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Unilateral swelling and hyperpigmented papules

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Abstract

Lymphangioendothelioma, also known as acquired progressive lymphangioma, is a rare vascular neoplasm of lymphatic origin. Although in light-skinned individuals lesions typically present as erythematous to violaceous papules or plaques, in dark-skinned patients lesions often appear hyperpigmented. Histopathologic distinction of lymphangioendothelioma from early Kaposi sarcoma and angiosarcoma is imperative considering the therapeutic and prognostic implications. Herein, we present a 71-year-old woman with slowly progressive hyperpigmented papules and histopathology demonstrating thin-walled vascular spaces interspersed between collagen bundles, consistent with lymphangioendothelioma. We describe the clinical and histologic findings of this rare entity and highlight histologic mimics that might result in diagnostic delay.

Keywords: acquired progressive lymphangioma, lymphangioendothelioma, skin of color

Introduction

Lymphangioendothelioma, also known as acquired progressive lymphangioma, is rare vascular anomaly of lymphatic origin with characteristic histopathologic features that needs to be distinguished from Kaposi sarcoma and well-differentiated angiosarcoma [1]. Although it typically presents as slowly progressive red-to-violaceous papules and plaques, its presentation as hyperpigmented papules or plaques in skin of color can further lead to diagnostic uncertainty in this already challenging to diagnose neoplasm. In this report, we discuss a case of benign lymphangioendothelioma in a dark-skinned patient and review clinical presentation and histopathologic mimics.

Case Synopsis

A 71-year-old woman presented for evaluation of asymmetric swelling and progressive lesions of the right thigh that started three years prior to presentation. Clinical examination revealed coalescing hyperpigmented papules on a background of woody induration of the anteromedial right thigh (**Figure 1**). There was no palpable pelvic lymphadenopathy and doppler ultrasound was negative for deep vein thrombosis. Magnetic resonance imaging of bilateral lower extremities showed abnormal enhancement throughout subcutaneous fat of the right thigh.

Punch biopsy revealed lymphatic and vascular endothelial proliferation diffusely dispersed within the full thickness of the dermis (**Figure 2**). There was no atypia of the endothelial cells identified. Endothelial cells were highlighted with D2-40 (**Figure 3**), CD31, and CD34 immunohistochemical stains. Human herpes virus-8 (HHV-8) stain was negative. The patient was diagnosed with lymphangioendothelioma. The patient was not considered a surgical candidate owing to the diffuse nature of her skin lesions.

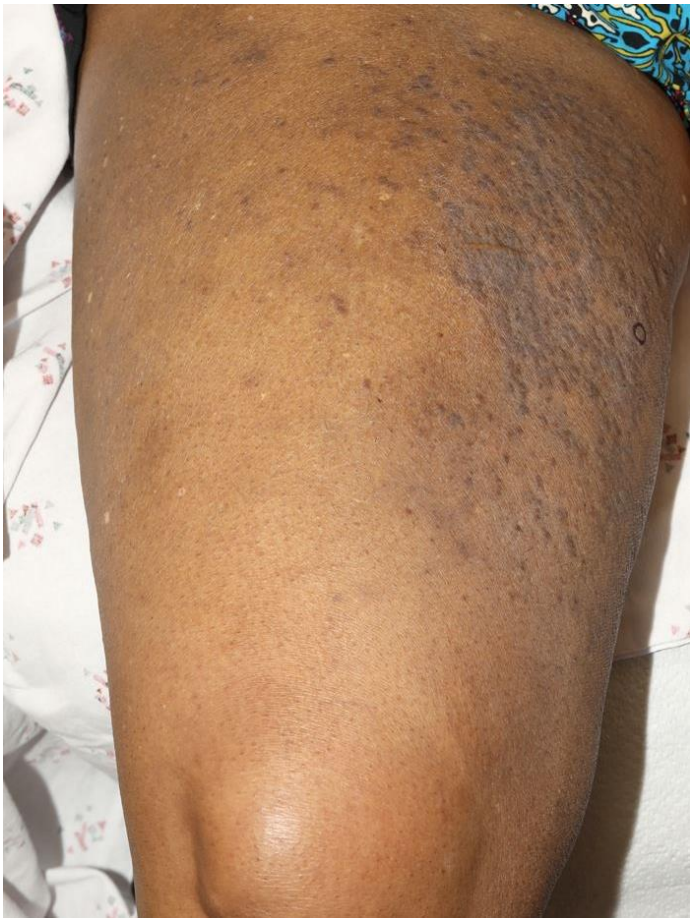

Figure 1. *Lymphangioendothelioma. Multiple, grouped 2-4mm hyperpigmented papules coalescing into a plaque on the patients' anteromedial right thigh.*

Case Discussion

First described by Jones et al. lymphangio-endothelioma, also known as acquired progressive lymphangioma, is a rare slowly progressive vascular anomaly of lymphatic origin [1]. Some reported inciting events are trauma, radiation, femoral arteriography, tick bite, and hip inflammation suggesting that lymphangioendothelioma may represent a response to inflammatory stimuli rather than a true neoplasm [2]. The development of lesions in pubescent and prepubescent patients suggest a role for a hormonal stimulus also serving as a trigger [3]. Finally, the presence of lymphatic vessels and blood vessels suggests that lymphangioendothelioma might represent a complex vascular hamartoma of both lymphatic and vascular origin.

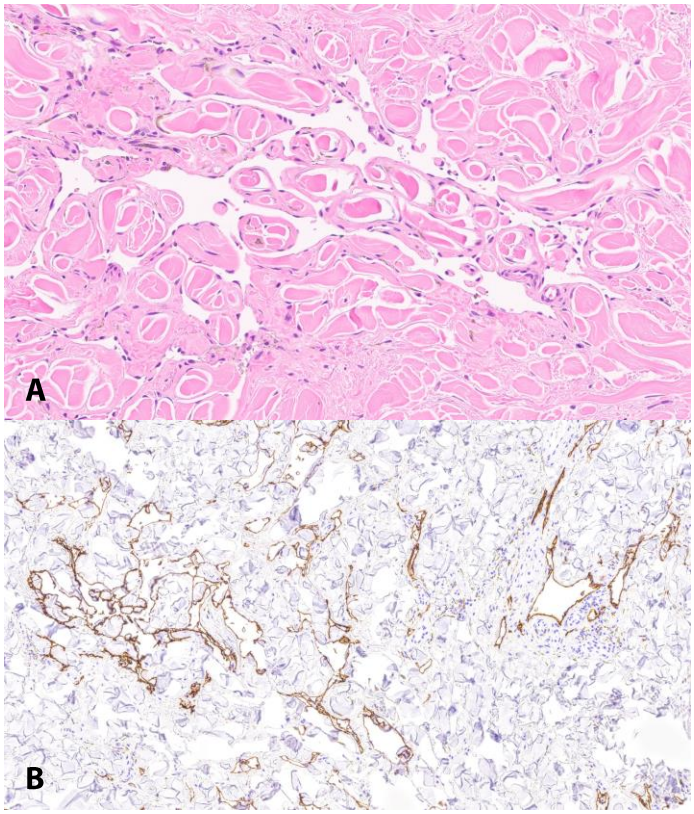

Figure 2. ***A)*** *Thin walled, endothelium lined irregular shaped dilated vascular spaces dissecting the collagen bundles in the dermis in patient with lymphangioendothelioma, H&E 200×.* ***B)*** *Irregular shaped dilated vascular spaces highlighted with D240, H&E 100×.*

In the literature, there is a reported predilection for both young and elderly individuals. Owing to its progressive nature, the reported age at diagnosis ranged from 17–90 years. Lesions may last for months to years or spontaneously regress [1,4]. two Clinically in individuals with Fitzpatrick I-IV types, lesions appear as erythematous to violaceous patches or plaques that slowly expand over time. However, in dark-skinned patients, lesions often appear hyperpigmented. The presentation of our patient's lymphangioendothelioma on the lower extremity is consistent with literature reports of the extremities as a commonly reported site of involvement. Other commonly reported locations include the head and neck.

Although the clinical appearance of lesions of lymphangioendothelioma are well characterized, histopathologic examination is required to make the diagnosis. On histopathology examination,

lymphangioendothelioma is a dermal based-infiltrative vascular proliferation comprised of thin-walled vascular spaces dissecting though collagen with no endothelial atypia or mitotic figures. Although the proliferation of irregular, thin-walled vascular spaces predominantly dissect dermal collagen bundles, these findings can extend deeper involving subcutaneous tissue and resulting in edema. In our patient the depth of the biopsy specimen did not extend into the subcutis preventing us from evaluating whether her woody edema was secondary to deeper proliferation of vascular spaces into the subcutaneous tissue. The endothelial cells are highlighted with CD31, CD34, and factor VII-related antigen, and D240 positivity supporting the lymphatic origin of the neoplasm. Smooth muscle and pericytes that may surround the vascular spaces can be highlighted with smooth muscle actin. Although lymphangioendothelioma is histologically similar to Kaposi sarcoma, it can be differentiated from Kaposi sarcoma because it lacks the dermal infiltration of lymphocytes and plasma cells [2]. In addition, this can be further supported by a negative HHV-8 stain. Although angiosarcoma may also appear histologically similar, lymphangioendothelioma lacks the cytologic atypia and prominent mitoses seen in angiosarcoma.

Although surgical excision is recommended for local disease, other therapeutic options have to be explored when surgery is not feasible due to extent of lesion involvement, as in our patient. There are no reported medical side effects of progression, but its consequence may limit treatment options. Alterative systemic agents that have been explored for the management of lymphangioendothelioma include sirolimus, pulsed-dye laser, and imiquimod treatments [5]. Sirolimus promotes normal cell development by acting on the phosphatidylinositol-3-kinase protein kinase B, the target of rapamycin. This is in keeping with growing evidence that vascular malformations may result from mutation in the rapamycin pathway. Our patient declined recommendation to initiate sirolimus because of concerns of potential side effect. Her disease remains stable one year after initial diagnosis confirming the slowly progressive nature of this vascular neoplasm.

Conclusion

We present the case of a dark-skinned woman with lymphangioendothelioma on the lower extremity, highlighting the clinical presentation and pertinent histologic features. Recognition of the clinical presentation of this rare entity in darker skin types and appropriate histologic characterization is critical to distinguishing it from other vascular histologic mimics that might result in diagnostic delay.

Potential conflicts of interest

The authors declare no conflicts of interest.

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