A RARE CASE OF POST-MASTECTOMY LYMPHANGIOSARCOMA

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Lymphangiosarcoma or Stewart-Treves syndrome is a rare and aggressive malignancy of the lymphatic vessels. It was first described as arising in chronically lymphoedematous extremities by Stewart and Treves (1948), who noted the condition in six females who had undergone radical mastectomy for breast carcinoma. Since this time, over 300 cases of lymphangiosarcoma arising from the site of chronic lymphoedema have been reported (Roy et al, 2004).

The majority of cases detailed in the literature occurred in the upper extremities of patients who had undergone mastectomies with axillary lymph node dissection for breast cancer. The incidence of post-mastectomy lymphangiosarcoma of the arm in this patient group varies between 0.07–0.45% (Shirga, 1962).

Lymphangiosarcoma of the lower extremities, occurring as a result of chronic lymphoedema due to filariasis, obesity, primary causes and pre-existing malignancies is less frequently reported. The discrepancy in incidence between upper and lower extremity lymphangiosarcoma is likely to be an effect of the high prevalence of breast cancer; its treatment brings with it an increased risk of lymphoedema. Lymphangiosarcoma may occur in other sites, such as the trunk, but this is even rarer (Arieke et al, 1995).

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Aetiology

The aetiology of lymphangiosarcoma is not completely understood. However, it is recognised that lymph node dissection complicated by lymphoedema, trauma and radiation are important risk factors in its development (Aygit et al, 1999). Martorell (1951) suggested that the lymphoedema is in itself tumour-inducing, while Shrieber et al (1972) speculated about the role of loco immunodeficiency in the oedematous extremity. Brady et al (1994) found that 19 of 22 patients with lymphangiosarcoma had been treated with radiotherapy post-mastectomy. The mean interval between mastectomy and/or radiotherapy and the development of lymphangiosarcoma is reported to be 10 years (Arieke et al, 1995).

If left untreated, the predicted survival of a patient with lymphangiosarcoma is less than 4–6 months (Roy et al, 2004). Lymphangiosarcoma has a poor prognosis and therapeutic options are few.

Presentation

Lymphangiosarcoma often first appears as a bruise mark with purple discoloration or as a tender nodule in the extremity, typically on the medial or anterior surface of the oedematous area. Initial presentation is commonly attributed to trauma.

The primary lesion tends to form satellites, which can remain isolated or can form larger lesions that can ulcerate and crust. As the disease progresses, extensive necrosis can spread throughout the whole arm and possibly extend into the chest wall. The lymphangiosarcoma can metastasise in an early stage of the disease, especially to the lung, which is the most common cause of death.

If left untreated, the predicted survival of a patient with lymphangiosarcoma is less than 4–6 months (Roy et al, 2004). Lymphangiosarcoma has a poor prognosis and therapeutic options are few. Arieke et al (1995) followed a series of eight patients with chronic lymphangiosarcoma; all but one case showed a typical rapid progression and fatal outcome.

Treatment

Radical amputation appears to offer the best chance of cure for lymphangiosarcoma (Roy et al, 2004). Heitmann and Ingianni (2000) and Roderich et al (2002) focused on two patients following radical operations: both had lymphangiosarcoma; were ≥15 years following amputation; and were free from cancer. In the studies by Heitmann and Ingianni (2000) and Roderich et al (2002), radical amputation therapy accomplished long-term survival in all cases studied. However, Brady et al (1994) found that only two out of 22 patients treated with amputation survived more than five years.

Radiotherapy often cannot be given because of previous therapy, while chemotherapy has been reported to prolong survival in a limited number of cases. Tong and Winter (1974) detailed two cases of

post-mastectomy lymphangiosarcoma treated with cyclophosphamide chemotherapy. Both patients showed a dramatic symptomatic improvement and tumour regression, however, there was a prompt reactivation of the tumour as soon as the cyclophosphamide was stopped.

Chemotherapy for the treatment of lymphangiosarcoma can be used and cyclophosphamide and/or another cytotoxic agent should be considered in patients whose tumours are too advanced for palliative treatment with either surgery or radiotherapy.

Although lymphangiosarcoma is very rare, it should be considered when treating patients with breast cancer-related chronic lymphoedema, as the following case report highlights.

Case report

Patient X, a 66-year-old female, was diagnosed in 1995 with grade 2 ductal adenocarcinoma of her right breast, for which she underwent a mastectomy and level 2 axillary clearance. She went on to undergo 15 fractions of radiotherapy and cyclophosphamide, methotrexate and fluorouracil chemotherapy, in addition to tamoxifen (*Table 1*).

Following the removal of a drain one week postoperatively, patient X developed a swelling to the right postaxillary pouch, which progressed into her arm, hand and fingers as a result of radiotherapy.

Patient X was referred to the lymphoedema service, and on initial examination, the swelling was soft and pitting in places, and she reported that it only occasionally affected her hand and fingers. There was a collection of oedema to the elbow, which fluctuated overnight. Patient X's arm shape and skin condition were good, and on measurement her right arm was 10.9% bigger than the contralateral limb; her body mass index (BMI) was 36. Brenda was prescribed a treatment plan of skin care, simple lymphatic drainage (SLD), exercise (she was a keen swimmer) and a class one combined armsleeve with handpiece. The prescription of this garment was a direct result of the nurse's lack of knowledge of best practice. When patient X was offered decongestive lymphatic therapy (DLT), she was only provided with a maximum of four days treatment with bandaging, skin care and exercise; she was not offered manual lymphatic drainage (MLD), which would be best practice according to the British Lymphology Society (2001).

As a result of her less than optimal management, the patient's arm size increased with time, and in 2000 her right arm was 62% bigger than the contralateral limb. Deepened skin folds had appeared to the base of her fingers, wrist and elbow, and her hand and fingers were continually swollen, making dextrous tasks difficult to perform. Some of the limb volume increase could be attributed to cellulitis and possibly some to a

Table 1

Key events in patient X's medical history

1995	Diagnosed with cancer in the right breast. Treated with surgery, radiotherapy, chemotherapy and tamoxifen. Post-operative removal of drain and immediate development of swelling to right postaxillary pouch
1997	Excision of flap under axilla (cosmetic)
April 1997	First fall, bruising right arm badly
December 1999	Cellulitis of right arm
October 2000/May 2001	Further falls, resulting in bad bruising to right arm
February 2002	Cellulitis of right arm
2003	Excellent reduction of limb volume with decongestive lymphatic therapy which was maintained for one year
July 2004	Cellulitis of right arm
May/June 2005	Fall in garden
July 2005	Referred to the breast care team
December 2005	Re-referred to breast care team
March 2006	Diagnosed with multiple nodules in the right arm (in line with lymphangiosarcoma) and referred to specialist centre
June 2006	Seen at specialist centre, confirmation of diagnosis of a high-grade epithelioid angiosarcoma
July 2006	Resection of subcutaneous tumour with split skin grafting Lymphoedema worse
September 2006	Recurrence of very painful cancer in the forearm
September 2006	Amputation
October 2006	Experiencing phantom pains
November 2006	Admitted to local hospice for symptom control of phantom pains and diagnosed with recurrence of the lymphangiosarcoma to the chest wall. Excision of the recurrent nodules to the chest wall
January 2007	Commenced a regimen of palliative chemotherapy

number of falls. Ultimately, patient X did not find the hosiery she had been supplied with comfortable, and with no alternatives forthcoming, she did not wear the hosiery most of the time, which would also have led to worsening of her lymphoedema.

In May 2003, the author took over as lead for patient X's lymphoedema care. On initial assessment, patient X's right arm was 95.2% bigger than her left and her BMI was 31.4. DLT was commenced three months later and following a two-week period of treatment her limb volume reduced from 3,982L to 3,343L (a 641ml reduction) (*Table 2*).

Patient X was fitted with a strong compression sleeve with a separate, full-fingered glove (all class 2); a second-layer combined armsleeve and handpiece were added for activities. Compliance was achieved as time was spent on fitting the garments so patient X would find them comfortable to wear. Patient X continued with skin care and exercise and attended four sessions of MLD over four months. As a result, the swelling was well controlled for 12 months after intensive treatment.

In July 2004, patient X developed cellulitis and was unable to wear the strong compression hosiery for a number of weeks, during which time her limb volume significantly increased (*Table 2*). A further two-week course of DLT was arranged, and her limb volume was reduced to 3,157L (*Table 2*). Patient X continued with skin care, exercise, SLD, the application of double-layered, strong compression hosiery and four sessions of MLD over four months, which resulted in the maintenance of the reduction in limb volume at a follow-up visit in February 2005.

At the six-month follow-up in July 2005, patient X stated that she had fallen a few weeks previously and had knocked the medial aspect of her right arm, and that the black-blue bruised area (measuring approximately 4x2cm) had never totally gone away. On examination, her arm was hard and lumpy from the inner elbow to the root of the limb, and patient X described it as feeling 'like a brick'. Her arm was painful, especially when held next to her body, and she was not able to tolerate wearing her compression hosiery or go swimming, leading to an increase in her limb volume.

Even following an aggressive approach with limb amputation, lymphangiosarcoma frequently recurs in the operation site and can spread further to the chest.

Patient X was referred to her breast surgeon for review, as unresolving blackish-blue lumps can be a sign of lymphangiosarcoma (Noguchi et al, 1987). The breast surgeon was satisfied that the blue-black area was simply bruising in the absence of any other symptoms, and referred patient X back to the lymphoedema clinic in September 2005 to continue her treatment. By this stage there had been a further increase in limb volume, although measurement was not carried out as the patient was not finding it helpful, but its shape and skin condition were satisfactory. Patient X was fitted with a lighter sleeve, and analgesia was arranged through her GP. When she was seen three months later (December 2005), she had developed a nodule to the still bruised area and was immediately re-referred to the breast care team. In March 2006, she was diagnosed with multiple nodules in her right arm in line with lymphangiosarcoma and was referred to a specialist centre. In June 2006, a diagnosis of high-grade epithelioid lymphangiosarcoma was confirmed.

Treatment

In July 2006, patient X underwent resection of the subcutaneous tumour with split skin grafting, and her lymphoedema worsened. In September, a very painful recurrence of the sarcoma was diagnosed in her forearm, followed some eight weeks later with radical disarticulation of the shoulder. Post amputation, patient X suffered extensive phantom limb pain, specifically of the fingers, and was admitted to a hospice for symptom control. This was an extremely distressing symptom that presented immediately after surgery, but was successfully managed with ketamine.

Even following an aggressive approach with limb amputation, lymphangiosarcoma frequently recurs in the operation site and can spread further to the chest. This happened to patient X, who in November 2006 was diagnosed with recurrence of lymphangiosarcoma to the anterior chest wall. The recurrent nodules were excised as a day case and the district nurses visited the patient daily at home to change her dressings.

Table 2

Patient X's limb volume reduction as a result of decongestive lymphatic therapy (DLT)

	Limb volume (L)	Excess (L)	Excess as a percentage
Before treatment (2003)	3982	1942	95.2
After treatment (2003)	3343	1136	51.5
After cellulitis (July 2004)	3679	1564	68.1
After second course DLT	3157	1047	38.0
December 2005	4516	1766	64.0

Currently patient X is undergoing chemotherapy in an attempt to extend her life. The regimens are making her extremely ill and she feels that she may not be able to continue. She is hugely unstable since the amputation and has sustained a number of falls. She is supported by a community Macmillan nurse and attends the local hospice day centre. It has been extremely difficult for both the patient and the lymphoedema clinic as we currently have no part to play in her management.

Discussion

It is possible that patient X's less than optimal lymphoedema management for a number of years, combined with recurrent cellulitis and a number of traumatic falls, put her at an increased risk of developing lymphangiosarcoma. Indeed, most of the literature focuses on untreated lymphoedema as a risk factor for the development of this aggressive malignancy. As there is still gross disparity in the way patients with lymphoedema are treated, it is important to consider other patients like patient X who may benefit from appropriate management that may ultimately prevent the development of lymphangiosarcoma. Patient X's condition was further complicated with a delayed diagnosis of lymphangiosarcoma, which was almost certainly due to the rarity of the condition. Due to the rapid progression of her disease, it is unlikely that earlier diagnosis would have changed the outcome in patient X's case, but this would have been likely to have had a positive psychological effect on this patient.

Conclusions

Lymphangiosarcoma is a very aggressive malignancy with a poor prognosis, that is particularly prevalent in patients with lymphoedema arising post-mastectomy. It should always be considered when treating patients with breast cancer-related lymphoedema.

As the combination of mastectomy or breast-conserving therapy with axillary clearance and radiotherapy of the axilla is rarely used now, it is hoped that a corresponding decrease in the occurrence of post-mastectomy lymphangiosarcoma will be observed.

However, It is possible that an increase in lymphangiosarcoma of the breast itself may be observed, due to the increased conservation and irradiation of the breast itself. The predicted survival of a patient with lymphangiosarcoma is less than 4–6 months (Roy et al, 2004). Amputation of the affected extremity is the most effective treatment, but radiotherapy and chemotherapy have been shown to prolong survival in a limited number of cases (Roy et al, 2004).

As the condition is so aggressive, and lacking in ideal treatments, it is important that practitioners are aware of the condition and its risk factors when treating and following-up patients with chronic oedema. Early detection and treatment are essential to lower the morbidity and mortality associated with this rare malignancy. JL

Key Points

- Lymphangiosarcoma is a rare and aggressive malignancy of the lymphatic vessels that arises in chronically oedematous extremities.
- The majority of cases occur in the upper extremities of patients who have undergone mastectomies with axillary lymph node dissection for breast cancer.
- If left untreated, the survival rate is less than 4–6 months. Amputation of the affected extremity offers the best outcome.
- It is important that practitioners are aware of the condition and its risk factors when treating and following-up patients with chronic oedema.
- Early detection and treatment are essential to lower the morbidity and mortality associated with this rare malignancy.

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