

REVIEW PAPER

REVIEW OF RENAL ANASTOMOSING HEMANGIOMA WITH FOCUS ON CLINICAL AND PATHOLOGICAL ASPECTS

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Renal anastomosing hemangiomas (RAH) has been recently proposed as a new entity. In this article, we summarize the clinicopathologic features of this tumor. RAH usually develops on a background of end-stage renal disease. Macroscopically, tumors are well-defined and their cut surface shows mahogany brown spongy tissue with epicenter in the renal medulla. Tumors are usually small, but larger lesions are reported. On microscopic examination, the tumor consists of sinusoid-like vascular channels lined by cuboidal endothelial cells with occasional hobnail-like appearance of endothelial cells closely mimicking splenic sinusoids. Eosinophilic hyaline globules may be present in the cytoplasm of neoplastic endothelial cells. Extramedullary hematopoiesis containing erythroid precursor and megakaryocytes may be present in the vascular lumens. Immunohistochemically, endothelial cells are positive for CD31 and CD34, but negative for D2-40, GLUT-1 and HHV8. The surrounding stroma around endothelial cells demonstrates positivity for α smooth muscle action. To date, there are no studies on molecular genetic aspects of RAH. This tumor is indolent based on site and size of the lesion, partial or nephrectomy is sufficient as a therapeutic modality.

Key words: anastomosing hemangioma, kidney, pathology.

Introduction

The concept of renal anastomosing hemangioma (RAH) has been introduced recently [1]. However, the awareness about this tumor entity among pathologists, radiologists and urologists is still limited. In this article, we review features of RAH with focus on clinical and pathological aspects.

Epidemiology and clinical features

The patient's age ranges from 15 to 83 years with a mean age of 50 years. There is a male predominance (68.8%) [2]. Renal anastomosing hemangioma commonly occurs in end-stage renal disease [3, 4, 5, 6]. The main symptoms are hematuria and abdominal pain. Some asymptomatic tumors are found inciden-

tally upon investigations for unrelated disease [2, 6]. Ultrasound sonography usually shows a hypoechoic mass [7]. The computed tomography scan examination typically show heterogeneous enhancement of a solid mass [2, 3, 6, 7, 8, 9]. The magnetic resonance imaging demonstrates well-defined solid mass with homogeneously hyper-intense effect by contrast enhancement [10]. However, some lesions, particularly smaller ones represented incidental histological findings in nephrectomy specimens performed for end-stage renal disease.

Pathologic findings

Macroscopic findings

Macroscopically, tumors are well-defined but not encapsulated and on cut surface show a mahogany brown color with a spongy appearance (Fig. 1A, B). The tumor size ranges from 0.1 to 5.0 cm, but most lesions are small [1, 2, 3, 8, 10, 11]. Tumors are often located in the renal medulla and occasionally protrude into renal sinus fat. However, the cortical parenchyma or perinephric area can be involved as well [2, 3, 4, 5, 6]. Bilateral and multiple lesions have been documented [2, 3, 4, 5, 6].

Microscopic findings

Microscopically, RAH may show either a circumscribed uninodular growth or a multinodular pattern being composed of multiple lobules of tumor tissue. The tumor is composed of splenic sinusoid-like frequently communicating vascular channels lined by cuboidal endothelial cells [1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11] (Fig. 2A). The endothelial cells often display hobnail-like appearance [2, 3, 4]. Occasionally, eosinophilic hyaline globules are noted in the cytoplasm of neoplastic endothelial cells [3, 4]. Foamy macrophages or mast cells occasionally infiltrate the stro-

ma [6]. Extramedullary hematopoiesis containing erythroid precursor and megakaryocytes may be seen within the vascular channels [2, 3, 4, 6] (Fig. 2B). Although well circumscribed at low power, RAH frequently contains entrapped tubules with the periphery of the tumor and these can be best highlighted by pancytokeratin stain. Intravascular growth pattern may be observed (Fig. 2C).

Histochemical findings

The eosinophilic globules in the cytoplasm of neoplastic endothelial cells show diffuse and strong positivity for PAS stain [3]. Although foci of hemorrhages are frequent, stromal hemosiderin is not a common feature in RAH.

Immunohistochemical findings

The tumor cells are usually positive for the pan-endothelial markers CD31, CD34, factor VIII-related antigen, FLI-1 and ERG but negative for the lymphatic endothelial marker, podoplanin (D2-40), CD8, cytokeratin, epithelial membrane antigen, Melanosome (HMB45) and human herpesvirus 8 [1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11]. The surrounding pericyte cell population and stroma around endothelial cells express α smooth muscle actin [2, 7, 8]. The Ki-67 index in tumorous endothelial cells is generally very low [5, 8, 9].

Ultrastructural findings

Electron-dense globules measuring from 170 to 450 nm and primary lysosomes are observed in the cytoplasm of endothelial cells [3].

Differential diagnosis

Several diseases are listed in the differential diagnosis including capillary hemangioma, arteriove-

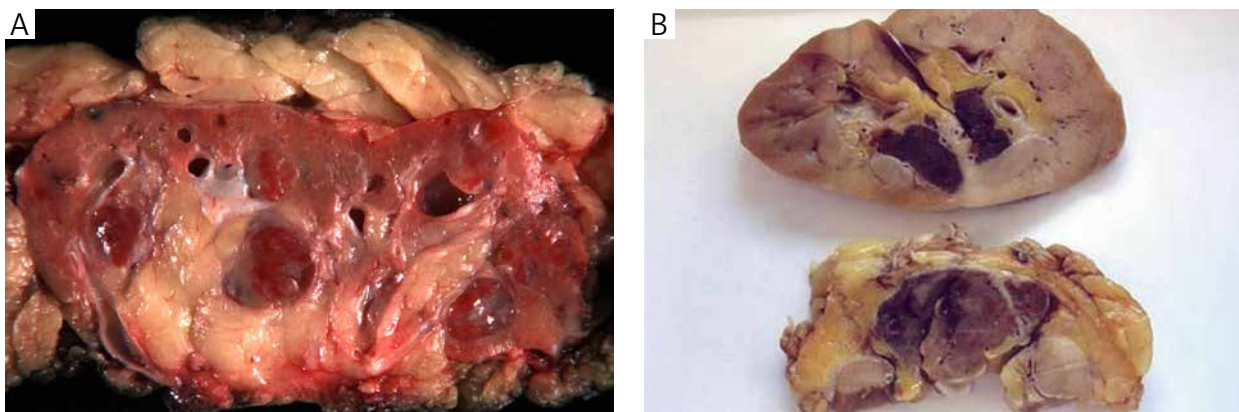


Fig. 1. Macroscopic findings. A) Before fixation. Gross image of anastomosing hemangioma showing numerous hemorrhagic circumscribed nodules distributed in the cortex and the medulla with extension into the surrounding fat. B) After fixation. The cut surface shows dark brown color

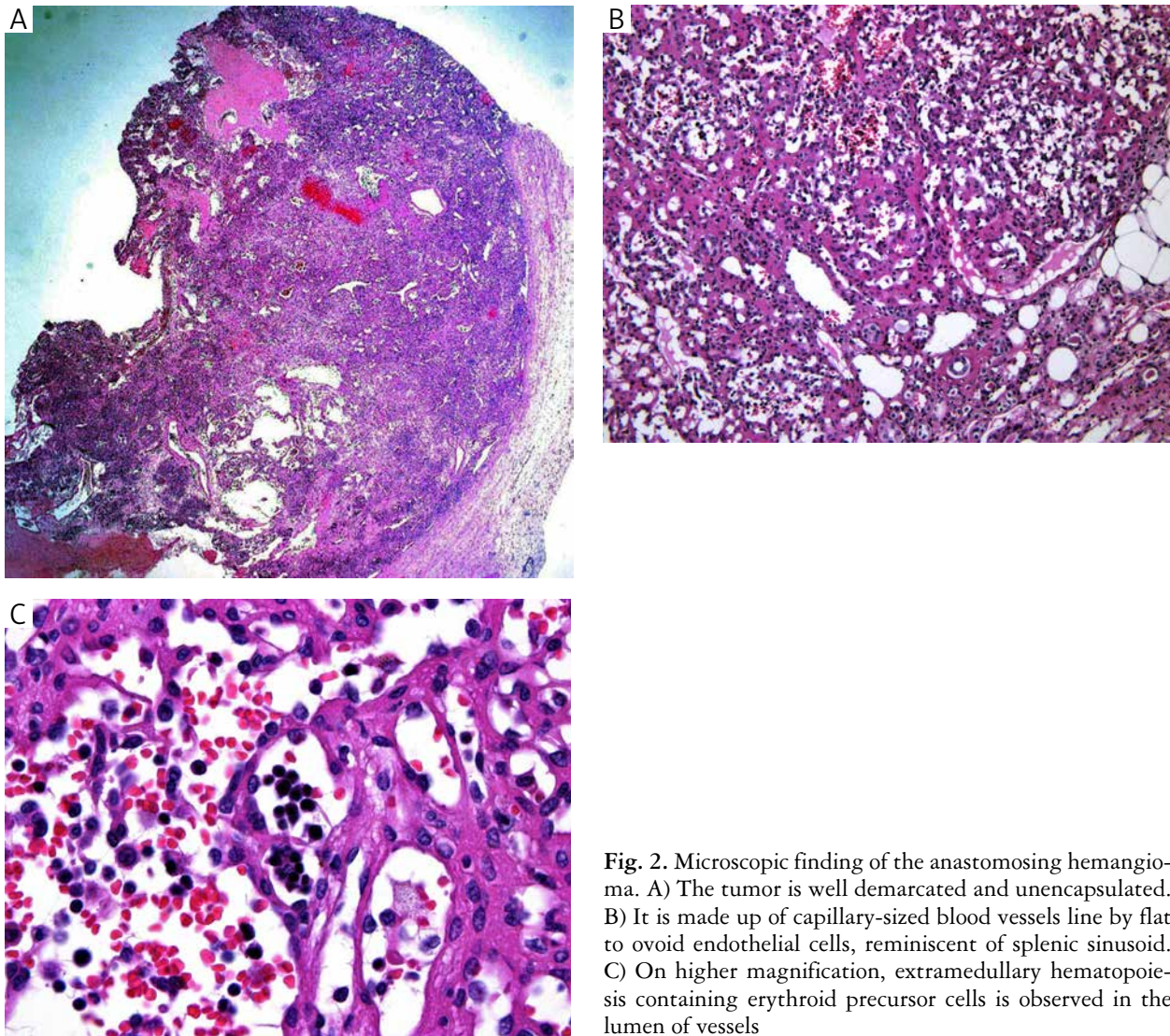


Fig. 2. Microscopic finding of the anastomosing hemangioma. A) The tumor is well demarcated and unencapsulated. B) It is made up of capillary-sized blood vessels lined by flat to ovoid endothelial cells, reminiscent of splenic sinusoid. C) On higher magnification, extramedullary hematopoiesis containing erythroid precursor cells is observed in the lumen of vessels

nous malformation, myopericytoma, glomus tumor, hemangioblastoma, Kaposi's sarcoma, angiosarcoma, sarcomatoid RCC, RCC with pseudoangiomatous (peliosis-like) changes and renal angiomyolipoma. In capillary hemangioma, tumor cells proliferate mostly in a distinctive lobular arrangement similar to capillary hemangiomas of skin and other sites [1]. In early lesions, vascular lumens are not prominent, and anastomosing pattern is generally absent. In arteriovenous malformation, a histological shunt between artery and vein can be highlighted by elastic Van Gieson stain [1, 11]. Myopericytoma is composed of medium-sized vessels, cuffed by concentric layers (onion skinning) of ovoid to bipolar spindle-shaped myopericytic cells [12, 13]. In glomus tumor, neoplastic cells are composed of sheets of small round to oval, uniform cells with distinctive cell borders set within a fibromyxoid background [14]. Hemangioblastoma consists of sheets of large polygonal cells traversed by arborizing thin-walled blood vessels [15, 16]. Although the prominent capillary vasculature of capil-

lary hemangioblastoma may closely mimic RAH, the lesional cells show characteristic xanthomatous clear cytoplasm and they express S-100 protein, but not endothelial markers. Presence of cytoplasmic hyaline globules in RAH if associated with increased cellularity might suggest Kaposi's sarcoma. However, Kaposi's sarcoma, in particular its visceral variant, occurs almost exclusively in HIV-patients and the tumor cells form compact fascicles entrapping slit-like vascular clefts. Immunohistochemically, they are uniformly positive for D2-40 and HHV8 [6]. Angiosarcoma probably is the most serious and frequently considered differential diagnosis of RAH. This is mainly due to the unusual communicating sinusoidal pattern and the limited familiarity with this lesion among pathologists. Angiosarcoma usually exhibits an infiltrative growth of mitotically-active endothelial cells with clear-cut atypia, nuclear enlargement, and endothelial tufting and multilayering [1, 8, 9, 10, 17]. The distinction from sarcomatoid RCC with angiosarcomatous differentiation is also important. The exclu-

sion of RCC component is crucial to establish the final diagnosis by extensive sampling of such rare cases [18, 19]. Angiomyolipoma has a fat component and tumor cells are immunoreactive for melanocytic markers HMB45 and/or Melan A [6, 20].

Therapy and clinical management

Nephrectomy was performed in the vast majority of previously reported cases [1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11]. However, if urologists and radiologists can suspect anastomosing hemangioma radiologically, partial resection or active surveillance may be feasible, if the risk of spontaneous tumor hemorrhage is judged as low. Needle biopsy for tumorous lesion cannot be recommended because this procedure carries the hazard of retroperitoneal or intra-renal bleeding in some cases.

Prognosis

This tumor pursues a benign clinical course. To the best of our knowledge, there is no report on recurrence, metastasis or malignant transformation to date [1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11]. Rare extension into thick-walled peripelvic veins seems not to affect prognosis and might indicate intravascular origin of some rare lesions (Agaimy *et al.*, unpublished data). As of to date, no recurrence or metastatic spread has been documented for this entity.

Future perspectives

Whether RAH is a variant of capillary hemangioma or not seems to be a controversial issue at the moment [1, 2]. Additionally, anastomosing growth pattern resembling splenic sinusoids seems to be a distinctive feature in hemangiomas arising in the kidney. However, it has been shown that RAH does not represent ectopic neoplasia derived from ectopic splenic tissue and it does not differentiate similar to or show phenotypic features of splenic sinusoids (the tumor cells being immunonegative with CD8) [2, 4]. Regarding the pathogenesis of RAH, there are no reports dealing with molecular genetic features. Therefore, further examination of RAH will be required in the future for a better understanding of etiology and biological behavior of this uncommon but distinctive vascular lesion.

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The authors declare no conflict of interest.

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