

Short Communication

A Case of Multiple Halo Cherry Hemangiomas: A Novel Entity with Histopathologic Correlation

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The diagnosis of halo cherry hemangioma is a newly described entity that has previously only been described in one patient that presented with one lesion. The diagnosis of halo hemangioma was made based on clinical and dermoscopic findings. This report describes a single patient with a novel entity of multiple halo hemangiomas. A biopsy of the patient's lesion was compared histologically to a biopsy of a non-halo cherry hemangioma taken from another patient. Multiple immunohistochemical studies and a Fontana-Masson special stain were carried out on both the patient's and on the control non-halo hemangioma. On comparison it was noted the halo hemangioma showed an increase of CD4 and CD8 T Cells, similar to halo nevus. Although the mechanism for both lesions is unknown, one could speculate that both share a similar mechanism of depigmentation. This case serves as a description of the clinical entity of multiple halo hemangiomas as well as provides a histologic description of the affected areas.

INTRODUCTION

Halo hemangioma was first reported in 2011 as a newly described entity [1]. Kocabas *et al.* reported on an 82 year old female that presented with one 0.5 x 0.5 cm asymptomatic red papule with a surrounding 1 x 1 cm area of depigmentation on the right pectoral region that was clinically and dermoscopically consistent with a halo hemangioma. This was the first clinical description of a "halo" of depigmentation surrounding a cherry hemangioma. To our knowledge there has not been a previously reported case of a single patient with multiple halo hemangiomas. This case report will provide a description of such a patient as well as provide the first histologic comparison of a halo to a non-halo cherry hemangioma.

CLINICAL PRESENTATION

An otherwise healthy 41 year old Caucasian man presented to outpatient clinic for removal of an irritated congenital nevus. Examination revealed numerous erythematous, shiny, papules of varying size (all measuring less than 0.5 cm x 0.5 cm in diameter) surrounded by sharply demarcated depigmented ring around each hemangioma, which were scattered across the abdomen. Dermoscopic examination revealed central erythematous lacunas with surrounding depigmented areas. Based on clinical presentation and dermoscopic evidence a diagnosis of multiple halo hemangiomas was made in this patient. Upon further questioning the patient was unsure of the duration of

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depigmentation and denied any associated symptoms. Other diseases and syndromes including Fabry's disease and senile leukoderma were excluded. The changes in pigmentation were also not directly attributed to aging of the skin.

A 5 mm punch biopsy was taken from a lesion on the right flank of the patient for a histologic confirmation of the diagnosis. A 3mm punch biopsy of a typical appearing (non-halo) cherry hemangioma was also preformed on a volunteer subject to serve as a control for comparison (Figure 1, Figure 2, Figure 3)



Figure 1 Multiple erythematous, shiny papules scattered across the abdomen with surrounding macules of depigmentation.

HISTOPATHOLOGIC FINDINGS

Specimen processing, including formalin fixation and subsequent staining of slides with hematoxylin and eosin, was carried out by standard laboratory protocols. Similarly, Fontana-Masson and immunohistochemical stains were performed by standard protocols using purchased antibodies.

Sections of the patient's specimen showed a circumscribed central hemangioma. The hemangioma was composed of lobules of small thin-walled vessels surround by an edematous stroma. There were a few lymphocytes seen along the dermoepidermal junction. A few melanophages were seen with mild melanin pigmentation. There were scattered interstitial and perivascular lymphocytes. Mast cells were noted in the section. Adjacent to the hemangioma, a follicle with an interface inflammatory infiltrate and lymphocytes within the follicular epithelium was noted. Histiocytes associated with this interface follicular inflammatory infiltrate demonstrated some mild melanin pigmentation. No significant cytologic atypia was seen. On the control, a similar proliferation of small thin-walled vessels was seen. A few perivascular lymphocytes were seen. Lymphocytes were not present along the dermoepidermal junction or in association with follicles.



Figure 2 An enlarged image of a single erythematous, shiny papule with a surrounding macule of depigmentation.



Figure 3 A dermoscopic photograph of erythematous lacunas of a cherry hemangioma with surrounding depigmentation.

Fontana Masson special stain of the patient's biopsy demonstrated very focal pigmentation within a few basilar keratinocytes and demonstrated pigment in scattered melanophages beneath the dermoepidermal junction. On the control biopsy widespread light melanin pigmentation was seen in most basilar keratinocytes as well as in scattered melanophages beneath the dermoepidermal junction.

MART1 (Melanoma antigen recognized by T cells 1) and MiTF (Microphthalmia-associated transcription factor) immunohistochemical stains of both biopsies (the halo cherry hemangioma and the control) demonstrated well spaced melanocytes at the dermoepidermal junction including over the hemangiomas. HMB45 (Human melanoma black 45) immunohistochemical stain of the patient's biopsy did not highlight melanocytes along the dermoepidermal junction, though the control showed melanocytes were identified in association with the deep portion of a follicle. The control was similar to the halo cherry hemangioma biopsy with HMB-45 highlighting only rare junctional melanocytes.

CD3 immunohistochemical stain of the halo cherry hemangioma biopsy demonstrated some perivascular lymphocytes and small foci of lymphocytes at the dermoepidermal junction. CD3 performed on the control biopsy showed scattered perivascular lymphocytes but none at the dermoepidermal junction.

CD4 immunohistochemical stain of the halo cherry hemangioma biopsy demonstrated a similar pattern to CD3; additionally, including a cluster of lymphocytes present at a follicle. The CD4 stained control showed few perivascular lymphocytes, but none at the dermoepidermal junction or in association with a follicle.

CD8 immunohistochemical stain of the patient's biopsy demonstrated a similar pattern to CD3, although staining fewer lymphocytes. CD8 also showed lymphocytes at the dermoepidermal junction. CD8 performed on the control biopsy showed scattered perivascular lymphocytes and rare single lymphocytes at the dermoepidermal junction.

More CD4 than CD8 positive lymphocytes were seen in the patient's halo cherry hemangioma. In contrast, more CD8 than CD4 positive lymphocytes were seen in the control non-halo cherry hemangioma.

CD20 immunohistochemical stain of the patient's biopsy demonstrated rare perivascular B-cells interspersed with in the hemangioma and a small focus deeper in the dermis. Also, CD20 performed on the control showed rare B-cells interspersed with in the hemangioma. The ratio of T cells:B cells was higher for the halo cherry hemangioma than for the control non-halo cherry hemangioma.

CD68 immunohistochemical stain of the patient's biopsy demonstrated some perivascular histiocytes. CD68 performed on the control showed fewer histiocytes but still demonstrated substantial perivascular staining.

Factor XIIIa immunohistochemical stain of the patient's biopsy demonstrated some perivascular "dermal dendrocytes"

including many just beneath the dermoepidermal junction. FactorXIIIa performed on the control showed fewer “dermal dendrocytes” but demonstrated the same dermal staining as the halo cherry hemangioma biopsy. There were significantly fewer FactorXIIIa positive cells just beneath the dermoepidermal junction in the control biopsy than were seen in the patient’s biopsy.

CD31 immunohistochemical stain of the patient’s biopsy highlighted (lesional) endothelial cells, which demonstrated the lesion to be well circumscribed. Adjacent areas appeared to show a normal distribution of blood vessels. CD31 performed on the control showed darker staining of endothelial cells. No adjacent normal tissue was available for comparison on the control slide as the hemangioma went to edges of this piece of tissue (Figure 4-7, Table 1).

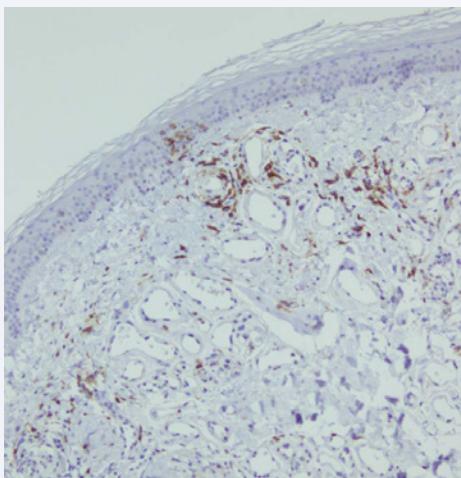


Figure 4 Halo hemangioma stained with CD4 stain at 400x showing perivascular CD4 T-cells and a small group of CD4 T-cells at the dermoepidermal junction.

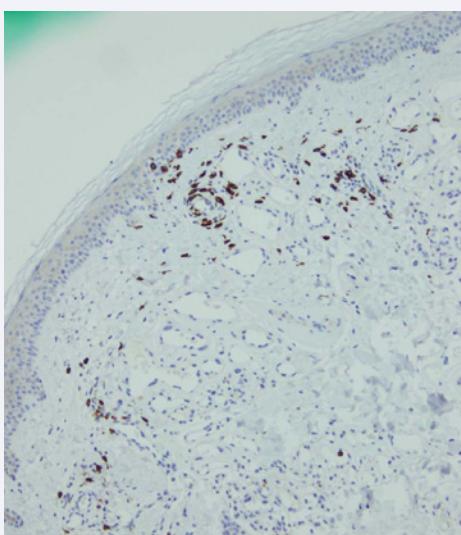


Figure 5 Halo hemangioma stained with CD8 stain at 400x showing perivascular CD8 T-cells and a small group of CD8 T-cells at the dermoepidermal junction.

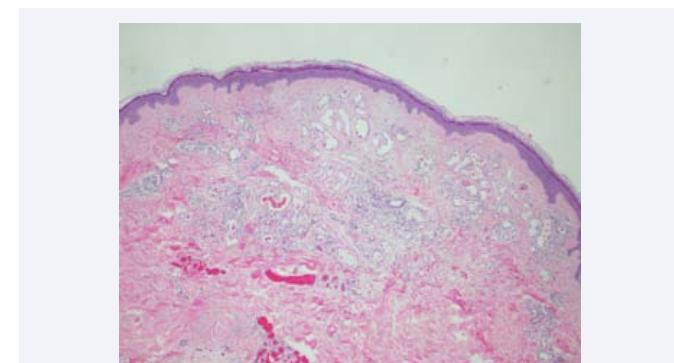


Figure 6 Halo hemangioma at 40x showing small dilated thin-walled vessels of a cherry hemangioma.

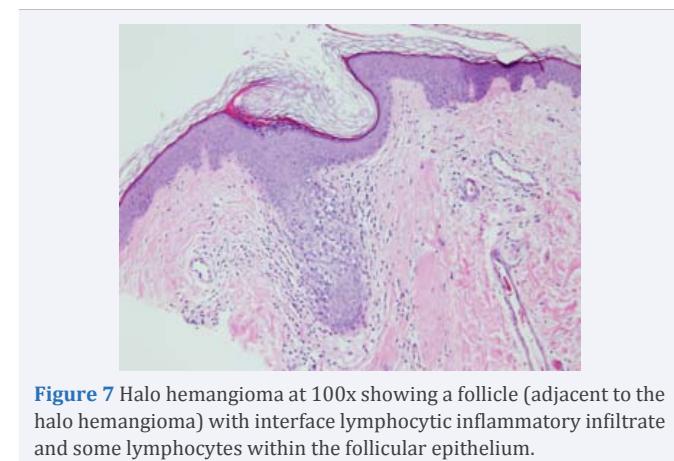


Figure 7 Halo hemangioma at 100x showing a follicle (adjacent to the halo hemangioma) with interface lymphocytic inflammatory infiltrate and some lymphocytes within the follicular epithelium.

DISCUSSION

Considering the diagnosis of multiple halo cherry hemangiomas made in the patient discussed in this case is a novel entity, other similar entities will be discussed for comparison.

Nevus anemicus is a congenital cause of hypopigmented macules that coalesce into patches often on the trunk of newborns. The areas of hypopigmentation are due to a hypersensitivity of dermal capillaries to catecholamines that produces subsequent vasoconstriction. There is no alteration of the melanocytes or melanin content in the affected areas [2]. Histologic examination of nevus anemicus reveals a normal epidermis with melanocytes in the basal layer [3,4].

A halo nevus is characterized as a central melanocytic nevus surrounded by a well-circumscribed area of hypo- or depigmentation. Over the course of weeks to months there is loss of pigment around acquired melanocytic lesions. Frequently located on the upper backs of children and young adults [1,2]. Histologically the depigmented halo of a halo nevus shows an absence of melanin pigment and melanocytes in the basal layer [5]. Lymphocytes are sometimes noted in close proximity to residual melanocytes in the halo zone of newly forming lesions, but they are not usually present in the basal layer of established lesions [5].

Cherry hemangiomas are described as red, dome-shaped papules that typically begin to appear in the third decade of life.

Table 1: This table is a summarization of the histopathologic findings created for ease of comparison for the reader.

Immunohistochemical Marker/Stain	Halo Hemangioma	Typical Cherry Hemangioma
CD3	Lymphocytes: Perivascular and at the dermoepidermal junction	Lymphocytes: Perivascular only
CD4	Lymphocytes: Perivascular, at the dermoepidermal junction, and clustered at a follicle	Lymphocytes: Perivascular only
CD8	Lymphocytes: Perivascular and at the dermoepidermal junction (Similar pattern to CD3 however fewer in number)	Lymphocytes: Perivascular only and a single lymphocyte at the dermoepidermal junction
CD20	Rare perivascular B Cell with small focus in dermis	Rare scattered B Cell
T Cell:B Cell Ratio	Higher	Lower
CD31	Lesional Endothelial cells (Well circumscribed)	Darker Staining of lesional endothelial cells. No adjacent tissue available.
CD68	Perivascular Histiocyte (More)	Perivascular Histiocyte (Less)
FactorXIIIa	Dermal Dendrocytes: Perivascular and many underneath the dermoepidermal junction	Dermal Dendrocytes: Perivascular and significantly fewer dendrocytes underneath the dermoepidermal junction
Fontana Masson	Focal pigmentation with a few basilar keratinocytes and scattered melanophages beneath the dermoepidermal junction.	Widespread melanin pigmentation in most basilar keratinocytes and scattered melanophages beneath the dermoepidermal junction.
MART1	Well spaced melanocytes at dermoepidermal junction	Well spaced melanocytes at dermoepidermal junction
MiTF	Well spaced melanocytes at dermoepidermal junction	Well spaced melanocytes at dermoepidermal junction
HMB45	No melanocytes stained along the dermoepidermal junction	Melanocytes indentified at the deep portion of the follicle

They are most often located on the proximal extremities and trunk. The appearance of the hemangiomas is due to dilated capillaries and postcapillary venules within the dermis. The pathogenesis is unknown; however, a hormonal influence has been suggested [2].

The histologic hallmark of cherry hemangioma describes ectatic capillaries and postcapillary venules in the dermis. Over time the endothelial cells of the vessel walls flatten causing an overall dilation in the diameters of the vessels [2]. In the halo hemangioma studied the junctional melanocytes were intact, demonstrated by immunohistochemical staining with MART1 and MiTF. There was a decrease in melanin in basilar keratinocytes by Fontana Masson special stain in the halo cherry hemangioma studied. It is interesting that when compared to the control the halo hemangioma demonstrated an increase number of CD3, CD4, and CD8 cells at the dermoepidermal junction as well as an increased ratio of T:B cells.

In comparison, Halo nevi have been shown to be infiltrated by an oligoclonal population of CD4 and CD8 T Cells that are thought to be specific to antigens within the nevus [3]. It is still unclear whether the immune cells surrounding halo nevi are involved in the destruction of the nevus cells or adjacent junctional melanocytes. As the population of immune cells surrounding halo nevi are similar to those seen in the biopsy our patient's halo hemangioma, it is possible that the pigmentary changes of a halo

hemangioma could be due to a similar mechanism as that of a halo nevus. However, these two diagnoses should be considered as separate entities.

As the diagnosis of multiple halo hemangiomas is a novel entity, the cause of the depigmentation surrounding the cherry hemangiomas in this patient is unclear. The description of this case is important as it provides the first histologic and immunohistochemical description of a halo hemangioma.

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