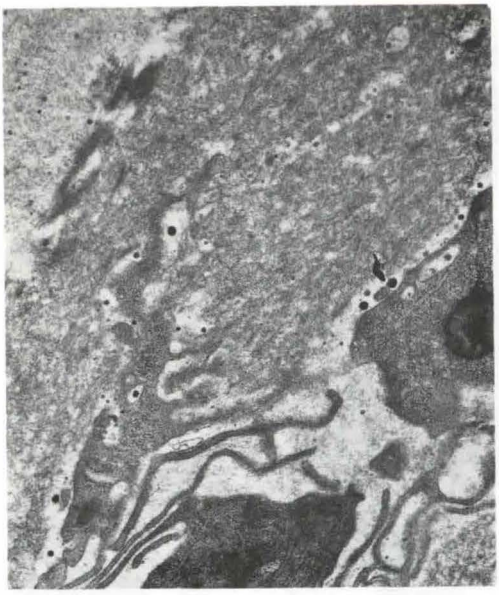

Fig. 6 As for Fig. 5, but in the interstitial tissue just deep to the impact region. The tissue channels are smaller and less frequent, as established by stereology. The tissue contains much amorphous proteinaceous material, together some fibrin-like deposits (much fibrin was shown, by light microscopy, in an adjacent region). There are portions of macrophages. 25,000x

Fig. 7 As for Fig. 5, but in the interstitial tissue in the oedematous region. The tissue channels are much more numerous and much larger, as was conformed by stereology. 25,000x

[2.3] and 0.018 μm^2 [0.0079], respectively. In the region just at the edge of the oedema (Fig. 7), they were much increased: 170 nm [22] and 10 μm^2 [2.6]. All these differences are significant at the 0.1% level. These results clearly show why fluid was not passing the region of impact, either in the lymphatic system or via the tissue channels.

Other portions of the biopsies were processed for light-microscopy, including using the DMAB-nitrate stain, for tryptophan, to locate fibrin (*Pearce* 1968, pp. 135–136). Unlike the usual difficulty of seeing the initial lymphatics in biopsies (*Huth* 1983, pp. 236–237, 319–322, 473) – as was also found with the normal leg – it was easy to see numerous, dilated, initial lymphatics in the specimen taken from the injured leg. This was because they were filled with fibrin thrombi, which prevented their contents running-out when the incisions were made. In addition, there was much fibrin in the interstitial tissue, and thrombi in many of the blood vessels. Other alterations were some inflammatory cells (almost all macrophages and some lymphocytes), and oedema in the oedematous region of the biopsy. It is evident that the material blocking so many of the initial lymphatics and the tissue channels was fibrin, from the damaged blood vessels.

Treatment

Psycho-therapy. The patient's state of mind was greatly improved by thrashing that damn horse up and down mountain-sides, chasing sheep.

Medical and Physical. The generalised oedema was treated with benzo-pyrones (150 mg coumarin and 900 mg troxerutin per day)*.

*Venalot Depot, 5 tablets, twice a day; Schaper & Brümmer, Bahnhofstrasse 35, 3320 Salzgitter 61-Ringelheim, West Germany.

I was too busy at the time to use lymphatic massage or bandaging. As mentioned, the generalised oedema rapidly disappeared, but the localised one persisted.

After the 7th. day, lymphatic massage (*Földi* 1982), bandaging, elevation of the leg, and the benzo-pyrones were used to treat the localised oedema. (I had then returned from mustering sheep to the more leasured life of an academic.) It was reduced from a 7 cm difference in circumference to a 6 cm one, by the 16th. day. By then I was getting worried and realised how much this injury resembled a model of chronic inflammation I use in rats (*Casley-Smith* and *Gaffney* 1981). I therefore commenced using Unguentum lymphaticum*, twice a day, as well. Over the next four days, the difference in circumference was reduced by 1 cm per day. By the 28 th. day no difference was detectable, clinically, between the two legs and all treatment was stopped, except that bandaging was continued for some weeks. At that time there was still no sign of a collateral lymph circulation in the dermis over the localised region, by dye-lymphography, although that over the rest of the leg was normal.

Remarks

The most important thing to emerge from this case is how easily, with relatively slight trauma, a lymphoedema may be caused – if the trauma is correctly applied. It is of interest that there were in fact two distinct lymphoedemas. One was generalised over the whole medial aspect of the leg and was no doubt caused by injury to the saphenous collecting lymphatics. (This was a true lymphoedema and had no venous component, as was shown by a complete absence of any signs of venous dilatation or hypertension.) It passed relatively swiftly, as the benzo-pyrones increased local tissue proteolysis. (It is unlikely that the collaterals had dilated enough to reduce the oedema by six days – and the dye-lymphography, at 13 days, showed no signs of dermal lymph flow.)

The other lymphoedema was more localised and prolonged. The fluid collected into a few large cavities, so that the macrophages in the surrounding tissues contacted little of it and hence were relatively powerless to lyse much of its protein (even though their activities, also, must have been increased by the benzo-pyrones). This lymphoedema was no doubt encouraged by the injury to the saphenous lymphatics, but was largely caused by local injury to, and fibrin deposition in, the initial lymphatics just under where the horse-shoes impacted, and by the deposition of fibrin in the tissues in this region.

The damage to the initial lymphatics was shown by the number of those found with thrombi in them. The deposition of fibrin was shown by the specific stain, and by the greatly reduced numbers and dimensions of the tissue channels – just where the shoes impacted. No doubt this fibrin originally came from broken blood vessels, which also gave the transient bruising. It is evident that the effects of such fibrin deposition can last long after the injured blood vessels have recovered.

Menkin (1940) proposed the hypothesis that fibrin deposition in the tissues formed a considerable barrier to the spread of inflammation. Recently his ideas have fallen out of favour – largely because such fibrin barriers are seldom seen (*Miles* 1964), and there are other explanations for the "fixation" of tracers in injured tissue (*Rusznyák* et al. 1967, pp. 416, 417), although thrombosed lymphatics are indeed seen in inflammation (*ibid.*, pp. 472, 508, 549–550). However this case, while not one of acute inflammation, shows that such fibrin barriers can indeed form in tissues under certain circumstances.

The fibrin not only blocked many of the initial lymphatics, but obviously also obstructed the tissue channels. This is the first confirmation of this idea which was independently proposed by *Földi* (1975) and *Ketterings* (1977, pers. com.). It is evident that this obstruction almost certainly contributed to this lymphoedema. True the lymphatics surrounding the area were obstructed and damaged but,

*Unguentum lymphaticum; PGM, Fürstenstrasse 6, 8000 München 2, West Germany.

in the absence of the blockage of tissue channels, the fluid could readily have moved to another region and been absorbed. This was shown by injecting some of the aspirated fluid into subcutaneous tissue of the normal leg, and its rapid disappearance.

No doubt such blockage of channels and initial lymphatics by fibrin occurs quite frequently during trauma. It has not been observed before for two reasons. One is that it is very rare for biopsies to be taken of a traumatic injury. The second is that most trauma occurs over a continuous area. Thus the tissue channels and lymphatics at its periphery will still be intact and can drain the excess protein away; only if fibrin deposition occurs in a circle will one notice the oedema and lymphostasis of the "normal" tissue inside. One wonders whether fibrinolysins would assist in such cases. I would have tried them, but the oedema had subsided before I thought of them.

There are frequent complaints that patients are inarticulate when trying to describe the pain of lymphoedema. It is rather humiliating to discover that I can do no better than they. The normal pain was a dull, bursting ache. One was always conscious of it and it was, in fact, quite wearing, as was the necessity to avoid jarring the leg. An acute, tearing, pain was caused by any considerable external pressure (when the fluid was tending to tear the tissues apart); this was also felt if the bandages were omitted and the oedematous area became very tense. The acute pain was more pronounced at 2–3 weeks than at the beginning, perhaps because the nerves were conducting better. It could cause nausea and considerable incapacity. Unfortunately there is no internationally recognised way of grading pain. The best I can do is to say that the acute pain was about 50% along a scale from no pain, to pain strong enough to cause suicide; the normal dull ache was about 20% along this. More information may be conveyed by observing that my testes have been frequently used as targets by many maliciously-inclined animals – from rugby foot-ballers, to cows and horses. I would estimate the acute pain as being about as severe as that caused by a moderate kick – enough to make one stop and rest almost no matter what one wished to do, but not enough to make one vomit. Certainly it was much more than an ulna with a closed fracture, which has about the intensity of the normal, dull ache. Of course, the pain in chronic lymphoedema may be quite different from these since the tissue then is fibrotic and hence better supported, however I am now certainly much more conscious of this aspect of lymphoedema.

Unfortunately, I was more concerned to use all means to remove the lymphoedema, than to test the various treatments. It really is not possible to say how much each contributed. I have given reasons why I think the benzopyrones, while reducing the generalised lymphoedema, were relatively ineffective with the localised collection of fluid. Probably, properly-trained masseurs could have reduce the latter more rapidly than I could by massage, but one wonders how much the deposits of fibrin would have impeded even their efforts. There was certainly a remarkable reduction in oedema after *Unguentum lymphaticum* was used; this is similar to the great reduction it produces in acute lymphoedema in rats (*Casley-Smith* and *Casley-Smith* 1983). It has also been reported to relieve the pain of lymphoedema very rapidly in patients (*Földi* and *Földi* 1983), although it did not (*Földi* 1982, pers. com.) reduce the oedema significantly more rapidly than complex physical therapy alone (*Földi* 1982). It is likely that this cream does more than just act like a benzo-pyrone, because poisoning the macrophages with silica does not completely prevent its activity (*Casley-Smith* and *Casley-Smith* 1983). This was also shown by its results on my leg, when the benzo-pyrones were much less effective than usual, because of the concentration of the fluid into large pools – with the macrophage only on their edges.

Concluding Remarks

Interested friends will be pleased to learn that

I no longer have a clinically-detectable lymphoedema: animal lovers will be delighted that the stallion is now reunited with his mares.

Acknowledgements

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