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Acquired lymphangiectasia ('lymphangioma circumscriptum') of the vulva: a report of eight cases

C. J. R. STEWART*, T. CHAN* AND M. PLATTEN†

*Department of Histopathology, King Edward Memorial Hospital, Perth, Western Australia, and †Divison of Anatomical Pathology, PathWest, The Sir Charles Gairdner Hospital, Perth, Western Australia

Summary

Aims: To present the clinico-pathological findings of eight cases of acquired vulval lymphangiectasia (AVL) with discussion of the terminology and differential diagnosis.

Methods: Vulvectomy or biopsy specimens from eight patients with AVL were reviewed. All patients had undergone surgery, lymphadenectomy and/or radiotherapy, most commonly for carcinoma of the cervix, up to 26 years prior to presentation with the lymphangiectatic lesions. Immunohistochemistry for CD31, CD34, D2-40, p53 and p16 was performed in each case.

Results: The original clinical and pathological diagnoses were most frequently 'lymphangioma circumscriptum' but viral infection was considered in some cases. All specimens showed dermal lymphangiectasia associated with marked reactive epidermal hyperplasia. The lymphatic endothelial cells showed CD31 and D2-40 expression but CD34 was negative. The keratinocytes showed focal p53 immunoreactivity in four cases.

Conclusions: AVL is the preferred nomenclature for the lesions presented herein. The clinical and histological features usually are characteristic but the differential diagnosis may include condyloma and differentiated type vulval intraepithelial neoplasia (VIN). Immunohistochemistry may be helpful but lack of CD34 expression should be noted and may prove useful in the differential diagnosis of other vulval vascular lesions. Focal p53 protein immunoreactivity should not be considered indicative of differentiated type VIN in this clinical setting.

Key words: Vulva, lymphangiectasia, lymphangioma.

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INTRODUCTION

Acquired or secondary lymphangiectasia of the vulva, sometimes referred to as lymphangioma circumscriptum or acquired lympangioma, is a rare long term complication of pelvic lymphatic obstruction.[1,2] Most commonly this follows surgery, lymphadenectomy and/or radiotherapy for carcinoma of the cervix but it may also occur after treatment of other tumours or result from lymphatic damage due to non-neoplastic conditions such as Crohn's disease or tuberculosis. The most characteristic clinical presentation is of multiple small raised bleb-like lesions ('frog spawn-like') that may ooze watery fluid, and there may be co-existent lymphoedema extending on to the adjacent abdominal or thigh skin. Some cases are complicated by recurrent infection. Reactive epidermal changes frequently occur and in some cases these are sufficiently florid to mask the underlying vascular abnormality. Thus, acquired vulval lymphangiectasia (AVL) can mimic human papillomavirus (HPV)-related condyloma, other viral or fungal infections, or specific dermatoses such as dermatitis herpertiformis.[3–5] Accurate diagnosis may also be hampered by the significant time interval between the initial disease process or treatment that caused the lymphatic damage and the presentation with AVL, so that details of the clinical history may be unavailable. Similarly, interpretation of the associated histological changes may be problematic when the clinical details are incomplete or if small and superficial biopsies lacking the characteristic vascular changes are submitted.

Descriptions of AVL are mainly restricted to clinical case studies and few reports have considered the potential differential diagnosis on microscopic examination.[6–14] Furthermore the nomenclature of lymphatic vascular lesions involving the vulva is confusing since different and partly overlapping classifications have been used. In this study we present a single centre experience of eight cases of AVL encountered over a 15-year period and discuss the terminology and pathological findings.

MATERIALS AND METHODS

The files of the Histopathology Department of King Edward Memorial Hospital, Perth, Western Australia, were searched for vulval lesions encoded as lymphangioma, lymphangioma circumscriptum or lymphangiectasia between January 1993 and December 2007. Eight cases fulfilling criteria for AVL where there was previously documented iatrogenic interference with pelvic lymphatic drainage were identified during this period. The clinical data including patient age, distribution of skin lesions, presence of associated lymphoedema, and presumptive diagnoses were obtained from the pathology request forms and/or from the case records. The cause of the lymphatic obstruction including any previous pelvic surgery, lymphadenectomy and/or radiotherapy was noted and the interval to presentation with the vulval skin lesions was documented. The initial histopathology diagnoses were also recorded.

All slides were reviewed and the following epidermal changes were noted: polypoid or papillomatous architecture, surface hyperkeratosis and/or parakeratosis, ulceration, spongiosis, acanthosis and pseudoepitheliomatous hyperplasia, deep (premature) keratinocyte maturation, nuclear atypia and associated inflammation. Changes noted within the dermis included the distribution and calibre of the dilated lymphatic channels (present by definition), and any associated fibrosis or

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inflammation. The presence of abnormal vessels within the subcutaneous tissue was also noted in those specimens that included deeper tissue.

Immunohistochemistry

One representative block from each case was examined using an auto-immunostainer (Benchmark XT; Ventana Medical Sytems, USA) with the following primary antisera: CD31 (dilution 1:150), CD34 (1:200), D2-40 (1:40), p16 (1:20) and p53 (1:2400). The CD31 and p53 antibodies were obtained from Dako (Australia), CD34 and p16 from Novocastra (UK) and D2-40 from Jomar Diagnostics (Australia). Each staining batch included appropriate positive and negative controls (omission of primary antiserum). All specimens also included internal positive controls for the vascular endothelial markers (normal vessels).

RESULTS

The clinical data are summarised in Table 1. The mean age at first presentation with AVL was 48.6 years (range 39–63 years). Six patients had a history of cervical carcinoma while one case each followed treatment for vulval carcinoma and cutaneous malignant melanoma. Most patients had undergone a combination of surgery, lymphadenectomy and post-operative radiotherapy. The mean interval between treatment of the initial neoplastic process and the first presentation with AVL was 11.6 years (range 7–26 years). Six patients had recurrent vulval lesions that were biopsied on between two and five occasions. In five cases wide local excision including partial vulvectomy was performed and the specimens ranged from 60 to 135 mm in greatest dimension, while three patients underwent only small excisional biopsies or punch biopsies. The presumptive clinical diagnosis provided with the specimens was most frequently lymphangioma circumscriptum or vulval oedema but the possibility of viral infection was raised in three cases (condyloma in two cases and molluscum contagiosum in one case). The pathological findings were usually reported as lymphangioma circumscriptum, lymphangiectasia and/or lymphatic cyst while the epidermal changes were interpreted variably as reactive hyperplasia, lichen simplex chronicus or, in two cases, squamous papilloma. None of the biopsies in this series was considered to represent a malignant process.

Macroscopic examination of the larger resection specimens showed focal to diffuse verrucous and polypoid skin changes usually separated by areas of normal appearing skin (Fig. 1). Ulcers up to 5 mm in diameter were recognised in two cases. Histologically, all specimens showed markedly dilated superficial dermal vessels associated with epidermal hyperplasia that corresponded to the exophytic macroscopic appearances (Fig. 2a). The epidermis showed hyperkeratosis, parakeratosis and irregular elongation of rete pegs that were often attenuated and appeared to branch and anastomose around the dilated dermal vessels (Fig. 2b). Two of the biopsies showed focal papillomatous epidermal changes (Fig. 3a). Spongiosis was commonly observed and the keratinocytes exhibited enlarged vesicular nuclei with prominent nucleoli. Cells with abundant eosinophilic cytoplasm were evident close to the basal layer in a few cases but there was only mild nuclear enlargement and atypia (Fig. 3b). HPV-associated changes including koilocytosis and multinucleation were not seen. Mitotic figures were infrequent and confined to the basal and parabasal zones. Superficial ulceration was identified in four specimens and appeared multifocal in distribution. Periodic acid-Schiff with diastase (PASD) stain for fungal organisms was negative in the three cases in which it was performed. The dilated lymphatics were of variable calibre and showed uneven distribution along the dermis with interspersed relatively normal areas. The most superficial vessels abutted the base of the epidermis and in

TABLE 1 Summary of previous history and original clinical and pathology diagnoses in eight cases of acquired lymphangiectasia of the vulva

Case (age, years)*	Previous tumour	Previous therapy			Interval (years)†	Clinical diagnosis	Other findings	Original pathology diagnosis
		SUR	RT	LND				
1 (58)	Stage 2A CA cervix	N	Y	N	26–32	'Vulval lump', ? molluscum contagiosum	CA clitoris age 50 and VAIN 3 age 63	Lymphatic cyst, squamous hyperplasia, lymphangiectasia
2 (44)	CA vulva	Y	Y	Y	16,22	? condyloma and papilloma	Bilateral leg oedema	Squamous papilloma, seborrhoeic keratoses, LC
3 (39)	Stage 1B CA cervix	Y	Y	Y	9,22,26	Warts, 'nodular lymphangioma', LC	Cellulitis, bilateral leg oedema, endometriosis	Squamous papilloma, lymphangiectasia, dermal fibrosis
4 (47)	Stage 1B CA cervix	Y	Y	Y	7,20	Chronic oedema	DCIS breast	Lymphoedema, lymphangiectasia, epidermal hyperplasia
5 (63)	Melanoma	Y	NK	Y	NK	? lymphatic obstruction	Recurrent vulval itch and oedema	Lichen simplex chronicus, lymphangiectasia
6 (39)	CA cervix	Y	Y	Y	9	Angiokeratoma	Bilateral leg oedema, cellulitis	LC
7 (50)	Stage 1B CA cervix	Y	Y	Y	7,14	LC	Watery vulval discharge	LC
8 (49)	CA cervix	Y	Y	Y	7,13	LC	Left leg oedema, cellulitis	LC

*Age at first presentation with AVL.
†Interval from tumour treatment to presentation with AVL.
CA, carcinoma; DCIS, ductal carcinoma *in situ*; LC, lymphangioma circumscriptum; LND, lymph node dissection; N, no; NK, not known; RT, radiotherapy; SUR, surgery; VAIN, vaginal intraepithelial neoplasia; Y, yes.