

Lymphangioma Circumscriptum of the Vulva in a Patient With Noonan Syndrome

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Practice Points

- Lymphatic malformations such as lymphedema and cystic hygroma are not uncommonly observed in patients with Noonan syndrome; there are rare reports of cutaneous lymphangioma in this population.
- Lymphangioma circumscriptum of the vulva should be considered when patients with Noonan syndrome present with grouped vesicular lesions in the vulvar region characterized by erythema, swelling, and/or drainage.
- The mainstay of treatment of lymphangioma circumscriptum of the vulva includes complete surgical resection of superficial lesions and deep communicating lymphatics.

Lymphangioma circumscriptum (LC) results from the development of abnormal lymphatic vasculature and is characterized by the presence of grouped vesicles filled with clear or colored fluid. Vulvar localization is uncommon. Abnormalities of the lymphatic system, such as lymphedema and cystic hygroma, are well-known features of genetic disorders such as Noonan syndrome (NS) and Turner syndrome. We report the case of a patient with NS who presented with LC of the vulva. We also discuss the expanding spectrum of clinical anomalies associated with the presentation of NS.

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The clinical manifestations of Noonan syndrome (NS) are seen in multiple organ systems and include cardiovascular, musculoskeletal, genitourinary, dermatologic, and gastrointestinal findings. Patients with NS may present with a wide range of features including ptosis of the eyelids, ocular hypertelorism, epicanthus, pterygium colli, undescended testicles in men, short stature, pectus excavatum or pectus carinatum, congenital heart defects, cubitus valgus, low-set ears, mental retardation, micrognathia, lymphedema, and cystic hygroma.^{1,2} Lymphatic dysplasia has been reported in up to 20% of patients with NS, with the most common presentation being lymphedema.¹ Although the association of NS with lymphedema and cystic hygroma have been well described, the finding of cutaneous lymphangioma in NS is rare.

We present a patient with NS who developed the uncommon finding of classic lymphangioma circumscriptum (LC) of the vulva. Due to the extensive nature of the vascular abnormalities in this case, the patient underwent surgical resection of the lesions.

Case Report

A 30-year-old woman presented to the dermatology clinic with vascular lesions on the vulva that had been present for several years. Although

the lesions remained unchanged in size, they had become increasingly bothersome due to persistent oozing and subsequently had negative effects on the patient's quality of life. Her primary concerns were the appearance of the lesions, pruritus, and weeping discharge from the affected area. The patient previously was referred to the urology department and then laser therapy for the lesion was attempted with minimal benefit. She also had been evaluated by a gynecologist who proposed an initial diagnosis of vulvar angiokeratoma and suggested surgical treatment.

The patient's medical history included NS, a heart murmur, and narrow-angle glaucoma. No

other concerns aside from cutaneous findings were elicited during a review of systems. Physical examination revealed erythema and swelling with a pink mammillated surface on the bilateral labia majora accompanied by a clear, yellow, lymphlike discharge. The lesions did not extend to the introitus but demonstrated substantial involvement of the bilateral vulvar tissue.

The patient was referred to the gynecology department for diagnostic hysteroscopy, dilation and curettage, vaginoscopy, and bilateral vulvectomy. Two weeks following surgery, dramatic improvement of the vulvar lesions was noted, with some edema of the genital region as well as residual scattered red and clear vesicular lesions of LC (Figure 1). A microscopic analysis of surgical specimens performed by a board-certified pathologist (R.T.C.) revealed superficial and deep infiltrative growth of irregularly outlined lymphatic channels that did not closely border the overlying epithelial basement membrane, resulting in the presence of a prominent grenz zone (Figure 2). On immunohistochemical evaluation of sections of the left labium majus, lymphatic channels and endothelial vasculature stained positive with CD31 (platelet-endothelial cell adhesion molecule), which stained both lymphatic and blood vessel endothelium as well as a subset of tissue macrophages (Figure 3A). A number of vascular channels stained positive with D2-40, a marker that is relatively



Figure 1. Edema and scattered red and clear vesicular lesions 2 weeks following bilateral vulvectomy for treatment of lymphangioma circumscriptum of the vulva.

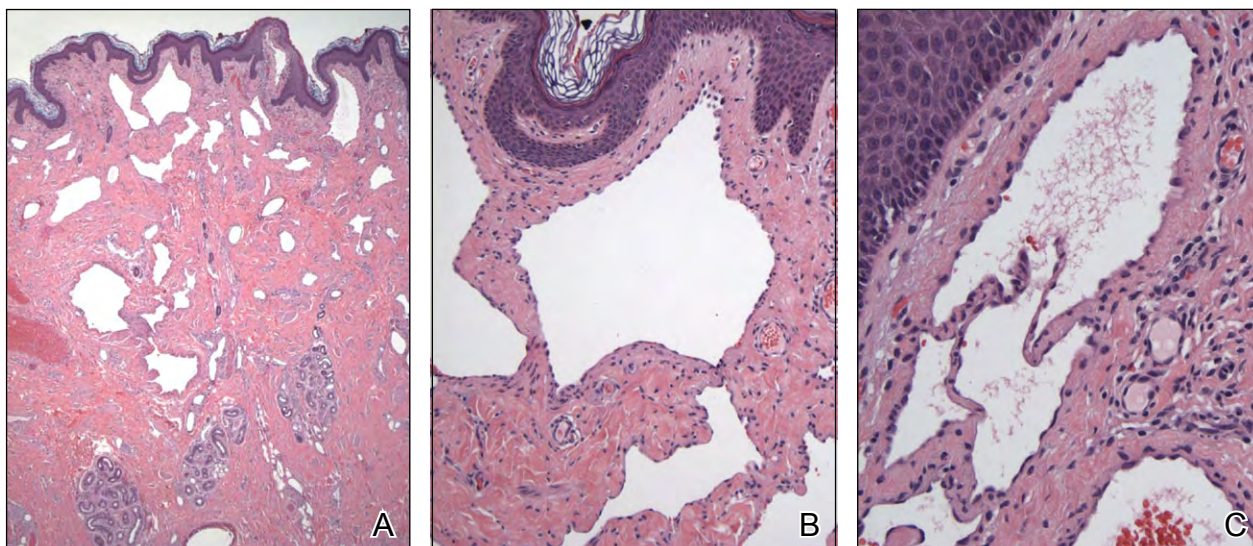


Figure 2. A tissue section from the left labium majus revealed superficial and deep dilated vascular channels with increased density in the superficial dermis beneath a mildly papillomatous epidermis (A)(H&E, original magnification $\times 2$); ectatically dilated, endothelial-lined vascular spaces separated from an overlying basement membrane zone by an intervening grenz zone (B)(H&E, original magnification $\times 10$); and dilated endothelial-lined vascular channels with intraluminal eosinophilic lymph in the lumen. Intraluminal valves were seen in the centrally located lymphatic vessel (C)(H&E, original magnification $\times 20$).

specific for lymphatic endothelium. The endothelial lining of adjacent capillaries demonstrated negative staining for D2-40 (Figure 3B). Histopathologically, these results were consistent with the diagnosis of LC of the vulva.

Comment

Lymphangiomas previously have been classified as superficial and deep lesions, with LC comprising the superficial group and cavernous lymphangiomas and cystic hygromas classified in the deep group. Lymphangioma circumscriptum generally presents as cutaneous vesicles ranging in color from pink to black depending on the amount of blood intermixed with the clear lymph fluid.³ In 1970, Peachey et al⁴ reviewed and characterized lesions in 65 patients with cutaneous LC. The 2 most commonly described variants of cutaneous LC are classic and localized LC. Classic LC generally is characterized by extensive lesions with affected areas of skin greater than 1 cm². The lesions tend to be concentrated over the proximal regions of limbs and adjacent to limb girdles; however, they can be found on almost any area of the body.⁴ Localized LC presents as single discrete lesions of vesicles comprising an area of less than 1 cm². Lesions do not consistently present in any particular areas of the body but tend to be absent from regions where classic LC is seen.⁴

The differential diagnosis of LC of the vulva should include condyloma acuminatum, herpes zoster, molluscum contagiosum, angiomyofibroma, and angiomyxoma. Lymphangioma circumscriptum of the vulva may be congenital or acquired and is

an uncommon finding. Vlastos et al⁵ reported only 11 cases of congenital LC of the vulva and 22 acquired cases. There have been additional reports of acquired LC of the vulva.⁶⁻¹³

Prior reports of lymphatic dysplasia associated with NS include the presence of cystic hygroma, lymphedema, intestinal lymphangiectasia, pulmonary lymphangiectasia, and facial cutaneous lymphangioma in NS.¹⁴⁻¹⁶ Our case provides additional evidence that the characteristic phenotypes involving lymphatic dysplasia in NS may be broadened to include cutaneous lymphangioma in addition to generalized lymphedema and cystic hygroma.

Management considerations for LC involve cosmetic effects, pain, swelling, persistent lymph fluid and blood leakage, and continued recurrence of infections.¹⁷ The mainstay of treatment of LC is surgical resection of the lesion with radical vulvectomy demonstrating the lowest recurrence rate following treatment of LC of the vulva.¹⁸ Complete surgical resection also should include excision of deep communicating lymphatics. Additional therapeutic options include abrasive therapy, sclerotherapy, and electrocoagulation; however, these methods commonly result in recurrence if the entire lesion and deep communicating system have not been destroyed by the treatment.¹⁸⁻²⁰

Conclusion

It is not uncommon for patients with NS to demonstrate features of lymphatic abnormalities, with lymphedema and cystic hygroma most often observed.¹ As demonstrated in this report, NS

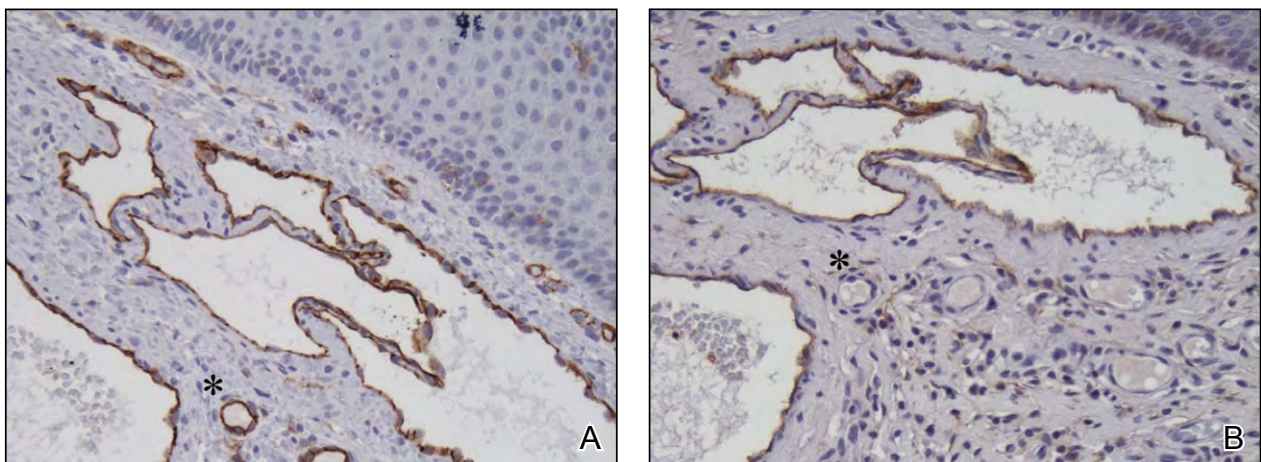


Figure 3. Immunohistochemical analysis of a tissue section from the left labium majus demonstrated positive staining for CD31 (platelet-endothelial cell adhesion molecule) and D2-40 in lymphatic channel endothelium. Numerous CD31⁺ dilated vessels, both lymphatic and endothelial vascular channels (asterisk), were seen in the superficial dermis as well as D2-40⁺ lymphatic channels (A)(original magnification $\times 20$). Adjacent capillaries (asterisk) showed negative staining for D2-40 (B)(original magnification $\times 20$).

patients also may present with cutaneous LC. Although it generally is an uncommon finding, LC of the vulva should be considered when patients with NS present with vesicular lesions in the vulvar region characterized by erythema, swelling, and/or drainage. Appropriate management of LC includes complete surgical resection of superficial lesions and deep communicating lymphatics.

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