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# Clinical Manifestations and Pathological Diagnosis of Anastomosing Hemangioma

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**Abstract:** *Objective*: To explore the clinical manifestations, histopathological features and differential diagnosis of anastomosing hemangioma. *Methods*: Histopathological observation and immunohistochemical study were performed on 3 cases of anastomosing hemangioma. *Results*: Among the 3 cases, 2 occurred in the adrenal gland and 1 in the mediastinum. The tumor had a thin fibrous capsule, with interlacing and anastomosing vascular-like arrangement. The vessel walls were irregular, with varying numbers of wall cells and uneven thickness, only a single layer of cells in the thin areas, while dense cell regions with abundant cells forming thick trabeculae. The cells were small with a low nuclear-cytoplasmic ratio, abundant eosinophilic cytoplasm, small round nuclei, thin nuclear membranes, fine chromatin and inconspicuous nucleoli. Eosinophilic edematous and fibrinoid stroma were visible. A small number of scattered irregular thick-walled blood vessels were found in the tumor; some areas resembled splenic medulla, some contained abundant edematous and hyaline stroma, and some endothelial cells could be hobnail-shaped. *Conclusion*: Anastomosing hemangioma is a newly reported benign vascular tumor, which is relatively rare. It generally has no obvious clinical symptoms and is occasionally found during physical examination. Due to the significant anastomosing arrangement of neoplastic blood vessels, it is easily misdiagnosed as angiosarcoma.

**Keywords:** Anastomosing hemangioma; Histopathology; Diagnosis

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## 1. Introduction

Anastomosing hemangioma (AH) is a recently reported benign vascular tumor that is relatively rare and not extensively documented in the literature. Due to its characteristic anastomosing and interlacing arrangement of neoplastic blood vessels, it is prone to misdiagnosis as angiosarcoma. To avoid overtreatment, it is essential to understand its clinical and pathological features. We collected three cases of anastomosing hemangioma encountered during routine external examinations at our hospital from 2017 to 2025. By analyzing their clinical manifestations, gross appearances of specimens, histological features, and immunohistochemical expression patterns, we aimed to summarize their clinicopathological characteristics. With a grasp of these key points, accurate diagnoses can generally be made.

## 2. Materials and Methods

### 2.1. General Information

The three cases of anastomosing hemangioma were sourced from external examination cases at the Pathology Department of the Affiliated Tumor Hospital of Harbin Medical University between 2017 and 2025. There were two females and one male, with a male-to-female ratio of 1:2. The patients' ages ranged from 45 to 62 years old, with an average age of 57 years old. Two tumors were located in the adrenal glands, and one was in the mediastinum.

### 2.2. Methods

Histological observations and immunohistochemical analyses were performed on the three cases of anastomosing hemangioma. Specimens were fixed in 10% formalin, routinely dehydrated, embedded in paraffin, sectioned at 4–5 μm thickness, and stained with routine hematoxylin and eosin (HE) for light microscopy. Antibodies, including FLi1, ERG, CD31, CD34, CK, PAX-8, and CA-9, were purchased from Fuzhou Maixin Biotechnology Co., Ltd.

## 3. Results

### 3.1. Clinical manifestations

Anastomosing hemangiomas predominantly occur in solid organs, most commonly in the urogenital system, such as the kidneys, adrenal glands, testes, and ovaries, but can also be found in the liver and gastrointestinal tract. The clinical manifestations of the cases in this study are as follows:

(1) Case 1: A 45-year-old female presented with a left adrenal mass discovered during a physical examination. She was in good general condition, alert, and cooperative during the examination. An external ultrasound showed a solid hypoechoic nodule in the left adrenal region, measuring approximately 34 mm × 29 mm, with clear borders and uneven internal echo. CT at our hospital revealed a left adrenal mass. Ultrasound showed a nodular mass in the left adrenal gland. After completing relevant examinations, she underwent surgical treatment, nutritional support, anti-inflammatory therapy, and symptomatic treatment.

(2) Case 2: A 64-year-old male was admitted with a "lung mass discovered during a physical examination two weeks ago." He did not have cough, sputum production, fever, night sweats, chest pain, dyspnea, or shortness of breath. Chest CT revealed a mass adjacent to the aortic arch in the upper-middle mediastinum, with micronodules in the upper lobes of both lungs. A PET report indicated a mass in the left upper mediastinum with possible local necrosis and a high-density nodule in the upper pole of the right kidney. The preliminary diagnosis was mediastinal tumor.

(3) Case 3: A 62-year-old female was admitted with a "left retroperitoneal tumor discovered during a physical examination one month ago." CT one month before admission showed a cystic-solid mass in the left retroperitoneum, measuring approximately 38 mm × 31 mm, with lobulated margins, uneven internal density, and significant enhancement of the solid component on contrast-enhanced scans. The boundaries with the left adrenal gland and left renal vein were unclear locally. During the course of the disease, she had normal diet and sleep, good mental state, normal bowel movements, and no significant weight loss.

### 3.2. Gross appearances of specimens

(1) Case 1: The left adrenal gland specimen measured 40 mm × 40 mm × 20 mm. Upon sectioning, a translucent, grayish-yellow mass measuring 15 mm in length was observed, with a soft texture.

(2) Case 2: The submitted mediastinal mass was nodular, measuring 35 mm × 22 mm × 15 mm. The central cut surface was light brown and glossy, with dark red, hemorrhagic margins. The mass was soft and encapsulated.

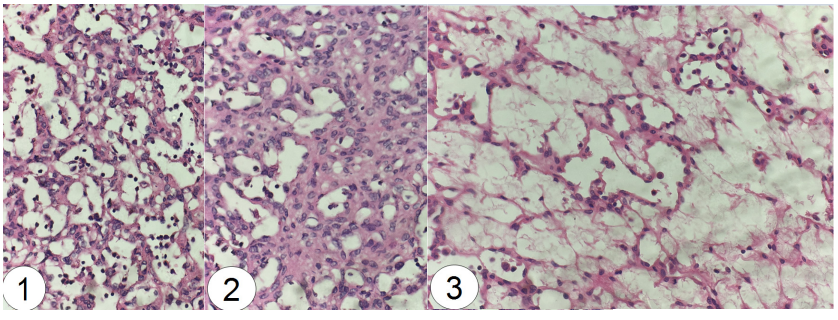
(3) Case 3: The submitted left adrenal gland specimen measured 70 mm × 50 mm × 40 mm. A nodular mass measuring 30 mm in length was observed on the cut surface, with a grayish-red, soft texture and relatively clear borders.

### 3.3. Microscopic findings

The histological features of the three tumors were generally similar. Some areas of the masses had a thin fibrous capsule, while others lacked a capsule but had clear boundaries with the surrounding tissue, without obvious “infiltrative” growth. The tumors were generally lobulated, with typical areas as well as loose and dense regions. The most prominent and characteristic feature was the tightly arranged, interconnected capillary lumens forming cell walls, with vascular walls composed of a single layer of cells. Some endothelial cells were hobnail-shaped, and some areas resembled the red pulp of the spleen. In the loose regions, the cellular and tissue structures were similar, but the vascular spaces were widened, with pink edema and fibrinous matrix visible inside. The dense regions had abundant cells, irregular vascular walls, and multilayered wall cells, sometimes arranged in thick cord-like structures. Some areas had hyaline stroma, and some cases had large areas of pink, edematous, acellular regions. Some regions had vascular walls connected in a network-like pattern, and some areas were accompanied by abundant collagenous stroma. Microthrombi were often visible within the vascular lumens. Scattered, few irregular, thick-walled blood vessels were seen within the tumors. The cells were small, with a low nuclear-to-cytoplasmic ratio, abundant eosinophilic cytoplasm, small, round nuclei, thin nuclear membranes, fine chromatin, and inconspicuous nucleoli. There was no obvious atypia, and mitotic figures were rare. Some cases showed extramedullary hematopoiesis and adipose metaplasia.

### 3.4. Immunohistochemistry

Tumor cells diffusely expressed FLi1, ERG, CD31, and CD34. When differentiating from vascular-rich renal cell carcinoma, additional staining with CK, PAX-8, and CA-9 was performed, all of which were negative.



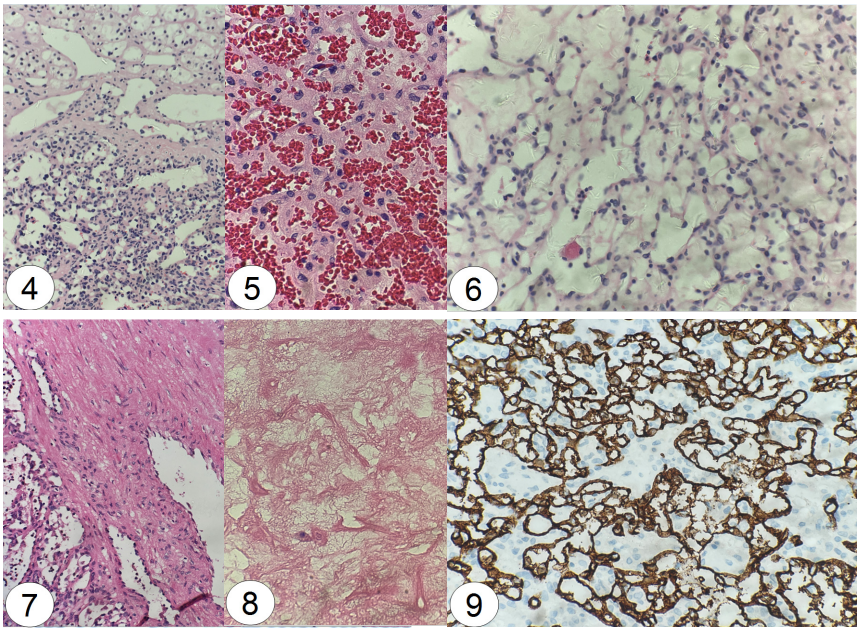



**Figure 1.** Typical morphology of anastomosing hemangioma (AH), with tightly packed, interconnected, and communicating capillary lumens forming the vessel walls;**Figure 2.** Dense cellular area;**Figure 3.** Loose cellular area;**Figure 4.** The upper part of the image shows normal adrenal tissue, while the lower part shows AH tumor tissue, with a clear boundary between the two;**Figure 5.** Prominent thrombosis;**Figure 6.** Vessel walls connected in a reticular pattern;**Figure 7.** Irregular thick-walled large vessels;**Figure 8.** Extensive pink-stained edematous acellular areas;**Figure 9.** Diffuse strong positivity for CD34 staining.

## 4. Discussion

Anastomosing hemangioma (AH), also known as interweaving hemangioma, is a rare benign vascular tumor first described by Montgomery and Epstein [1] in 2009. It primarily occurs in parenchymal organs, with the urogenital system, such as the kidneys, adrenal glands, testes, and ovaries, being the most common sites. It can also be found in the liver, gastrointestinal tract, and paraspinal regions [2, 3]. Currently, only a few reports have documented AH occurring in the skin and subcutaneous tissues [4]. The age range of patients is broad, from 2 to 85 years old (mean age 55.9 years, median age 56 years), with a slight female predominance [5]. Clinically, most patients are asymptomatic and are often incidentally discovered during physical examinations. The second case in our series was admitted with a “lung mass discovered during a physical examination two weeks ago.” Chest CT revealed a space-occupying lesion adjacent to the aortic arch in the upper-middle mediastinum, and PET imaging suggested a mass in the left upper mediastinum with possible local necrosis, leading to an initial diagnosis of mediastinal tumor. This indicates that tumors occurring in the lungs and mediastinum can sometimes overlap in imaging findings. The masses are generally small and often present as well-defined nodules. Masses located in parenchymal organs such as the kidneys and adrenal glands rarely have a capsule, but the second case in our series, which occurred in the mediastinum, had a capsule. The primary morphological feature is tightly packed, interconnected, and communicating capillary lumens forming the vessel walls, with a clear boundary and no “infiltrative” growth pattern. Since the growth pattern of interconnected and communicating capillary lumens forming the vessel walls is typical of angiosarcoma, the clear boundary of AH plays a crucial role in accurate diagnosis. The microscopic tissue

morphology of the tumor is generally similar. It usually lacks a capsule but has a clear boundary with the surrounding tissue, often presenting as indistinct, blurred lobules with typical areas, as well as loose and dense regions. The typical areas have vessel walls composed of a single layer of cells; some endothelial cells are hobnail-shaped; some areas resemble the red pulp of the spleen; the loose areas have similar cellular and tissue structures but with widened vascular spaces, containing pink-stained edema and fibrinous matrix; the dense areas are rich in cells with irregular vessel walls, and the vessel wall cells can be multilayered or even arranged in thick trabecular cords; some areas contain hyaline stroma; some cases may have extensive pink-stained and edematous acellular areas; some areas have vessel walls connected in a reticular pattern; some areas may be accompanied by abundant collagen fiber stroma; microthrombi are often visible within the vascular lumens; the cells are small with a low nuclear-to-cytoplasmic ratio, eosinophilic cytoplasm, small, round nuclei with thin nuclear membranes, fine chromatin, inconspicuous nucleoli, no obvious atypia, and rare mitotic figures; some cases may show extramedullary hematopoiesis and adipose metaplasia; when irregular thick-walled vessels are scattered within the tumor, it can be easily confused with renal angiomyolipoma [6]; immunohistochemical staining shows diffuse strong positivity for vascular endothelial markers such as CD34, CD31, ERG, F8, and Fli-1, while Ki-67 staining indicates low proliferative activity of tumor cells [7-8]. The vast majority of AH cases have somatic mutations in the GNAQ or GNAI4 genes, supporting its classification as a neoplastic lesion [9-11].

## 5. Differential diagnosis

(1) Well-differentiated angiosarcoma: This is the most important differential diagnosis for AH in clinical practice. Well-differentiated angiosarcoma shares significant morphological similarities with AH, sometimes lacking obvious cellular atypia, and including interconnected and interwoven vascular lumens. However, the primary characteristic of well-differentiated angiosarcoma is infiltrative growth into the surrounding normal tissue. Moreover, most well-differentiated angiosarcomas exhibit some degree of cellular atypia, with cells of varying sizes, disorganized arrangement, thick nuclear membranes, clumped chromatin, small nucleoli, frequent multilayered vessel walls, easily visible mitotic figures, and possible necrosis.

(2) Kaposi sarcoma: AH, with its clear boundary and often visible eosinophilic hyaline bodies, may be confused with Kaposi sarcoma. However, Kaposi sarcoma primarily occurs on the skin of the extremities, presenting as spindle cell fascicles with rare anastomosing or interwoven arrangements, indistinct vascular lumens, and significant extravasation of red blood cells between cells, which can serve as an important diagnostic clue. Additionally, Kaposi sarcoma is generally associated with HIV infection or the use of iatrogenic immunosuppressants. Immunohistochemical staining positive for HHV8 is diagnostic.

(3) Hobnail hemangioma: This presents with a characteristic biphasic morphology, with significantly dilated, thin-walled vascular lumens lined by prominent hobnail endothelial cells visible in the superficial dermis, and slit-like vascular lumens in the deep dermis, often surrounded by hemosiderin deposition. Hobnail morphology is relatively rare in AH. Furthermore, a hobnail hemangioma primarily occurs on the skin, while an AH primarily occurs in abdominal visceral organs.

(4) Reticular hemangioendothelioma: This often involves the superficial skin and is composed of slender, branching vascular lumens resembling the rete testis structure; the vascular lumens are

lined by prominent hobnail endothelial cells, similar to some cases of AH; it may form intraluminal papillary structures with hyaline axial changes and is often surrounded by lymphocyte infiltration in the stroma, overlapping with the morphology of Dabska tumor. Hobnail (Dabska reticular) hemangioendothelioma is the preferred term connecting Dabska-type hemangioendothelioma and reticular hemangioendothelioma due to their many overlapping features, particularly the hobnail endothelial cells. Dabska-type hemangioendothelioma was first described in 1969 [12] and is primarily a tumor occurring in the skin and subcutaneous tissues of infants and young children. Reticular-type hemangioendothelioma shares histological similarities with AH but occurs in adults and is characterized by long "reticular" vascular lumens lined by hobnail endothelial cells [13].

(5) Renal clear cell renal cell carcinoma: A small number of renal clear cell renal cell carcinomas are highly vascular but have small cells, making an initial diagnosis of a vascular tumor tempting. However, clear cell renal cell carcinoma is characterized by abundant blood sinuses without anastomosing or interwoven vessels. A small number of clear cell renal cell carcinomas may show significant shrinkage and degeneration, presenting with extensive acellular areas, which can be confused with some cases of AH. In such cases, careful search for residual small clear cells or additional sampling to find more typical areas is necessary. Additionally, immunohistochemistry is very helpful in differentiating the two. Clear cell renal cell carcinoma expresses PAX2, PAX8, CD10, and CAIX positively but does not express vascular endothelial markers such as CD34, CD31, and ERG.

(6) Hemangioblastoma: This primarily occurs in the central nervous system, most commonly in the cerebellum, but can occasionally occur in the kidneys. Hemangioblastoma is characterized by epithelioid stromal cells among abundant capillaries, with vessels lacking interwoven and anastomosing features. Immunohistochemical staining positive for α-inhibin can also aid in differentiating it from AH. According to current research, the biological behavior of AH is benign, with no reports of recurrence or metastasis.

## 6. Conclusion

Anastomosing hemangioma is a recently discovered rare, benign tumor with only a few reports in the literature and has not yet been included in the latest (fifth) edition of the WHO classification of soft tissue tumors. It commonly occurs in visceral organs, particularly the kidneys and adrenal glands. The primary and most important morphological feature is tightly packed, interconnected, and communicating capillary lumens. Since this interconnected and communicating growth pattern is characteristic of angiosarcoma, inexperienced pathologists may easily misdiagnose it as angiosarcoma. However, the most crucial differentiating point is that AH has a clear boundary and lacks an "infiltrative" growth pattern. Therefore, the clear boundary of AH plays a pivotal role in accurate diagnosis.

## Disclosure statement

The authors declare no conflict of interest.

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