A poisoned cherry: Migratory cutaneous intravascular large B-cell lymphoma with subsequent systemic nodal lymphoma.

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INTRODUCTION

Cherry angiomas are the most common acquired vascular proliferation of the skin. Occurring in 75% of adults over age 75, these benign neoplasms hardly elicit anything more than cosmetic concern.[1] Yet, occasionally, these lesions may be associated with a more serious disease. Here we present a case of intravascular large B-cell lymphoma (IVLBCL) that presented in a solitary cutaneous angioma, later diffusely involving the skin and terminating as a nodal and central nervous system lymphoma.

CASE REPORT

A 76-year-old white woman presented with a newly developed 4-mm cherry-red papule on her neck. The lesion was clinically suspected to be a cherry angioma but because of its increasing size was precautionarily biopsied. Biopsy found some large cells with multiple prominent nuclei and mitotic figures in the hemangioma capillaries underlying the skin (Figs 1 and 2). Further staining identified these as abnormal large B cells, leading to a diagnosis of non-germinal center-like, IVLBCL, involving a hemangioma. Aside from the solitary skin lesion, the patient had no other signs or symptoms of lymphoma.

A comprehensive workup was undertaken. Laboratory results were within normal limits, and diagnostic imaging came back negative. Medical history and family history were deemed noncontributory. No treatment was given, and the patient was instructed to follow up biannually. At these 6-month visits, the patient continued to deny any signs or symptoms of lymphoma, with her lactic dehydrogenase and complete blood count staying within normal limits.

Abbreviations used:

IVLBCL: intravascular large B-cell lymphoma
CT: computed tomography

After two and a half years, a crop of 2- to 3-mm cherry-red angiomas appeared, this time on her right flank. Two of the lesions were biopsied with abnormal large B cells once again being seen intravascularly (Figs 3 and 4). Given the absence of any other symptoms, no treatment was initiated.

Over the course of the next 3.5 years, these crops of angiomas episodically disappeared and reappeared, migrating from her flank to her back before ultimately covering her entire body. During this period, the patient's serum monoclonal IgM-λ protein continued to be produced. However, her serum IgM was increased, serum IgA decreased, lactate hydrogenase increased, and platelet count decreased. Despite these abnormalities, no treatment was initiated due to the absence of any other symptoms.

Six years after her initial presentation, the patient was found unconscious at home. After being hospitalized, computed tomography (CT) imaging of the

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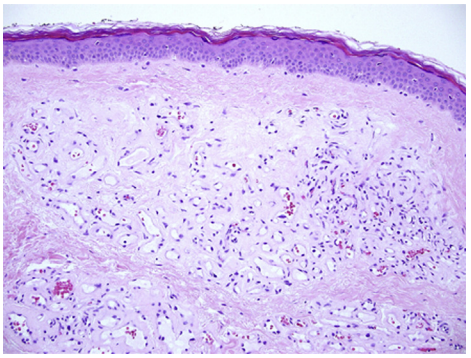

Fig 1. Lobules of capillaries in the papillary dermis. (Hematoxylin-eosin stain; original magnification: ×40.)

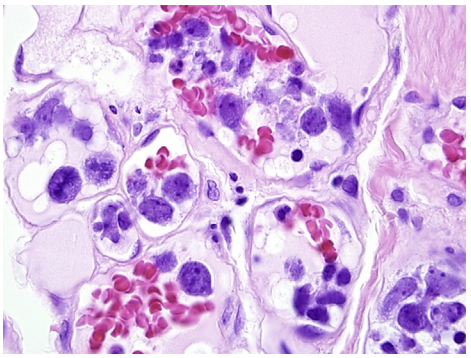

Fig 2. Large cells in the lumens of the capillaries in the reticular dermis. (Hematoxylin-eosin stain; original magnification: ×1000.)

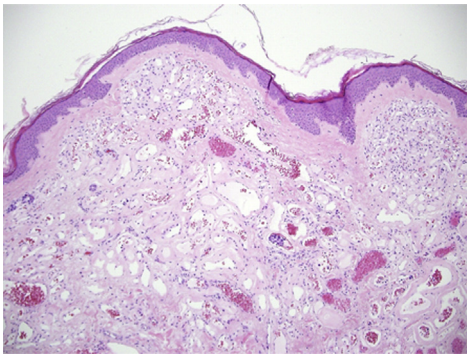

Fig 3. Lobules of capillaries in the papillary dermis and intravascular large cells in some of them (second biopsy). (Hematoxylin-eosin stain; original magnification: ×40.)

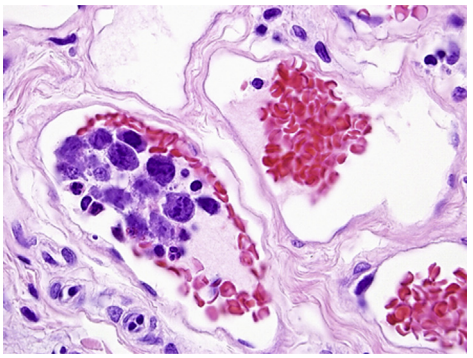

Fig 4. Intravascular large cells (second biopsy). (Hematoxylin-eosin stain; original magnification: ×1000.)

head was performed, finding possible ischemic lesions in the white matter of the brain. CT imaging of the chest and abdomen found generalized lymphadenopathy as well. The patient died 2 days later with no autopsy being performed. A postmortem diagnosis of migratory cutaneous IVLBCL with probable termination as systemic nodal lymphoma with central nervous system involvement was made.

DISCUSSION

First described by Campbell de Morgan, cherry angiomas are common cutaneous vascular papules whose prevalence increases with age.[1] They are benign neoplasms that, barring cosmetic concerns, are generally left untreated. In stark contrast, IVLBCL is a rare variant of extranodal non-Hodgkin lymphoma in which there is malignant proliferation of large B lymphocytes within the lumina of capillaries, small arteries, and veins. These lymphocytes can plug the vessels, leading to ischemia and infraction (as suspected as the cause of the ischemic changes seen in the head CT of our patient).

Although IVLBCL is known as a "mimicker of many maladies" and can manifest in multiple ways, 2 general types have been described, a Western form and an Asian variant.[2]

In the Western form, skin and neurologic involvement are common, and patients generally lack the B symptoms, pancytopenia, hemophagocytosis, and multiorgan failure associated with the Asian variant.[3] A subtype of the Western form of IVLBCL with only cutaneous symptoms at presentation, like in our case, has been described. Interestingly, it seems to occur exclusively in women and has a far better prognosis than other forms of IVLBCL.[3]

The cutaneous manifestations of IVLBCL are wide ranging, most commonly presenting as skin nodules, plaques, or macules of red or blue to livid color on the thigh, leg, and trunk.[4] A fundamental question to consider is whether IVLBCL promotes the development of these skin lesions or simply appears in them. Saurel et. al[5] demonstrated that a subset of IVLBCL cells contain angiogenic factors SPP1 and vascular endothelial growth factor perhaps allowing them to form pseudohemangiomoformative lesions.[5] Given that classical cherry angiomas do not typically regress, the disappearance and reappearance of our patient's lesions would also seem to suggest that

IVLBCL may actually induce angioma formation. We theorize that subsequent regression of the lesions is likely caused by the angiogenic lymphocytes being knocked out of the angiomas, only to create new angiomas after migrating to a different site. Recognizing the lack of sufficient evidence of this phenomenon, we hope to investigate this further.

Our case is unique for several reasons. First, although any case of IVLBCL is a rarity, those of the cutaneous variant are rarities within rarities, comprising only about 25% of all cases.[6] Second, the cutaneous variant generally occurs in younger women, with a mean age of 59 years.[6] Our patient who first presented at age 76, is thus significantly older than the mean. Third, although most cases of cutaneous IVLBCL that exhibited terminal generalized lymphadenopathy or extravascular lymphoma saw that lymphadenopathy appear antecedently or concomitantly to the skin findings, only a handful have reported lymphadenopathy appearing subsequent to the cutaneous manifestations.[7,8] Thus, our case of cutaneous IVLBCL appearing 7 years before the generalized lymphadenopathy seen on our patient's final abdomen and chest CT scan is an important contribution to the existing literature.

Our case once again highlights the important role of the dermatologist in the diagnosis of IVLBCL. If a cherry angioma continues to increase in size or episodically disappears and reappears, a differential diagnosis of IVLBCL should be considered, and a precautionary biopsy of the lesion should be performed. Our case is also testament to the fact that cutaneous IVLBCL, despite not having signs or symptoms, can be lethal if not treated. Although much remains to be learned about this mysterious malady, recent studies finding successful treatment regimens signal a promising future.[6]

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