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**Case Report**

# The Pleural Origin of Retiform Hemangioendothelioma: An Unusual Origin of a Rare Diagnosis

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**Keywords**
Pleura · Retiform hemangioendothelioma · Vascular neoplasm

## Abstract

***Introduction:*** Vascular malignancies are categorized into benign hemangiomas, malignant angiosarcomas, and tumors of intermediate malignancy. Retiform hemangioendothelioma (RH) is one of the rare diagnoses belonging to the class of intermediate malignancies that was initially diagnosed. ***Case Presentation:*** In this case report, we have reported a rare case of RH, a locally aggressive, vascular tumor of malignant potential presenting at an unusual site. The most observed locations of this soft tissue tumor are skin and subcutaneous tissues of extremities; however, this case of RH was observed in an unusual site called pleura, which is a rare occurrence related to this tumor. The presence of cell surface markers like CD31 and ERG of vascular and endothelial origin and the presence of hobnail appearance of endothelial channels on the biopsy profile supported the vascular origin of the tumor; the clinical features and imaging studies further confirmed the diagnosis of RH. ***Conclusion:*** In this case report, a rare case of RH with an unusual site of origin was highlighted. RH is a vascular neoplasm; commonly observed sites of this vascular tumor were skin and subcutaneous tissue of the extremities; however, in this case, the site was unusually different, which was the pleura of the left lung.



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## Introduction

Vascular malignancies are categorized into benign hemangiomas, malignant angiosarcomas, and tumors of intermediate malignancy. Retiform hemangioendothelioma (RH) is one of the rare diagnoses belonging to the class of intermediate malignancies that was initially diagnosed in 1994 by Calonje et al. [1]. RH is characterized by its high rate of local recurrence and low potential for metastasis to remote sites [2]. RH, an exophytic dermal tumor, is most located over the skin and subcutaneous tissues of the extremities [3, 4]. The variation in origin of RH at various locations can have different sets of underlying pathologies; however, the studies have shown the involvement of genetic component as well. Studies have demonstrated a special gene mix-up called YAP1-MAML2 in pathogenesis of RH; hence, the diagnosis of RH should also be highlighted not only on clinical but genetic basis as well. We are here presenting a rare case of RH that originates from an unusual, rare site of pleura as opposed to the other commonly reported locations.

## Case Presentation

A 50-year-old female presented to the medical OPD with primary complaints of cough and shortness of breath for 8 months. The cough was non-productive and dry in nature and associated with worsening dyspnea. The patient otherwise was vitally stable with only other significant complaints of fatigue and undocumented weight loss. The patient was initially evaluated with a CXR, which revealed nonspecific loss of volume on the left lung with the lateral displacement of the left hilum. There were no signs of consolidations or pleural effusions on either side. The diagnosis of other vascular tumors like angiosarcoma and Kaposi sarcoma was also considered; however, patient was having no history of any chemical exposure and no history of HIV infection in past. The contrast-enhanced CT scan chest showed heterogeneously enhancing mass in the left para-cardiac region measuring 13.9 × 7.7 cm causing compression on the pericardium with encasement of the pulmonary trunk and superior vena vava. CECT also demonstrated a sub-segmental collapse of the right middle and left middle and lower lobes of the lungs. Though the most common differential diagnosis like angiosarcoma can initially present in similar pattern, however, it is differentiated on the basis of irregular soft tissue mass enhancement with invasion of adjacent tissues and organs. The presence of soft tissue calcification may be found in angiosarcoma as compared to RH. Further correlational core biopsy was performed.

Histopathology reports revealed interconnected vascular channels with areas of prominent glomeruloid appearance. The channels were lined by a single layer of cells with a prominent hobnail pattern of nuclei. The nuclei were uniformly arranged with a scant amount of cytoplasm. No mitotic figures were visualized within the examined sections of cores. The histopathology findings all advocated for a low-grade vascular lesion, which inclined toward the diagnosis of RH as shown in Figure 1 and 2.

In addition, the immunohistochemistry testing came back positive for CD31 and ERG cell markers, both of which are vascular endothelial differentiation markers confirming the origin of the tumor to be vascular and supporting the diagnosis of RH. The rest of the stains studied are tabulated in Table 1.

The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000539771). Given the above-discussed investigations and histopathology reports, the final

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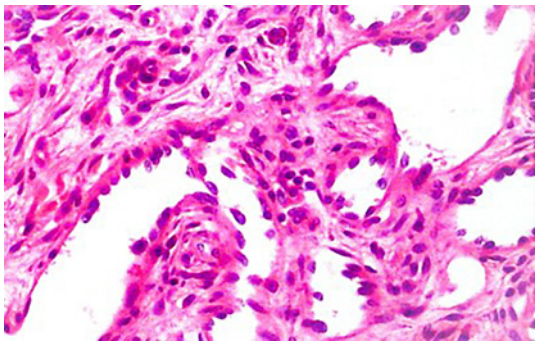

**Fig. 1.** Showing the histological profile of RH with ill-defined vascular channels.

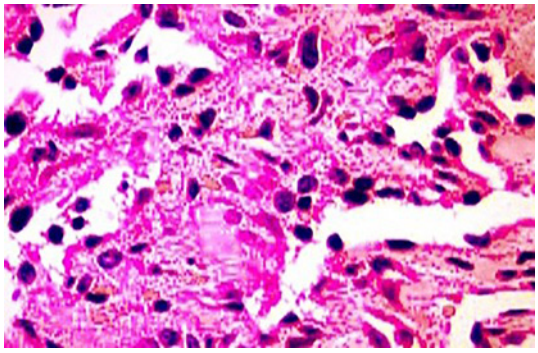

**Fig. 2.** The H&E stain also shows the hobnailing of endothelial channels.

diagnosis of RH was made and the tumor was classified as locally invasive with less predisposition for metastasis. However, the site of this vascular tumor was pleura, which was an unusual site according to the WHO classification of soft tissue tumors.

## Discussion

Hemangioendothelioma is an intermediate class of vascular tumors whose features lie in between benign hemangiomas and malignant angiosarcoma, hence the name to the name hemangioendothelioma. Subclasses further include epithelioid, Kaposi form, retiform, composite, and pseudomyogenic [5]. The diagnosis of the exact histological and morphological variety of hemangioendothelioma is based on the histopathology and immunohistochemistry of the lesion. As published in various literatures, the most involved sites of hemangioendothelioma are skin and soft tissues; however, exceptions do exist as shown in this literature and others [2]. The involvement of pleura and lungs has been investigated in hemangioendothelioma of epithelioid variety; however, there has never been a description of its counterpart RH on pleura. To date, no specific cause or association of this form of vascular tumor has been identified.

RH is characterized as an intermediate variety of vascular tumors that has a high rate of local recurrence and low potential for metastasis [1]. As observed in the literature, RH has been shown to have a strong predilection toward the female gender. RH is most observed over extremities, genitalia, and scalp rather than the pleura, as reported in our case [6]. The exact diagnosis involves the utilization of CECT, histopathology, and immunohistochemistry of the lesion. According to the literature, the presence of disorganized vascular channels along with nuclear hobnailing of the

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**Table 1.** Showing the immunohistochemistry profile of RH

| Stain | Results |
|---|---|
| CD31 | Positive |
| ERG | Positive |
| CKAE1/AE3 | Negative |
| EAM | Negative |
| TTF-1 | Negative |
| Calretinin | Negative |
| WT-1 | Negative |

endothelial cells, with no mitotic figure, confirmed the diagnosis of RH, which is in concordance with our biopsy findings [7]. Similarly, various histological markers of vascular and endothelial genesis like CD31, CD34, D2-40, and ERG have been known to aid in precisely devising the diagnosis of RH. Among the above-mentioned markers, CD31 and ERG were found to be positive in our study, validating the diagnosis of RH [8]. In comparison to RH, the Kaposi sarcoma and angiosarcoma are most commonly observed differential diagnoses; other than being the vascular tumor, they are more aggressive and are associated with significant metastatic potential [9]. KS is linked to HHV8, mainly affecting those with weakened immune systems, especially patients with low T-cell counts. The virus induces new blood vessel formation and alters the DNA of infected cells, resulting in the uncontrolled growth of altered endothelial cells. In contrast, angiosarcomas are characterized by epigenetic alterations, oncogenic mutations, and UV damage markers [10].

As far as the prognosis of this tumor is concerned, to date, no deaths have been reported in the literature from RH. Although the tumor tends to be locally invasive, it has a low frequency of distant metastasis, which accounts for the associated low rates of mortality. The management of this variety of tumors includes adjuvant immunotherapy and radiotherapy in addition to the more definitive treatment of complete excision of the lesion [11, 12]. However, studies have shown the effectiveness of surgical excision combined with immunotherapy or radiotherapy as compared to either surgical excision or radiotherapy, validating the effectiveness of this combination in effective management of RH. There is very limited literature regarding the reason of development of a vascular tumor like RH in pleura and that needs not only genetic but pathogenetic, epigenetic, and detailed oncologic review of the tumor in future studies for better understanding of a rare tumor, that too at a rare location. In our study, the diagnosis of HIV was ruled out; however, HHV-8 serologic markers were not done in diagnostic workup and we strongly recommend this as well for better understanding of disease pathology.

## Conclusion

In this case report, a rare case of RH with an unusual site of origin was highlighted. RH is a vascular neoplasm that is characterized by a low frequency of distant metastasis, but it tends to grow and is locally invasive spreading to the surrounding structures. Commonly observed sites of this vascular tumor were skin and subcutaneous tissue of the extremities; however, in this case, the site was unusually different, which was the pleura of the left lung. The histopathology and immunohistochemistry of the presented lesion were in concordance with the diagnosis at an unusual site, the pleura.

## Acknowledgment

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## Statement of Ethics

Written informed consent was obtained from the parent of the patient for publication of the details of their medical case and any accompanying images. Ethical approval is not required for this study in accordance with local or national guidelines. The patient was given a clear description of the nature of the project and informed consent for publication of this case was taken from the patient. Ethical approval is not required for this study in accordance with local or national guidelines.

## Conflict of Interest Statement

The authors of this case report have no conflicts of interest to disclose.

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No funding was taken and utilized at any step of the project.

## Author Contributions

Hidayat Ullah, Imran Khan, Aria Khan, Apoorva Tangri, Saral Lamichhane, and Shahzaib Maqbool: conceptualization, data curation, writing – original draft preparation, and writing – reviewing and editing. Abdulqadir J. Nashwan: writing – reviewing and editing. All authors have read, reviewed, and approved the final version of the manuscript prior to submission, and each author accepts full responsibility for their respective contributions.

## Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

## References

1 Calonje E, Fletcher CD, Wilson-Jones E, Rosai J. Retiform Hemangioendothelioma. A distinctive form of low-grade angiosarcoma delineated in a series of 15 cases. Am J Surg Pathol. 1994;18(2):115–25. https://doi.org/10.1097/00000478-199402000-00001
2 Liu Q, Ouyang R, Chen P, Zhou R. A case report of retiform hemangioendothelioma as pleural nodules with literature review. Diagn Pathol. 2015;10:194. https://doi.org/10.1186/s13000-015-0433-7
3 Zhang G, Lu Q, Yin H, Wen H, Su Y, Li D, et al. A case of retiform hemangioendothelioma with unusual presentation and aggressive clinical features. Int J Clin Exp Pathol. 2010;3(5):528–33.
4 Paral K, Krausz T. Vascular tumors of the mediastinum. Mediastinum. 2020;4:25. https://doi.org/10.21037/med-20-40

5 Doyle LA. Sarcoma classification: an update based on the 2013 World Health Organization Classification of Tumors of Soft Tissue and Bone. Cancer. 2014;120(12):1763–74. https://doi.org/10.1002/cncr.28657
6 Askari E, Yaghmaei S, Haseli S, Pouradollah Totkaboni M. Primary pleural hemangioendothelioma: a case report and literature review. Case Rep Oncol. 2021;14(2):1201–11. https://doi.org/10.1159/000518243
7 Tan D, Kraybill W, Cheney RT, Khoury T. Retiform hemangioendothelioma: a case report and review of the literature. J Cutan Pathol. 2005;32(9):634–7. https://doi.org/10.1111/j.0303-6987.2005.00379.x
8 O'Duffy F, Timon C, Toner M. A rare angiosarcoma: retiform haemangioendothelioma. J Laryngol Otol. 2012; 126(2):200–2. https://doi.org/10.1017/S0022215111002398
9 Radu O, Pantanowitz L. Kaposi sarcoma. Arch Pathol Lab Med. 2013;137(2):289–94. https://doi.org/10.5858/arpa.2012-0101-RS
10 Torrence D, Antonescu CR. The genetics of vascular tumours: an update. Histopathology. 2022;80(1):19–32. https://doi.org/10.1111/his.14458
11 Hirsh AZ, Yan W, Wei L, Wernicke AG, Parashar B. Unresectable retiform hemangioendothelioma treated with external beam radiation therapy and chemotherapy: a case report and review of the literature. Sarcoma. 2010; 2010:756246–3. https://doi.org/10.1155/2010/756246
12 Al-Faky Y, Al-Mosallam A, Al-Rikabi A, Al-Sohaibani M. Medial canthus retiform hemangioendothelioma. Indian J Ophthalmol. 2014;62(4):491–3. https://doi.org/10.4103/0301-4738.126995