Case Reports in Dermatology

Case Rep Dermatol 2014;6:274–278

DOI: 10.1159/000369992
Published online: November 26, 2014

1662–6567/14/0063–0274$39.50/0
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The 'Pantie' Tumour

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Key Words
Angiosarcoma · Radiation · Sarcoma · Vascular tumour

Abstract
We present a case of radiation-associated angiosarcoma. A 67-year-old Thai woman was diagnosed with endometrium carcinoma stage IC and was treated with surgery and radiations. Ten years later, she presented with a gradually enlarging mass on the pubic area, in the shape of a pair of panties. Skin biopsy of lesions confirmed angiosarcoma. The diagnosis was radiation-associated angiosarcoma. She was treated with chemotherapy due to unresectable tumour. The chemotherapy was started with paclitaxel 70 mg/m^2 every 2 weeks. After completing the fifth cycle of paclitaxel, the lesion was markedly decreased in size and the symptoms previously described were also completely resolved.

Case Report

A 67-year-old Thai woman was diagnosed with endometrium carcinoma stage IC. She underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy followed by pelvic radiation in 2004. The total radiation dose was 50 Gy.

In 2014, she presented with a gradually enlarging mass on the pubic area extending to the mons pubis for the past 2 months. It also was painful on palpation and bled easily. The affected site was within the field of prior radiation. She had a history of loss of appetite and weight loss of 3 kg within 2 months. She denied any history of trauma and was not taking any medication.

Clinical examination revealed a large well-defined firm violaceous plaque, 12 × 25 cm in size, and several bluish nodules on the mons pubis and labia majora, in the shape of a pair of

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panties (fig. 1). Pelvic examination was not performed due to the obstructing mass. There was no palpable lymphadenopathy.

Histopathology showed poorly circumscribed dermal tumours extending to the subcutaneous tissue (fig. 2a), composed of multiple cords and strands of atypical cells with little mitosis, some forming irregular dissecting anastomosing lumen and papillary projection into the lumen (fig. 2b). These atypical cells were positive for CD31, but negative for AE1/AE3 and HHV-8.

The diagnosis was radiation-associated angiosarcoma (RAAS). In our patient, the large tumour could not be resected; chemotherapy was started with paclitaxel 70 mg/m^2 every 2 weeks. After completing the fifth cycle of paclitaxel, the lesion was markedly decreased in size and the symptoms previously described were also completely resolved.

Discussion

Angiosarcoma is a rare aggressive malignant mesenchymal tumour with endothelial differentiation that accounts for 2% of all soft tissue sarcomas [1]. The majority of patients develop angiosarcoma at advanced age on sun-exposed skin, with predilection for the scalp. The known risk factors for developing secondary angiosarcoma include chronic lymphedema and prior radiation. The frequency of RAAS is 17–25% of all angiosarcoma cases [2]. The diagnostic criteria for radiation-induced sarcomas include previous history of radiotherapy with a latency period of more than 3–4 years, development of sarcoma within a previously irradiated field or in the tissues adjacent to the field, and histologic confirmation [3]. The most frequent clinical setting is the treatment of breast carcinoma, predominantly after radiotherapy in breast conservative therapy, followed by gynaecological malignancies such as ovarian, endometrial or cervical carcinoma. Rare reasons for radiation treatment include acne, ringworm, graft radiation of a renal transplant, congenital hemangioma, Hodgkin's disease, multiple myeloma and melanoma [4].

Almost all of the patients are female. The median age at presentation is 68 years; the median radiation dose is 40–60 Gy. The latency between radiation and diagnosis of RAAS is approximately 5–6 years, ranging from 1 to 40 years. The latency period is shorter in patients treated for breast carcinoma than in patients receiving radiation for other reasons (median latency 5.5 and 30 years, respectively) [4]. The clinical presentation is quite variable, including violaceous or erythematous patches, plaques, nodules or bruise-like discolouration, overlying a painless area of induration. They occasionally bleed or ulcerate. Most are multifocal lesions and the size varies from a few millimetres to more than 20 cm (median 7.5 cm) [4]. The histologic features range from well to poorly differentiated and can vary within a single case. These lesions are poorly circumscribed, involve the dermis and sometimes subcutaneous tissues. Well-differentiated angiosarcoma consists of irregular interanastomosing channels that infiltrate surrounding tissue, diffusely dissecting the dermal collagen. The atypical endothelial cells are usually multilayered, with enlarged and hyperchromatic nuclei and sometimes nucleoli. Sieve-like architecture is a common feature. Moderately and poorly differentiated angiosarcoma has very heterogeneous cytoarchitectural features. The cytologic appearance can be epithelioid, spindled or pleomorphic. Blood-filled spaces are a frequent feature in these less well-differentiated lesions. Areas of necrosis are frequently present and the mitotic index is high. In poorly differentiated ones, the diagnosis is difficult [5]. Immunohistochemistry is often necessary to confirm the diagnosis. It shows positive staining with antibodies against endothelial markers including CD31, CD34, FVIII-related antigen and von Willebrand factor [4]. CD31 is the best marker with a

high sensitivity and specificity. D2-40 (podoplanin), known as a lymphatic marker, is positive focally less frequently in angiosarcoma. Cytokeratin positivity may be observed occasionally in epithelioid areas [6]. Proliferative activity detected by ≥50% Ki-67 nuclear staining is also found [7].

Angiosarcoma is a very aggressive tumour. Unfortunately, the treatment options are relatively limited, including surgery, radiation, chemotherapy and combinations thereof. Currently, surgery with complete tumour resection is considered to be a standard treatment. However, when surgery is not possible, re-irradiation and chemotherapy have also proved to be beneficial. Anthracyclines alone or in conjunction with ifosfamide have led to disease control after several months, always in combination with previous surgery [8]. Over the past few years, paclitaxel has been used in advanced-stage and/or metastatic angiosarcoma [9].

RAAS has a poor prognosis. The 5-year survival rates vary from 28 to 54%, and the overall 5-year local recurrence-free interval is 32%. Depla et al. [10] found that tumour size and age are the prognostic factors for local recurrence and that adding re-irradiation to surgery improves local control. However, some studies suggest a more indolent behaviour of RAAS compared with the conventional or lymphedema-associated variants [4, 11]. RAAS shows a high rate of recurrence rather than distant metastasis. RAAS of the breast has a significantly better prognosis more than that in other locations (overall survival >60 months and 7 months, respectively) [11].

Summary

RAAS is an angiosarcoma developing within a previously irradiated field, and the latency period is approximately 5–6 years. Most of the patients incurred RAAS after the treatment of breast carcinoma, followed by gynaecological malignancies. The clinical presentations are multiple, rarely solitary large violaceous or erythematous patches, plaques, nodules or bruise-like discolouration. However, the clinical and histopathological findings are undistinguishable from primary angiosarcoma. Treatment options include surgery, radiation, chemotherapy and combinations thereof. However, the response to treatment is usually poor.

Acknowledgment

The authors acknowledge the assistance of Dr. Marinya Pongpudpunth in histopathological consultation.

Disclosure Statement

The authors report no conflict of interest. There was no funding.

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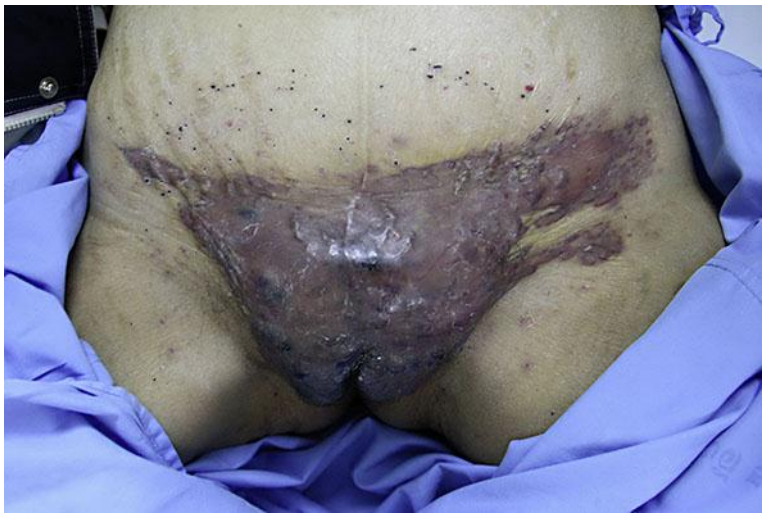

Fig. 1. A large indurated violaceous plaque on the suprapubic area.

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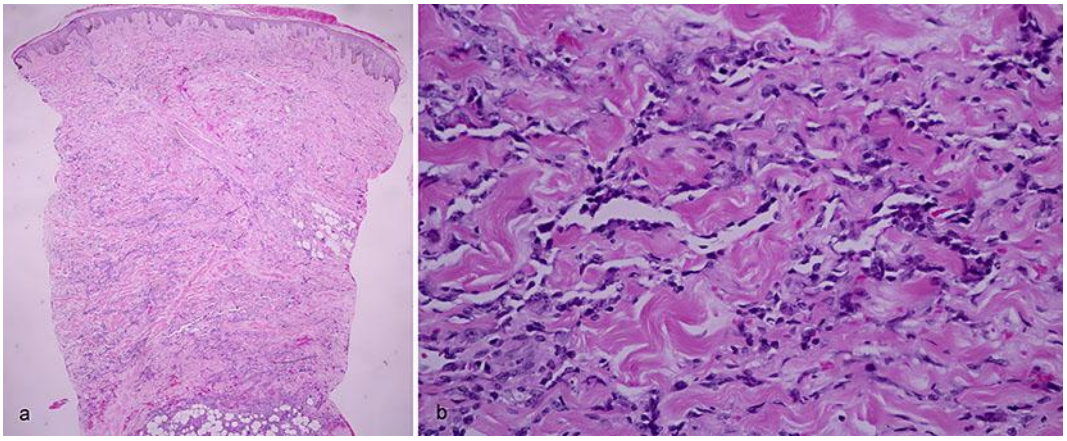

Fig. 2. **a** Poorly circumscribed dermal tumours extending to the subcutaneous tissue. Haematoxylin and eosin, original magnification ×40. **b** Atypical cells with little mitosis, some forming irregular dissecting anastomosing lumen. Haematoxylin and eosin, original magnification ×600.