Lymphangiosarcoma arising in chronic congenital and idiopathic lymphoedema

D. H. MACKENZIE

From the Department of Morbid Anatomy, Westminster Medical School, London

SYNOPSIS A case of lymphangiosarcoma arising in chronic congenital and idiopathic lymphoedema is presented. The literature is reviewed and the diagnosis discussed.

Malignant tumours arising from the endothelium of blood vessels or lymphatics are rare. While haemangiosarcoma is accepted as a definite if uncommon entity, considerable controversy has surrounded the lymphangiosarcoma. Most of the literature has been concerned with tumours arising in oedematous arms following radical mastectomy (Stewart and Treves, 1948; Taswell, Soule, and Coventry, 1962). There has, however, been a number of reports of lymphangiosarcomas arising in limbs affected by congenital or chronic idiopathic lymphoedema in the absence of any other detectable malignant disease, and it is with this group only that the present communication is concerned.

Taswell *et al* (1962) listed four cases from the literature which they regarded as acceptable and added two more of their own. They also listed five probable ones. To these must be added the cases of Francis and Lindquist (1960), Scott, Nydick, and Conway (1960), Vandaele and van Craeynest (1963), Baes (1967), and McBride, Reeder, and Smith (1969).

Received for publication 26 November 1970.

These include cases diagnosed as lymphangiosarcoma and angiosarcoma. There is a close relationship between the two, and Evans (1966) has suggested that the term 'angiosarcoma' should be used for all malignant tumours of endothelium. Details of the 16 cases are given in Table I.

Opinions regarding these cases have ranged from general acceptance to wholesale rejection by Salm (1963). In view of the wide differences of opinion the presentation of a further case and a review of the other cases seemed justified.

Case Report

The patient, a man aged 64, had suffered from an oedematous right leg since birth. Two months before admission the leg became heavier, more oedematous, painful, and ulcerated.

On examination the right leg was grossly oedematous, particularly below the knee, and there was a large ulcer on the outer aspect of the calf (Fig. 1). There was some oedema of the thigh and the skin

Case	Author	Cause of Oedema	Age	Sex	Site	Onset of Tumour to Death (yr)
1	Lowenstein (1906)	Trauma	56	F	Upper limb	?
2	Kettle (1918)	Congenital	44	F	Lower limb	?
3	Nather (1921)	Trauma	59	F	Lower limb	?
4	Aegerter and Peale (1942)	Multiple surgical procedures	40	F	Lower limb	6
5	Martorell (1951)	Old fracture and infection	44	F	Lower limb	4
6	Raven and Christie (1954)	Multiple surgical procedures	56	F	Upper limb	Died postoperatively
7	Aird <i>et al</i> (1956)	Idiopathic bilateral	60	F	Lower limb	3
8	Liszaauer and Ross (1957)	Congenital	28	M	Lower limb	8/12
9	Whittle (1959)	Meningitis followed by oedema	31	M	Lower limb	6/12
10	Scott <i>et al</i> (1960)	Oedema following vaccination	50	F	Upper limb	1
11	Francis and Lindquist (1960)	Surgical procedures	52	F	Lower limb	?
12	Taswell <i>et al</i> (1962)	Congenital	17	M	Upper limb	2
13	Taswell <i>et al</i> (1962)	Unknown	65	F	Lower limb	?
14	Vandaele and Van Craeynest (1963)	Idiopathic	46	F	Upper limb	?
15	Baes (1967)	Unknown	44	F	Lower limb	1
16	McBride <i>et al</i> (1969)	?	?	F	Lower limb	?

Table I Cases diagnosed as lymphangiosarcoma arising in chronic lymphoedema

Fig. 1 Lower part of affected leg.

Fig. 2 Dilated lymphatic spaces lined by endothelium. Haematoxylin and eosin $\times 40$.

texture was abnormal up to the groin. In addition to the oedema and ulceration there were multiple nodular lesions of the skin and subcutaneous tissues from the foot to the knee. The patient was extensively investigated but no other lesion was demonstrable anywhere else in the body.

A hindquarter amputation was performed. Post-operatively the patient's general condition improved rapidly and on discharge he was reasonably active on crutches. He received postoperative supervoltage radiotherapy to the right inguinal and right paraortic areas. The patient is alive and well after two years.

Pathology

The operation specimen consisted of the right lower limb removed by hindquarter amputation. The appearances have been described above but, in addition, there were a number of enlarged external iliac lymph nodes.

Microscopy

Sections were stained with haematoxylin and eosin,

van Gieson, Gomori's reticulin stain, Sheridan's elastic stain, and by Sudan black for fat.

Numerous well defined channels lined by a single layer of endothelium were seen in many sections (Fig. 2). They were empty of blood. In many areas the endothelial cells were larger and more hyperchromatic and were clearly proliferating within the channels and within their reticulin sheaths (Figs. 3 and 4). In some fields the tumour assumed a more solid and clearly malignant appearance (Figs. 5 and 6). Some sections showed a fine honeycomb structure which appeared to be due to a sponge-work of channels of capillary size forming in the tumour tissue (Fig. 7). Fat stains were negative. Two external iliac lymph nodes attached to the specimen showed metastatic deposits (Figs. 8 and 9). The appearances were those of a lymphangiosarcoma arising in a chronically oedematous limb.

Review of Previous Cases

Inadequate documentation is the main problem facing a reviewer of the literature. It is often im-

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 3 *Proliferating endothelial cells within lymphatic channels. Haematoxylin and eosin $\times 86$.*

Fig. 4 *Proliferating endothelial cells within reticulin sheaths. Gomori's reticulin stain $\times 80$.*

Fig. 5 *A malignant proliferation of closely packed endothelial cells. Haematoxylin and eosin $\times 86$.*

Fig. 6.

Fig. 7.

Fig. 8.

Fig. 6 A modified reticulin pattern in a cellular area of tumour. Gomori's reticulin stain $\times 80$.

Fig. 7 A spongework of capillary channels near a focus of solid tumour. Haematoxylin and eosin $\times 86$.

Fig. 8 Metastatic tumour in iliac lymph node. Haematoxylin and eosin $\times 56$.

Fig. 9 Reticulin pattern in a solid area of metastatic tumour. Gomori's reticulin stain $\times 86$.

possible for him to examine the actual slides on which the diagnosis was based and he is, therefore, dependent entirely upon the photomicrographs in the relevant papers. It is clearly the duty of an author to prove his case beyond reasonable doubt, and this is particularly important with rare entities such as lymphangiosarcoma which may be very closely imitated by metastatic carcinoma. In fact Salm (1963) rejected not only the cases of Stewart and Treves (1948) but also those accepted by Taswell *et al* (1962) in the most recent available review of the subject in English. It is necessary to reconsider the cases listed in Table I.

The cases reported by Löwenstein (1906), Nather (1921), Martorell (1951), Liszauer and Ross (1957), and Vandaele and van Craeynest (1963) are excluded either because the reports are devoid of illustrations or because the quality of the photomicrographs is too poor to substantiate the diagnosis or to exclude the possibility of carcinoma. The cases described by Francis and Lindquist (1960)

and by McBride *et al* (1969) were known to have had other primary tumours and the photomicrographs do not exclude the possibility of metastases. The case of Aegerter and Peale (1942) appears to have been an example of Kaposi's sarcoma while that of Raven and Christie (1954) concerned malignant change in a benign angioma with no mention of oedema at the initial presentation. These are, therefore, excluded. In the case of Scott *et al* (1960) the tumours were variously diagnosed as papilloma, sclerosing angioma, lymphangiosarcoma, and, on two occasions, as synovial sarcoma. The photomicrographs are not conclusive and their Fig. 6 would certainly do for a monophasic area in a synovial sarcoma. This case must also be excluded.

The remaining six cases are, in my opinion, acceptable. Through the courtesy of Professor Harrison and Professor Weinbren I have been able to examine the postmortem sections of the case reported by Aird, Weinbren, and Walter (1956) and these, together with the photomicrographs shown in the paper, appear to confirm the diagnosis. Through the courtesy of Dr A. Stansfeld I have been able to examine the initial section of the case of Whittle (1959). This was undoubtedly a vasoformative tumour and in no way suggested a carcinoma of the skin. The evidence in the other four cases, while not entirely conclusive, seems to justify their inclusion. The acceptable cases are shown in Table II.

Case No.	Author
1	Kettle (1908)
2	Aird <i>et al</i> (1956)
3	Whittle (1959)
4	Taswell <i>et al</i> (1962), case 12
5	Taswell <i>et al</i> (1962), case 13
6	Bacs (1967)

Table II Acceptable cases of lymphangiosarcoma and angiosarcoma arising in chronic lymphoedema

Discussion

In reducing the number of acceptable cases from 16 to six it must be admitted that injustice may have been done to a number of authors. A study of these cases shows a remarkable consistency in the clinical picture and in the naked-eye appearances of the affected limbs. This suggests, but does not prove, the accuracy of the diagnosis. Authors have an obligation to provide conclusive photomicrographs in support of their suggested diagnosis. One of the most unfortunate features of the photomicrographs shown in these cases has been the lack of a reticulin stain to illustrate the vasoformative nature of the neoplasm and to show that the proliferating tumour

cells do indeed lie within the reticulin sheaths. In this connexion it must be stressed that in highly cellular endothelial neoplasms the diagnostic reticulin pattern may be modified or lost and such reticulin variations are shown in Figures 4, 6, and 9. In the majority of cases, however, the examination of multiple sections will provide the vital information. Reticulin stains must be carried out in all suspected cases and these are particularly important if the patient has previously suffered from a primary neoplasm elsewhere. Willis (1967) has rightly stressed the importance of applying the very strictest criteria before the diagnosis of angiosarcoma or lymphangiosarcoma can be accepted.

I am indebted to Mr E. Stanley Lee for permission to publish this case. I wish to thank Professor R. A. Willis for reviewing the sections and confirming the diagnosis. My thanks are also due to the Department of Medical Photography, Westminster Hospital.

References

- Aegerter, E. E., and Peale, A. R. (1942). Kaposi's sarcoma. *Arch. Path.*, **34**, 413-422.
- Aird, I., Weinbren, K., and Walter, L. (1956). Angiosarcoma in a limb the seat of spontaneous lymphoedema. *Brit. J. Cancer*, **10**, 424-430.
- Baes, H. (1967). Angiosarcoma in a chronic lymphoedematous leg. *Dermatologica (Basel)*, **132**, 331-336.
- Evans, R. W. (1966). *Histological Appearances of Tumours*, p. 107. Livingstone, Edinburgh and London.
- Francis, K. C., and Lindquist, H. D. (1960). Lymphangiosarcoma of the lower extremity involved with chronic lymphedema. *Amer. J. Surg.*, **100**, 617-619.
- Kettle, E. H. (1918). Tumours arising from endothelium. *Proc. roy. Soc. Med.*, **11**, 19-34.
- Lisauer, S., and Ross, R. C. (1957). Lymphangiosarcoma in lymphoedema. *Canad. med. Ass. J.*, **76**, 475-477.
- Löwenstein, S. (1906). Der ätiologische Zusammenhang zwischen akutem einmaligem Trauma und Sarkom: Ein Beitrag zur Ätiologie der malignen Tumoren. *Brunn's Beitr. Klin. Chir.*, **48**, 780-824.
- Martorell, F. (1951). Tumorigenic lymphedema. *Angiology*, **2**, 386-392.
- McBride, C. M., Reeder, J. W., and Smith, J. L. (1969). Angiosarcoma in the lymphoedematous limb. *St. med. J.*, **62**, 378-380.
- Nather, K. (1921). Ueber ein malignes Lymphangioendotheliom der Haut des Fusses. *Virchows Arch. path. Anat.*, **231**, 540-556.
- Raven, R. W., and Christie, A. C. (1954). Haemangiosarcoma: a case with lymphatic and haematogenous metastases. *Brit. J. Surg.*, **41**, 483-489.
- Salm, R. (1963). The nature of the so-called postmastectomy lymphangiosarcoma. *J. Path. Bact.*, **85**, 445-456.
- Scott, R. B., Nydick, I., and Conway, H. (1960). Lymphangiosarcoma arising in lymphedema. *Amer. J. Med.*, **28**, 1008-1012.
- Stewart, F. W., and Treves, N. (1948). Lymphangiosarcoma in post-mastectomy lymphedema. A report of 6 cases in elephantiasis chirurgica. *Cancer (Philad.)*, **1**, 64-81.
- Taswell, H. F., Soule, E. H., and Coventry, M. B. (1962). Lymphangiosarcoma arising in chronic lymphoedematous extremities. *J. Bone Jt Surg.*, **44a**, 277-294.
- Vandaele, R., and van Craeynest, W. (1963). Lymphangiosarcome sur lymphoedème primitif du bras. *Bull. Soc. franç. Derm. Syph.*, **70**, 722-725.
- Whittle, R. J. M. (1959). An angiosarcoma associated with an oedematous limb. A case report. *J. Fac. Radiol. (Lond.)*, **10**, 111-112.
- Willis, R. A. (1967). *Pathology of Tumours*, p. 244. Butterworths, London.