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Hobnail cell change in reactive angioendotheliomatosis, a potential diagnostic pitfall

Neha A[1], **Shobana B**[2*]

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Authors' Affiliation:
[1]Postgraduate, Department of Pathology, Sree Balaji Medical College and Hospital, Chennai, India; Email: nehakwel82@gmail.com, Orcid: 0000 0002 5236 4573
[2]Associate Professor, Department of Pathology, Sree Balaji Medical College and Hospital, Chennai, India; Email: shobdr@gmail.com, Orcid: 0000 0003 4880 7279

[*]**Corresponding author**
Associate Professor, Department of Pathology, Sree Balaji Medical College and Hospital,
Chennai, India;
Email: shobdr@gmail.com

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ABSTRACT

Reactive angioendotheliomatosis (RAE) is a rare angio-proliferative disease which commonly exists with some underlying systemic disease. RAE clinically presents as an ulcerated lesion which can be single or multifocal. It can also present as violaceous papules or plaques. The rarity of hobnail cell change in RAE can cause confusion with other vascular neoplasms which exhibit these changes like Endovascular papillary angioendothelioma also called Dabska Tumor, hobnail hemangioma and angiosarcoma etc. Most of the lesions of RAE are superficial in location but occurrence in deeper tissues is also known. We describe here a case of a young man presenting with a swelling in the first web space of right hand that has been diagnosed with arteriovenous malformation and was given the histological diagnosis of intravascular reactive angioendotheliomatosis with focal areas showing hobnail cell change. Also, all the lesions in differential diagnoses should be ruled out before making the diagnosis of RAE and before starting the treatment. Here, we review the usual presentation of RAE, with rare phenomenon of focal hobnail cell change which poses a diagnostic pitfall and the criteria to rule out other possible differential diagnosis that has to be taken into consideration in this setting.

Keywords: Reactive Angioendotheliomatosis, hobnail cell change.

1. INTRODUCTION

Reactive angioendotheliomatosis (RAE) is an uncommon disease with no age preponderance and can be seen at any age (Gleason & Hornick, 2013). However it is known to occur in relation to the underlying systemic disease (Gupta et al., 2020). It is believed to occur as a result of hypoxia of the tissue which triggers the release of circulating growth factors (Gleason & Hornick, 2013). Hobnail cell change in RAE is a furthermore rare phenomenon which poses a potential diagnostic pitfall and all the vascular lesions with hobnail cell change will come into the differential diagnosis. Here, we are reporting a rare case of Intravascular Reactive Angioendotheliomatosis with focal hobnail cell change which is a very rare phenomenon in a young man over first web space of right hand.

DISCOVERY SCIENTIFIC SOCIETY

2. CASE REPORT

A 24-year-old male came to the dermatology department with complaints of swelling over first web space of right hand for last one year. There was a gradual increase in the size of the swelling associated with pricking type of pain which was intermittent in nature. On clinical examination, a 2x2cm swelling was seen in first web space of right hand, firm in consistency with smooth surface and well-defined margins. On Magnetic Resonance Imaging (MRI), it showed a well-defined lesion with lobulated margins, intermediate signal intensity on T1 and heterogenous signal intensity on T2WI in first intermetacarpal space. Location of the lesion was distal aspect of flexor pollicis brevis muscle and extends into intermuscular plane between flexor pollicis brevis and first dorsal interosseous muscle. Multiple nodular T2 hypointense areas within lesion were noted.

Gross examination showed a single globular brownish black soft tissue measuring 2.5x2.5x1cm. Cut section revealed dark brown hemorrhagic area with focal yellowish areas. Microscopic examination showed multiple dilated blood vessels which are lined by the flattened endothelial cells with hyalinized wall. There was predominantly intravascular dense proliferation of endothelial cells (figure 1) with cytoplasmic neovascular lumen formation admixed with areas of hemorrhage and foci of papillary architecture with hyalinized fibrovascular core (figure 2 and 3). Focal area showed foamy histiocytes and hobnail cell change (figure 4). Some of the cytoplasmic neovascular lumens were filled with RBCs and the dilated vessel walls showed organizing thrombus formation (figure 1). Collections of hemosiderin pigment were also seen, which was confirmed by positive Perl's stain (Figure 5). Thus, with these features the histopathological diagnosis was given as intravascular reactive angioendotheliomatosis.

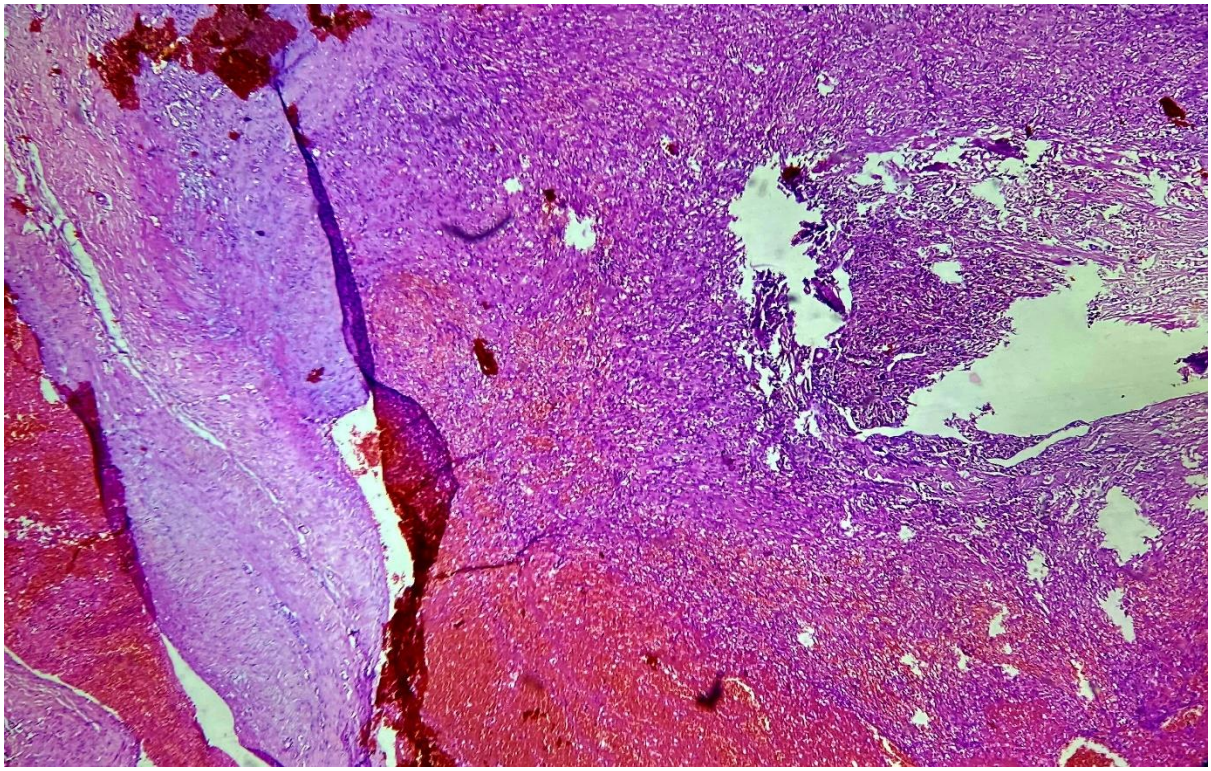

Figure 1 Scanner views shows thickened vessel wall (arrow) with intravascular proliferation of endothelial cells along with thrombus (arrowhead) formation.

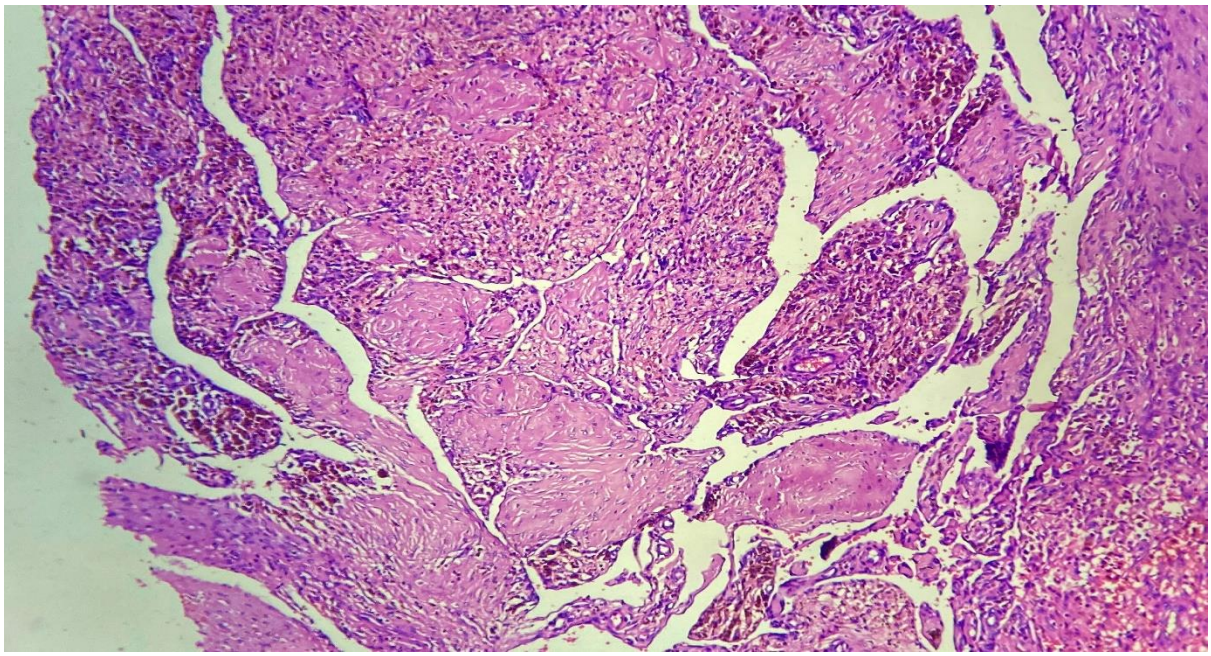

Figure 2 Low power view showing intravascular proliferation of endothelial cells with hyalinization (arrowhead) and hemosiderin deposition (arrow)

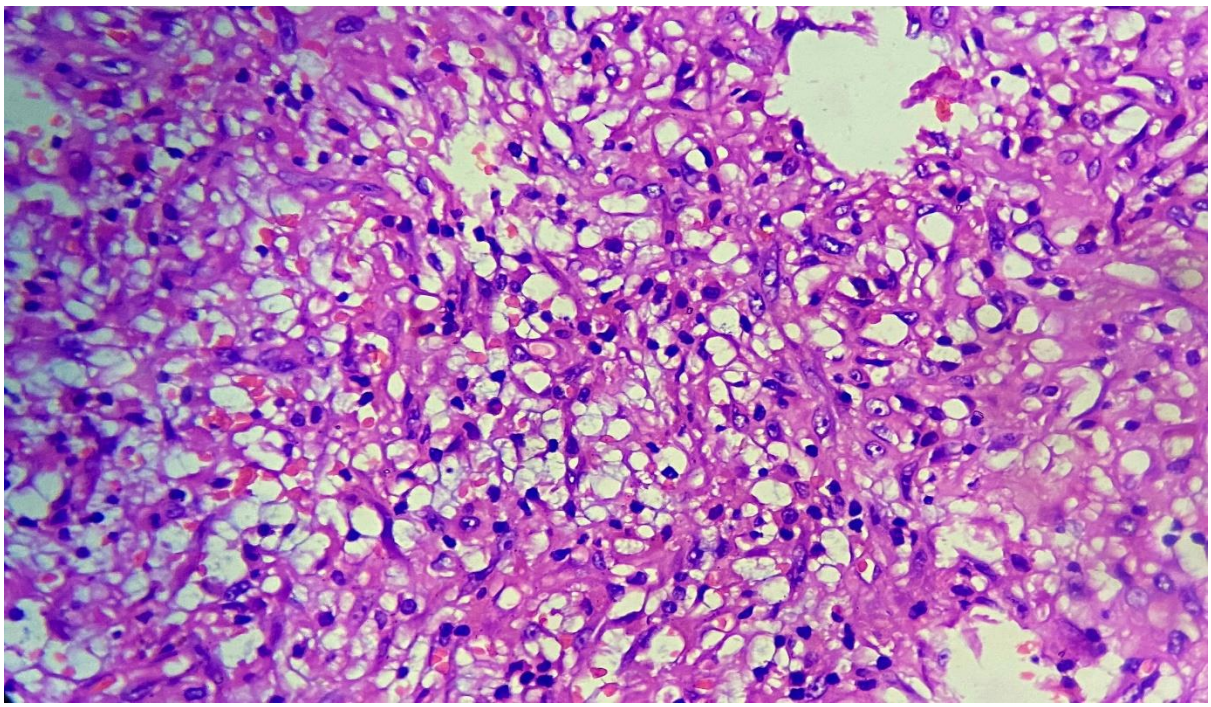

Figure 3 High Power View shows endothelial cells with cytoplasmic neovascular lumens (arrow)

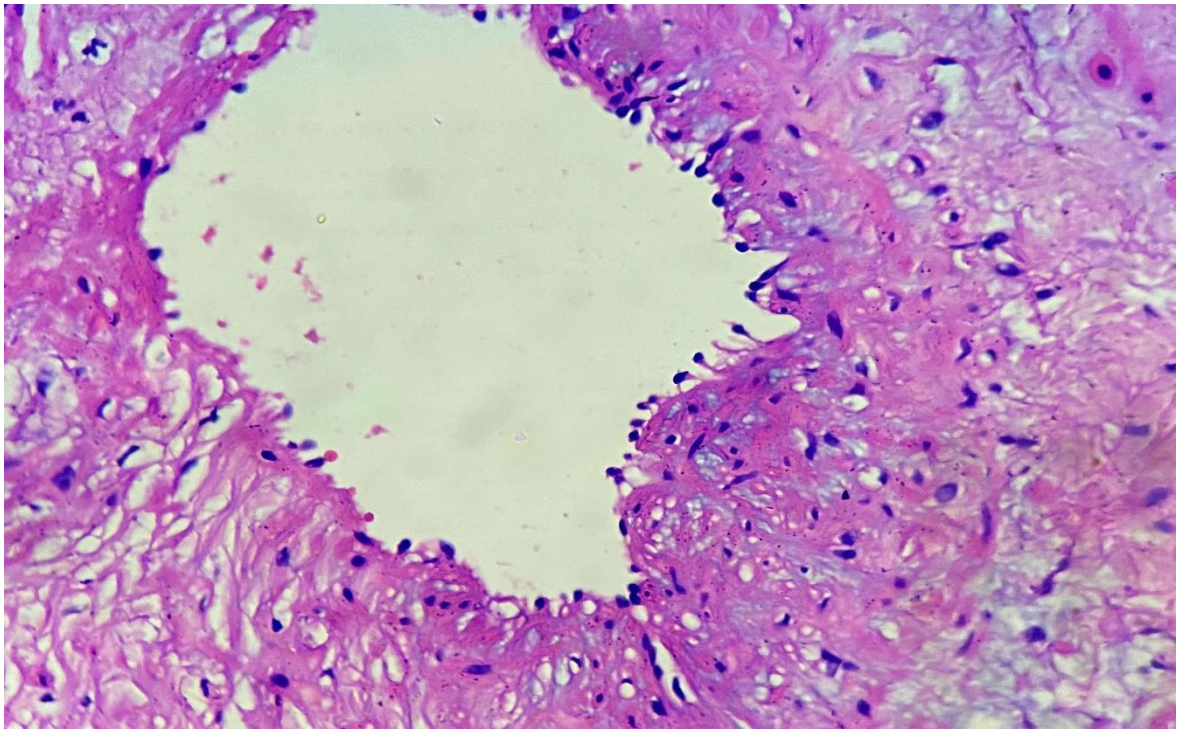

Figure 4 High power view showing hobnail cell change of endothelial cells in focal area

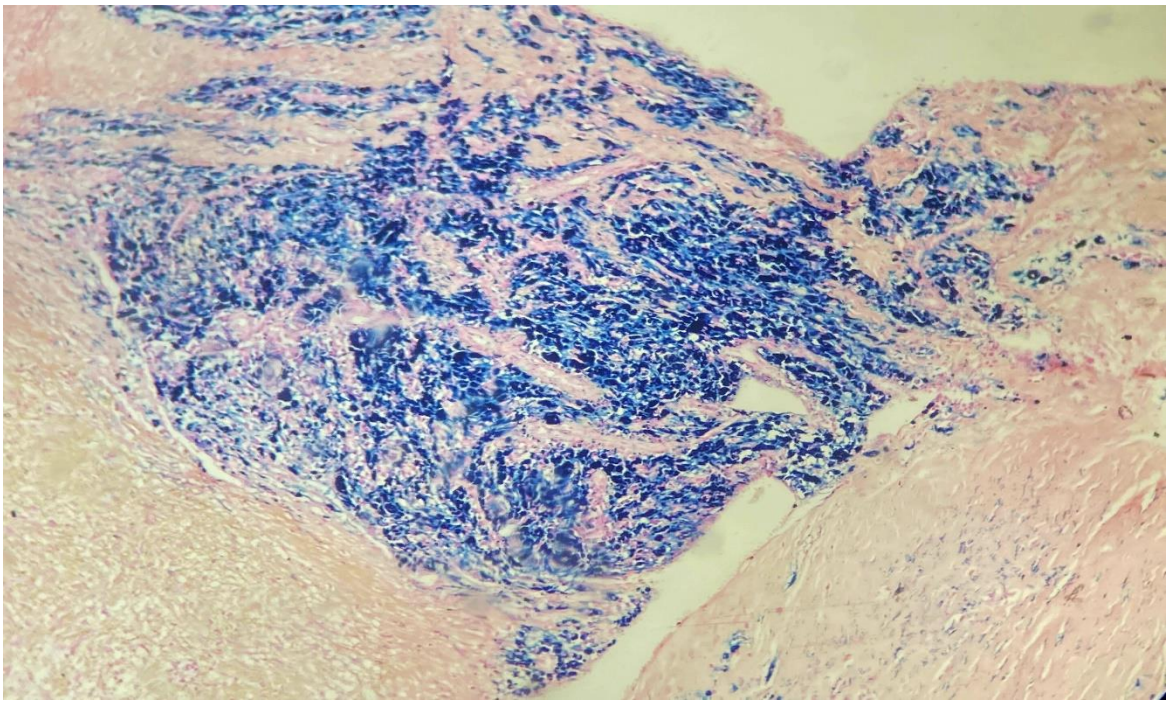

Figure 5 Perl's stain highlights the hemosiderin deposition (arrow)

3. DISCUSSION

Reactive Angioendotheliomatosis (RAE) is an uncommon, benign condition which is defined by the development of reactive proliferation of endothelial cells both intravascularly and extra vascularly and usually seen in patients with coexisting systemic diseases (Gupta et al., 2020; McMenamin & Fletcher, 2002). Ulcerated purpuric plaques, purpuric papules and erythematous macules remain the clinical presentation in such patients (McMenamin & Fletcher, 2002). It is usually seen in adults and very rare cases of children being affected is noted. Although patient mostly presents with lesion on the limbs, face and trunk are also

involved as the disease has wide anatomical distribution (Lazova et al., 1996; McMenamin & Fletcher, 2002; Rongioletti & Rebora, 2003). Many patients present with symptoms like fever and weight loss for which systemic examination is done to rule out the underlying systemic disease (Aung et al., 2015; Gupta et al., 2020). Laboratory findings show raised erythrocyte sedimentation rate (Lazova et al., 1996). Diseases that can co-exist include vascular abnormalities, hematologic disorders, infectious diseases, monoclonal gammapathies and other systemic diseases (Gleason & Hornick, 2013). In spite of pathogenesis not being fully known, alterations in portal and systemic hemodynamics and response to local hypoxia can be the probable factor behind the disease (Gupta et al., 2020).

RAE is a benign proliferation of endothelial cells intraluminal in location on histopathology, which could obstruct the vascular lumen which is also observed in our case (Kim et al., 2002; Mazloom et al., 2017). The vessels are typically dilated as well (Aung et al., 2015). In addition to the thrombus inside the vessel, subcutaneous fat also shows vascular occlusion with cells and fibrin (Lazova et al., 1996). This feature is present in our case too. Clinically, the differential diagnosis consists of Kaposi sarcoma, Calciphylaxis especially in patients having underlying renal failure (Gleason & Hornick, 2013; Schwartz et al., 2008). Thus the diagnosis has often been challenging to the pathologist because of its varying morphological characteristics, its rarity and due to its multifocality. Other variety of RAE shows tightly packed capillaries forming discrete tufted lobules, scattered throughout the dermis (Gleason & Hornick, 2013).

Microscopically, RAE must be distinguished from intravascular papillary endothelial hyperplasia, also called as Masson's tumor where the lesions show complete intravascular proliferation of endothelial cells in a papillary configuration with underlying thrombus formation (Katz et al., 1988; Rongioletti & Rebora, 2003). Though our case showed thrombus formation along with focal hobnail cell changes, typical papillary structures with hyalinized fibrovascular core exclusively seen in Masson's tumor were absent. In addition, varied histomorphology including intravascular and extravascular endothelial proliferation with deposition of hemosiderin and foamy histiocytes indicates the reactive nature of our case (Mazloom et al., 2017).

Although our case does not demonstrate the tufted angioma-like pattern of reactive angioendotheliomatosis, it is differentiated from tufted angioma because of the absence of crescentic lymphatic vessels at periphery of the capillary tufts and also by the clinical presentation (Mazloom et al., 2017). Another histopathological differential diagnosis remains Intralymphatic histiocytosis which is characterised by histiocytic accumulation within lymphatics and clinically the patient present with asymmetric plaques and macules (Barba et al., 2015). The major differentiating feature of RAE from Intralymphatic histiocytosis remains intraluminal glomeruli-like tufts of capillaries in RAE whereas in intralymphatic histiocytosis there will be intraluminal histiocytic proliferation with occlusion (Gleason & Hornick, 2013; Rongioletti & Rebora, 2003) and also show positivity for CD68 and are negative for CD31 / CD34 (Rongioletti & Rebora, 2003).

Another differential diagnosis considered can be Kaposi Sarcoma. In the early stage, Kaposi Sarcoma presents with small vessel proliferation and resembles granulation tissue as in our case whereas well developed lesions show vessels with endothelial proliferation along with slit like spaces which are cuffed by spindle and oval cells (Dabska, 1969; Schwartz et al., 2008). Angiosarcoma is a malignant neoplasm that can clinically present as hematoma. It is also found to be a complication of long-standinglymphedema (Shustef et al., 2017). The presences of poorly defined margins, varying histologic features, absence of increased/ abnormal mitosis are few diagnostic clues to a reactive etiology in our case (Mazloom et al., 2017). Though cytological atypia may be seen in reactive angioendotheliomatosis; the absence of endothelial multilayering and presence of pericytes around each vessel points against the diagnosis of angiosarcoma.

Hobnail hemangioma, another differential diagnosis is a vascular lesion which is very rare and presents with bland looking cells having hobnail appearance with biphasic pattern of growth having slit-like and superficially dilated blood vessels in deeper site of the lesion which can lead to misdiagnosis (Hejnold et al., 2012). In our case, the hobnail cell change is a focal and there is monophasic proliferation of endothelial cells. The finding of RAE with hobnail cell change has to be differentiated from Dabska tumor which is a rare vascular neoplasm seen in skin and subcutaneous tissues mostly in children (Dabska, 1969). Manivel et al., (1986) found that Dabska tumor belongs to the family of vascular neoplasms which are represented by the presence of characteristic cells with hobnail appearance, which indicates high endothelial cell differentiation. Although it is low grade slow-growing tumor, it has high tendency of local recurrence (Yamada, 1998; Enzinger and Weiss's, 2019).

On histopathology, this tumor is identified by localisation in the dermis and/or subcutaneous tissue and composed of thin-walled intercomposite vessels whose lining is formed by endothelial hobnail cells unlike the present case where there is proliferation of endothelial cells with neovascular lumen formation, and the hobnail cell change is only focally seen (Bhatia et al., 2006). Lymphatic differentiation is confirmed by the immunohistochemical positivity of VEGFR-3 and podoplanin (D2-40) positivity in Dabska tumor (Bhatia et al., 2006; Enzinger and Weiss's 2019). However, it can be locally invasive, with rare cases showing dissemination to regional lymph nodes and even distant metastases (Enzinger and Weiss's 2019). The gold standard

treatment for dabska tumor stands as the surgical excision with free margins. Thus, it is mandatory to differentiate this reactive condition from dabska tumour for early diagnosis and appropriate management. Also, a detailed long term clinical follow-up of these patients is necessary (Enzinger and Weiss's, 2019).

4. CONCLUSION

This case is being presented here to describe the unusual occurrence of intravascular reactive endothelial proliferation, intravascular reactive angioendotheliomatosis with focal hobnail cell change in a young adult. These conditions are recognized by endothelial cells with cytoplasmic neovascular lumens and intravascular proliferation. The hobnail cell change in our instance needs to be distinguished from other vascular neoplasms with hobnail cell change to avoid a potential diagnostic trap. By correctly recognizing histopathological findings, this rare entity can be identified, sparing patients from over diagnosis and treatment and also to look for any underlying or associated systemic illnesses. Our patient is being followed up and doing well so far.

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Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

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Conflict of interest

The authors declare that there is no conflict of interests

Data and materials availability

All data associated with this study are present in the paper.

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