Papules arising after radiotherapy for rhabdomyosarcoma

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SUMMARY

Radiation therapy, even at low doses, can induce a wide spectrum of vascular skin proliferations ranging from nonmalignant ones, such as benign lymphangiomatous papules (BLAP), to frankly malignant pathologies, such as angiosarcoma. We describe a 50-year-old Caucasian woman with a past history of uterine rhabdomyosarcoma, treated 22 years prior with surgical excision, chemotherapy, and radiotherapy. She presented with a few skin-colored papules and a clear discharge located in the previously irradiated area (right inguinal region). Histopathology showed a proliferation of irregular, interanastomosing vascular channels, thin walled and lined by prominent endothelial cells with focally hobnail features. Cytological atypia of endothelial cells, mitotic figures, hemorrhagic areas, and necrosis were not observed. The endothelial cells expressed D2-40 and CD31. A diagnosis of BLAP following radiotherapy for uterine rhabdomyosarcoma was made. The patient was treated with complete excision using electrodessication. At the 20-month follow-up visit the patient was still free of recurrence.

KEY WORDS

benign lymphangiomatous papules, radiotherapy, atypical vascular proliferation, rhabdom yosarcoma

Introduction

Recently, attention has been drawn to the onset of post-radiotherapy skin lesions. Radiation therapy, even at low doses, can induce a wide spectrum of vascular skin proliferations from benign to frankly malignant pathologies, such as cutaneous angiosarcoma (1). In 1994 Fineberg and Rosen documented some postradiation vascular lesions that were atypical but not really malignant, calling the vascular proliferations that were assumed to be benign "atypical vascular lesions" (AVL) (2, 3). Subsequently, in 199 Diaz-Cascajo et al. and in 2002 Requena et al. confirmed these results and the term "benign lymphangiomatous papules" (BLAP) after radiotherapy was proposed to designate these lesions (4, 5). Over the past 20 years, various terminology has been assigned to this entity, including acquired lymphangiectasis, acquired (progressive) lymphangioma, lymphangioma circumscriptum, and benign lymphangioendothelioma (1). Postradiation-associated vascular lesions seem to be part of a spectrum starting from BLAP with a benign course and finishing with an-

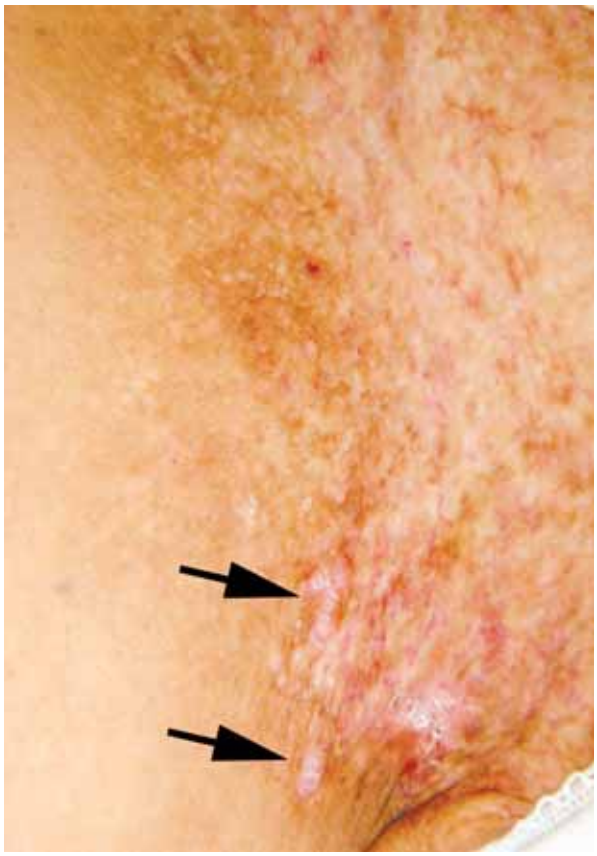

Figure 1. Close-up of the papules (arrows), surrounded by hypopigmented scleroatrophic skin.

giosarcoma (AS), a very aggressive cutaneous tumor with a high metastatic rate and a poor 5-year survival rate of only approximately 10% (1, 2, 6–11).

We describe a case of BLAP associated with uterine rhabdomyosarcoma that developed 22 years post-treatment.

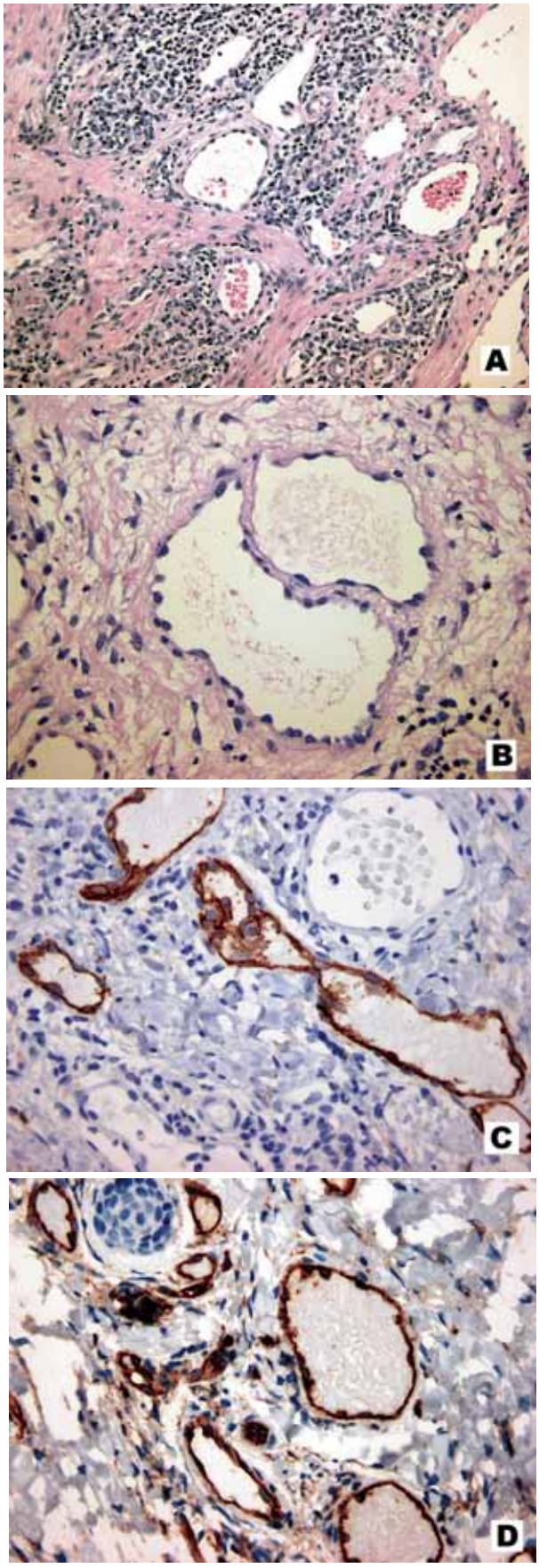

Figure 2. a: Proliferation of irregular interanastomosing vascular channels of various diameters surrounded by an inflammatory cell infiltrate composed of lymphohistiocytes and plasma cells (hematoxylin and eosin; original magnification ×100). b: Thin-walled hobnailed endothelial cells containing eosinophilic proteinaceous substance (hematoxylin and eosin; original magnification ×200). c: Positive staining for D2-40 (original magnification ×200). d: Positive staining for CD31 (original magnification ×200).

Case report

In October 2005 we examined a 50-year-old Caucasian woman with a past history of uterine rhabdomyosarcoma, diagnosed in 1983 and treated with wide surgical excision, chemotherapy, and radiotherapy (cumulative dose unknown). In 2003 she noticed the onset of skin-colored papules with a clear discharge, located on the previously irradiated area (right inguinal region). Physical examination revealed a few circumscribed, tender, skin-colored to erythematous papules almost resembling vesicles, approximately 3 to 8 mm in diameter, located on top of hypopigmented, scleroatrophic skin that corresponded to the previously irradiated area (Figure 1). We performed a shave biopsy of one of the multiple dome-shaped lesions.

Histopathologic examination showed a dome-shaped exophytic lesion projecting over the skin surface. Epidermal hyperplasia with focal parakeratosis was observed. A proliferation of irregular, interanastomosing vascular channels of various diameters was seen in the upper and mid-dermis (Figure 2a). The dilated vessels were thin-walled, lined by prominent endothelial cells with plump monomorphous hyperchromatic nuclei and with focally hobnail features. Some vessels contained an eosinophilic proteinaceous substance resembling lymph (Figure 2b). An increased number of fibroblasts in the stroma and a conspicuous inflammatory cell infiltrate, consisting of lymphohistiocytes and plasma cells surrounding the vascular proliferation, were evident. Cytological atypia of endothelial cells, mitotic figures, hemorrhagic areas, and necrosis were not observed. The endothelial cells expressed CD31 and D2-40 (Figures 2c and 2d). On the basis of clinical, histopathological, and immunohistochemical findings, a diagnosis of postradiation BLAP was made. A complete excision of the all remaining lesions was performed by electrodessication. During the follow-up visit at month 20, no recurrence was observed.

Discussion

BLAP represents a benign lymphatic vessel proliferation, seen after a variable latency period ranging from 6 months to 30 years after radiotherapy and characterized by rare relapses after local excision, and a typically asymptomatic course (1–11). Over the past 20 years, various terms have been assigned to this entity, including acquired (progressive) lymphangioma, lymphangioma circumscriptum, and benign lymphangioendothelioma (1). BLAP has been described in females that have undergone radiotherapy, most often as treatment for breast cancer (more than 50 cases reported in the literature); only a few cases have been associated with other neoplastic disorders (1–11). Our case is unusual because of the location (inguinal region) and the associated neoplasia (uterine rhabdomyosarcoma). BLAP presents as solitary or few papules or vesicles, skin-colored or slightly erythematous, with a diameter usually less than 5 mm, arising typically within the previously irradiated field (1–11). Histology discloses a wedge-shaped lesion composed of dilated vascular spaces located in the upper part of the dermis. Vessels are lined by endothelial cells with plump oval or flattened nuclei. Focally, endothelial cells may protrude into the lumen composing a hobnail pattern. Mitoses are not found and the stroma contains a moderately dense lymphohistiocytic infiltrate with plasma cells. The endothelial cells stain for CD31, CD34, and D2-40 (1–11). BLAP pathogenesis is unknown. Some authors hypothesize that BLAP are dilatations of the existing lymphatic ducts as a result of the disruption of the lymphatic flow produced by scarring after surgery or radiotherapy (3). Other authors believe that BLAP are reactive proliferations of lymphatic vessels induced by the tissue damage to the endothelial cells of lymph vessels provoked by mechanical damage from either surgery or radiotherapy (6).

Postradiation-associated vascular proliferation represents a well-documented complication following radiation exposure. They comprise a spectrum of vascular lesions given various labels including AVL, BLAP, lymphangioma circumscriptum, acquired lymphangioma, benign lymphangioendothelioma (acquired progressive lymphangioma), and AS (1, 6, 11). The lesions on the benign side of the spectrum show overlapping features among themselves and with well-differentiated AS, and at least some represent different names for the same entity. The development of cutaneous AS in the setting of radiation therapy has been well described in the literature (1, 6, 11).

The main differential diagnosis of BLAP is with postradiation cutaneous AS, which clinically appears as single or multiple indurated plaques, papules, or nodules associated with swelling and ecchymosis. Microscopically, BLAP and cutaneous AS share overlapping features but findings of cutaneous AS not seen in BLAP include irregular growth, hemorrhagic areas, significant cellular atypia of endothelial cells together with prominent nucleoli and increased mitotic activity, infiltration and destruction of cutaneous adnexa, solid areas of neoplastic endothelial cells, and necrosis. Features of BLAP absent in AS are relative circumscription, vertical wedge-shaped growth, monomorphous nuclei of endothelial cells with small or no nucleoli, and absence of mitotic features (1, 6, 8, 11). Recently, Mattoch et al. reported a series of 11 cases of post-radiotherapy vascular proliferations and found no unequivocal clinical or histologic criteria to differentiate the benign lesions from AS (11). Indeed, these entities are on a continuum (11). These authors propose the definition of AVL for lesions that can be entirely visualized and that meet the criteria of

Fineberg and Rosen (2, 6, 11). Otherwise, a nonspecific term such as "atypical vascular proliferation" should be used (11). The clinical and histological overlap between benign and malignant post-radiotherapy vascular proliferations poses such a clinical management risk that, until the clinical behavior of these lesions is more certain, all patients should undergo a complete excision with close clinical follow-up and biopsy of any newer lesion. Our patient was treated with complete excision using electrodessication. At 20 months after the last follow-up visit the patient is still free of recurrence.

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