Case Report

Concurrent diagnosis of vulvar angiokeratoma with recurrent squamous cell carcinoma after radical vulvectomy and radiation therapy

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Introduction

Angiokeratomas are uncommon benign vascular lesions diagnosed more often in males than females (Schiller and Itin, 1996). While the overall prevalence of angiokeratomas has been documented as 0.16% (Naranjo-Sintes et al., 1988), the actual incidence of vulvar angiokeratoma in the population at large is unknown (Wilkinson and Stone, 2008), with less than 50 cases last reported as of 2002 (Haidopoulos et al., 2002).

Herein, we report the case of a patient diagnosed with both vulvar angiokeratoma and squamous cell carcinoma in situ after being treated with radical vulvectomy and adjuvant radiation therapy for invasive squamous cell carcinoma of the vulva eleven years prior. To our knowledge, this is the first case involving concurrent diagnosis of angiokeratoma with a malignant lesion, and only the third documented case in the literature of vulvar angiokeratoma occurring after staging surgery and radiation therapy.

Case report

The patient is a 50-year-old Caucasian woman gravida 2, para 2 with a history of invasive squamous cell carcinoma of the vulva, which was adequately treated with radical vulvectomy, inguinofemoral lymphadenectomy, and adjuvant external radiation therapy. Subsequently, the patient developed bullous lesions on the vulvar region necessitating surgical removal of the tip of the clitoris and other vulvar skin. Even after complete post-operative healing, she continued to experience persistent discomfort, pruritis, and intermittent bleeding. Mere contact of the affected area with her underwear resulted in constant irritation and chronic infections. Repeated episodes of cellulitis often required hospitalization for intravenous antibiotic treatment.

Progressive worsening of symptoms and extension of the involved area brought the patient to the office in psychological and emotional distress. Examination revealed bilateral, microcystic lesions of the vulvar region. A red, firm, neoplastic-appearing, verrucous lesion involved most of the left side and measured approximately 30 mm in width and 40 mm in length. Other firm, thickened areas were also appreciated, but appeared to be more consistent with scar tissue from the initial staging surgery (Fig. 1). Biopsy of the solid lesion on the left vulvar region was performed which returned a diagnosis of angiokeratoma.

Prior radical vulvectomy left the bony structures of the pelvis covered only by skin and a thin subcutaneous layer which made simple activities such as sitting very uncomfortable for the patient. Sexual intercourse was also painful due to scarring and stenosis of the vaginal introitus. After considering the anatomic distortion and extensive involvement of the lesions, the decision was made to proceed with a bilateral, wide local excisional procedure followed by reconstruction of the acquired defect with gracilis myocutaneous flaps.

The pathology report included descriptions of the left vulvar specimen with multi-focal angiokeratoma involvement, and the right vulvar specimen containing both angiokeratoma and squamous cell carcinoma in situ with negative margins (Figs. 2, 3).

Discussion

Vulvar angiokeratomas usually affect women in their reproductive years up to age 50 (Nomelini et al., 2010), but most commonly between ages 20 and 40 years (Kontogianni-Katsaros et al., 2006). Primarily located on the labia majora, and more rarely on the clitoris, vulvar angiokeratomas may appear as solitary or multiple, unilateral or bilateral lesions, however most are multiple, unilateral, and located on the left side of the vulva (Kontogianni-Katsaros et al., 2006). Lesions usually range in size from 2 to 20 mm (Novick, 1985), with the majority measuring less than 1 cm in diameter (Kontogianni-Katsaros et al., 2006). These benign vascular tumors may have a smooth, papular,
nodular, lobulated, or verrucous morphology (Cohen et al., 1989), with colors varying from violet, red, brown, blue-black, and gray (Smith et al., 2004). They usually present as bright red in the early stages and progress to a bluish, brown or black appearance as the lesions enlarge and age (Clark and Wheelock, 1988).

Proposed mechanisms responsible for the development of angio-keratomas include primary degeneration of the vascular elastic tissue, increased venous pressure with consequent destruction of elastic fibers, local injury to papillary capillaries resulting in overdistention, and chronic inflammation causing phlebectasia (Smith et al., 2004). Histologic characteristics include papillomatosis, vascular dilatation in the papillary dermis, and secondary epithelial proliferation causing acanthosis and hyperkeratosis (Cohen et al., 1989; Smith et al., 2004).

Almost two-thirds of the women with angiokeratomas are asymptomatic (Cohen et al., 1989), but symptoms may include intermittent bleeding, vulvar pruritis, pain, and discomfort (Smith et al., 2004). A review of the literature showed that symptomatic patients sought medical attention sooner (Cohen et al., 1989), resulting in earlier work-up, diagnosis and treatment. It is possible that the largely asymptomatic nature and often benign appearance of angiokeratomas might help to explain the low documented incidence of this benign vascular tumor if we consider that there might be missed diagnoses and under-reporting due to lack of biopsy-proven confirmation.

Given that the gross appearance and clinical presentation of these benign lesions can vary widely among patients, proper diagnosis is often extremely difficult. The long list of differentials includes both benign and malignant conditions, thus emphasizing the importance of excisional biopsy and histological examination. Treatment is diagnosis-dependent and can range from conservative management such as reassurance with close monitoring and follow-up to more aggressive approaches including vulvectomy, chemotherapy and radiation. Definitive and accurate diagnosis is therefore imperative in differentiating neoplastic from non-neoplastic lesions and ensuring appropriate management.

Conditions presumed to be associated with angiokeratomas include pregnancy, post-hysterectomy, acute suppurrative Bartholinitis, chronic inflammation, hemorrhoids, and vulvar varicosities (Cohen et al., 1989). Two cases have been reported of vulvar angiokeratomas developing after staging laparotomy and radiation therapy for neoplastic processes (Haidopoulos et al., 2002; Smith et al., 2004). Our patient did not have a prior laparotomy, but radical vulvectomy could similarly cause increased

Fig. 1. Photograph of vulva with gross pre-operative lesions.

Fig. 2. Angiokeratoma with dilated vascular spaces in the superficial dermis and keratotic epidermal surface.

Fig. 3. Squamous carcinoma in situ; arrow indicates mitosis in upper epidermis.
venous pressure and secondary vascular dilatation. Also, chronic inflammation due to repeated episodes of vulvar cellulitis, radiation-induced damage to venous blood vessels, and compromised blood return with increasing venous blood pressure are all factors known to contribute to the development of angiokeratomas (Smith et al., 2004).

Although this is the third documented case of vulvar angiokeratoma occurring after surgical staging and radiation therapy, it is the only one not involving prior laparotomy and including concomitant benign and malignant diagnoses. This patient's history, presentation, diagnosis and treatment are all somewhat atypical. Vulvar angiokeratoma should be considered when presented with vulvar lesions, especially if given a history of conditions that may cause degeneration of perivascular elastic tissue and increased venous pressure and dilatation. Given the unanticipated finding of both angiokeratoma and recurrent squamous cell carcinoma in our patient, we wish to reemphasize the importance of single or multiple biopsies when assessing and diagnosing vulvar lesions.

Two years after this procedure, the patient reported vaginal bleeding. Pelvic ultrasound was performed and revealed a markedly thickened, inhomogeneous endometrium measuring 2 cm. Endometrial biopsy diagnosed carcinosarcoma (malignant mixed mesodermal tumor). The patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and abdominal washings. Surgical pathology returned Stage III carcinosarcoma with the tumor confined to the uterus, however washings were positive.

**Ethical consent**

Consent was obtained from the patient to publish this report.

**Conflict of interest statement**

The authors declare that there are no conflicts of interest.

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**References**