Clinicopathological features of unusual vascular lesions of the pelvis, retroperitoneum and colon in females: a report of five cases and review of the literature

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Summary

Vascular lesions comprise benign and malignant neoplasms as well as non-neoplastic conditions that may be located in various sites but only rarely in the pelvis or the retroperitoneum. In our study we describe five diverse and unusual cases of vascular lesions of the pelvis, retroperitoneum and colon in female patients: a case of retroperitoneal angiosarcoma, pelvic hemangioendothelioma, pelvic angiomyxoma, retroperitoneal lymphangioleiomyomatosis and a case of diffuse cavernous hemangiomatosis of the colon, with emphasis on their clinicopathological features and differential diagnosis. The recent literature on the subject is also briefly reviewed.

Key words: Vascular lesions; Pelvis; Retroperitoneum; Hemangiomatosis; Colon; Angiosarcoma; Lymphangioleiomyomatosis.

Introduction

Vascular lesions encompass a heterogeneous group of neoplasms and non neoplastic conditions, whose origin, symptomatology and biological behavior vary significantly. They may be benign or malignant, asymptomatic or symptom producing and located in various sites, but only rarely in the pelvis or the retroperitoneum. Vascular neoplasms arise from the endothelium, smooth muscle cells and pericytes of the arterial, venous or lymphatic pathways [1]. Their malignant counterpart is to blame for significant morbidity and mortality. However, benign vascular neoplasms of deep soft tissue structures or the colon may also cause severe symptoms or even death, secondary to complications including pulmonary embolism due to deep vein thrombosis, intestinal obstruction and perforation or massive rectal bleeding [1, 2]. Early diagnoses and optimal treatment of these lesions are therefore of the utmost importance for the avoidance of an adverse outcome. Their management however is a difficult, almost challenging task for the surgeon, not only because of the complexity and high level of complication risks of operative procedures and the detailed preoperative planning required, but also because of the high recurrence rate [3]. Pathological diagnosis may also be demanding and often requires the use of immunohistochemistry, because of the extreme diversity of vascular lesions.

In our study, we present five cases of unusual vascular lesions of the female pelvis, retroperitoneum and colon, and discuss the clinicopathological and immunohistochemical features, with emphasis on the differential diagnosis. The recent literature on the subject is also briefly reviewed.

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Presentation of clinicopathological and immunohistochemical features of our case material

Case 1

A 39-year-old woman was admitted to our hospital complaining of lower abdominal pain of one month's duration. Speculum examination revealed a mass protruding under the left vaginal wall. The gynecological examination revealed a normal sized uterus displaced to the right and normal adnexae. Physical examination showed bilaterally enlarged lymph nodes. Computed tomography (CT) of the pelvis suggested the presence of a reproperitoneal mass, consisting of both solid and cystic elements, which was pressing the bladder and the vaginal vault and displacing the uterus to the right. An exploratory laparotomy was performed which revealed that the left pelvic wall was occupied retroperitoneally by a dark colored mass which extended from the middle of the psoas muscle to the posterior surface of the pubis, enveloping the hypogastric and external iliac vessels, reaching to the pelvic floor and occupying the space between the pubis and the bladder, up to the median line. No attempt to remove the mass was made because of the danger of sectioning the large vessels. Frozen section biopsy of the tumor showed a malignant tumor consistent with a high-grade carcinoma or most probably an epithelioid angiosarcoma. The enlarged inguinal nodes were sampled. The examined specimen consisted of three right inguinal lymph nodes and two left iliac lymph nodes with a diameter ranging from 0.8-2 cm. The consistency was firm and the section surface red and sponge-like. Histological examination showed extensive infiltration of all examined lymph nodes by large, epithelioid malignant cells (Figure 1) arranged in trabecular,

solid, grandular and papillary structures with cytoplasmic eosinophilic globules. The nuclei were large with prominent nucleoli. There were many slit-like spaces covered by the neoplastic cells and focally filled with erythrocytes. The connective tissue between the neoplastic structure was myxoid and loose. An immunohistochemical study was performed. The neoplastic cells were immunoreactive for CD31, CD34, factor VIII and EMA and negative for S100, MK1, melane, HMB45, CEA and LCA. Based on these findings the diagnosis of an epithelioid angiosarcoma was definitively made, and adjuvant radiotherapy was proposed but the patient refused any therapy. The tumor recurred one year after surgery and the patient was lost to follow-up afterwards.

Case 2

A 52-year-old woman was admitted to our hospital due to a feeling of abdominal weight over a 5-month period accompanied by uterine bleeding. At palpation a painless mass in the left lower quadrant of the abdomen was found.

CT examination of the abdomen and pelvis revealed a uterine leiomyoma measuring 14.5 x 20 cm. Another mass was located in the right retroperitoneal space that extended from the pelvis to the lower pole of the right kidney. It was anterior to the right psoas muscle, the inferior vena cava and the aorta and was cystic with homogeneous water-density content giving the impression of an ovarian mass. In addition, in the left kidney there was an angiomyolipoma. There was no ascites. Chest radiography was normal.

At exploratory laparotomy a total hysterectomy was performed. The retroperitoneal mass had a gelatinous consistency. It was not adherent to the adjacent tissues so it was removed easily.

Pathological examination confirmed the diagnosis of uterine leiomyoma. The retroperitoneal specimen was a multiloculated mass 18 x 8 x 5 cm in size. On the external surface lobules of fatty tissue were observed. The cystic spaces, measuring 0.5-3.5 cm in their greatest diameter were filled with serous or sanguineous fluid. The thickness of their walls was 0.3-0.7 cm.

Histologically there was an irregular cystic pattern lined by endothelial cells, mostly flattened. The walls consisted of fibrous tissue and smooth muscle fibers (Figure 2). Dense lymphocytic infiltration was observed focally. An immunohistochemical study was undertaken to define the nature of the tumour. Positive reactivity to factor VIII, vimentin and smooth muscle markers, while negative for keratin, confirmed the diagnosis of lymphangiomyoma.After the diagnosis CT of the thorax was performed without showing any abnormality.

Three years after surgery the patient is well without any recurrence.

Case 3

A 40-year old woman was admitted to our hospital for a programed follow-up, one year after the removal of a pelvic hemangiopericytoma. CT examination of the abdomen and pelvis revealed two separate cystic masses, one in the pelvis and the other in the retroperitoneal space, measuring 5 and 7 cm, respectively. These findings gave rise to the suspicion of a recurrence and led to the performance of an exploratory laparotomy. During the procedure the two masses were found and removed intact. The left adnexa was also removed due to the presence of a hemorrhagic nodule, adjacent to the salpinx. Hemorrhagic nodules were also found in the surface of the greater omentum which was excised and sent to the pathology laboratory in two segments. On macroscopic examination the two masses measured 8 and 10 cm in the largest diameter, were partly cystic and filled with blood. The hemorrhagic nodules were of the same consistency. Histologically the tumors consisted of highly cellular areas with spindle-shaped cells of varying size, mild cellular atypia and rare mitotic activity (less than 0-1MF/10HPF), and areas with a cystic pattern, simulating vascular spaces, either sphenoid or cavernous, which were either filled with blood or thrombosed. The nodules shared the same cystic pattern. The adnexa was free of neoplastic infiltration. Immunohistochemistry was positive for vascular markers (CD34, CD31, factor VIII) and negative for keratin. Reticulin staining did not show the typical distribution of hemangiopericytoma. The final diagnosis was spindle cell hemangioendothelioma.

The tumor recurred within a year after surgery and the patient was lost to follow-up after that.

Case 4

A 38-year-old woman was admitted to our hospital for re-evaluation of a mass which was found in the right side of the minor pelvis one year before during cesarean section. The mass was soft and initially considered as an hematoma. Ultrasound (US) and CT showed an increase in the size of the tumor so exploratory laparotomy was performed. During the procedure a soft retroperitoneal mass, measuring 15 x 12 x 6 cm was found in front of the intrapelvic part of the right ureter, displacing the uterus and the rectum. The lower end of the tumour was in close contact to the pelvic ground. The mass was extremely soft and fragile but circumscribed and was easily removed from the adjacent structures without rupture of the surrounding capsule. The postoperative course was uneventful.

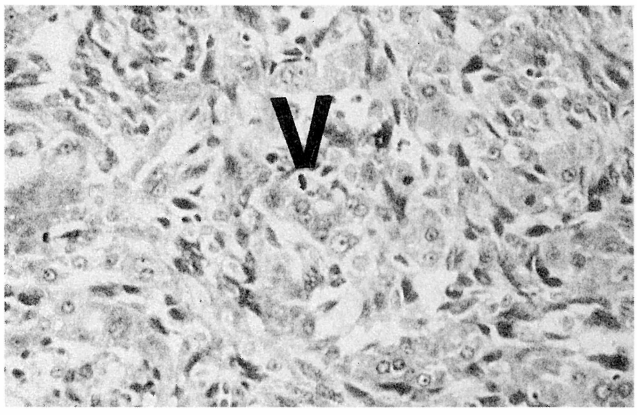
Pathological examination showed that the tumor had a polycystic structure and a focal myxomatous eosinophilic consistency. Histologically, a loose myxomatous eosinophilic background was found containing spindle-shaped cells with enlarged, hyperchromatic, atypical and focally lobular nuclei (Figure 3). Mitoses were not observed. Extensive cystic degeneration with areas of increased cellularity and hyaline degeneration of the stroma was observed. A rich vascular network, ranging from capillary to medium sized vessels was found throughout the whole tumor. In the periphery of the tumor a pseudocapsule was formed from contracted fibers of connective tissue. The neoplastic cells infiltrated the tumor margins. The consistency and location of the tumour, as well as the absence of fibroblasts, polymorphy and neural differentiation, favored the diagnosis of angiomyxoma. Immunohistochemistry for S-100 was negative. Factor VIII staining was positive for vessels, while negative for tumor cells. Positive perivascular staining was also observed for actin, desmin and vimentin. The final diagnosis was angiomyxoma of the pelvis.

The patient is well five years after surgery without any recurrence.

Case 5

A 39-year old woman came to the out one patient department of our hospital, because of a vague abdominal pain of a month's duration. Clinical examination showed a sensitivity in the right lower abdomen. Subsequent ultrasound examination of the upper abdomen revealed the presence of hemangiomas in the right liver lobe. CT of the abdomen showed a tumorous mass located in the right iliac fossa, measuring 5 x 5 cm as well as

Fig. 1



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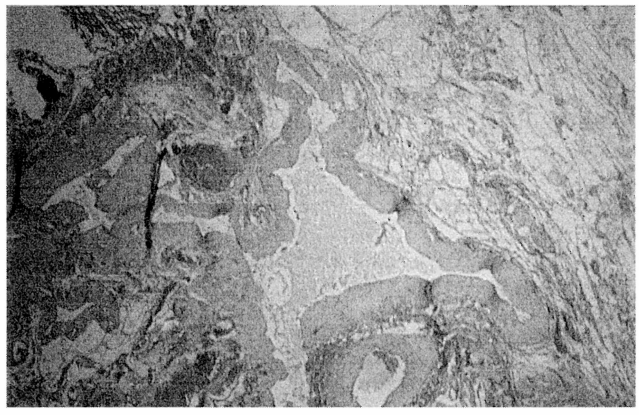
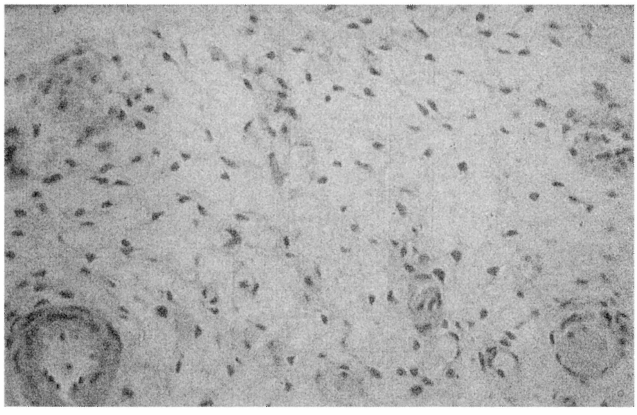


Fig. 3



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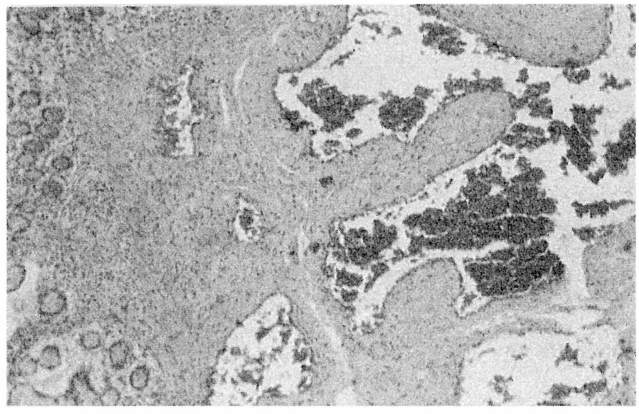

Figure 1. — Histological section of epithelioid angiosarcoma. Arrow points at a neoplastic cell cluster in fibrous stroma (H-E x 250).
Figure 2. — Histological section of lymphangiomyoma showing cystic spaces with a fibromuscular wall (H-E x 25).
Figure 3. — Histological section of angiomyxoma showing spindle cells in angiomatous stroma (H-E x 100).
Figure 4. — Histological section of colonic wall showing angiomatous elements into the muscle wall (H-E x 25).

multiple small liver hemangiomas. These findings led to an exploratory laparotomy. During the procedure, an extensive right hemicolectomy was performed. The specimen was sent to our pathology laboratory, and presented grossly a reddish-hemorrhagic tumor of the ileocolic valve level, measuring 5 x 4 cm. The tumor had a sponge-like consistency and infiltrated the whole wall thickness extending in the surrounding fatty tissue. The mesocolic and mesenteric fat, as well as the greater omentum, presented multiple hemorrhagic nodules measuring 0.6-1 cm in the largest diameter. Microscopic examination led to the diagnosis of diffuse hemangiomatosis, of cavernous type (Figure 4) of the colonic and enteric wall with concomitant lymphangiectatic lesions of the submucosa and infiltration of the mesocolic and mesenteric fat and the greatest omentum. No mitotic activity, remarkable cellular and nuclear atypia or necrosis of the lesion were observed.

The patient is well 18 months after surgery.

Discussion

Vascular tumors of the pelvis and the retroperitoneum are extremely rare neoplasms usually detected with the use of imaging techniques such as CT MRI or angiography, either as accidental findings or during the investigation of accompanying symptoms [1]. Due to the extreme diversity of these lesions, their clinicopathological features as well as the diagnostic and therapeutic approach are studied separately.

Retroperitoneal angiosarcomas are extremely rare tumors occurring mainly in patients aged between 60 and 70 years [4-6]. They belong to the group of deep soft tissue angiosarcomas which are generally characterized by aggressive biological behavior [7]. Surgical excision of the tumor remains the treatment of choice, although radiotherapy given as adjuvant to surgical therapy may provide local control or improved quality of life [1]. Although chemotherapy was generally considered in the past as ineffective in the management of angiosarcomas, recent studies reveal that administration of certain chemotherapeutic agents (such as paclitaxel and doxorubicin) in angiosarcoma patients – and especially those with unresectable disease – may result in major responses or even complete remission [8, 9]. Metastases occur early in these patients and account for the poor prognosis of these neoplasms [1]. Our reported case of a retroperitoneal angiosarcoma presented with lymph node metastases and was diagnosed during the evaluation of lower abdominal pain. Pathological examination of the resected inguinal and iliac lymph nodes and frozen section biopsy of the tumor revealed a high-grade neoplasm forming

compact sheets of large epithelioid cells suggesting carcinoma. The presence of papillary structures in rugged spaces filled with blood and especially the presence of eosinophilic globules in the neoplastic cell cytoplasm suggested the diagnosis of epithelioid angiosarcoma. According to Vuletin *et al.,* these globules indicate the presence of an angiosarcoma [10]. For a differential diagnosis between high-grade carcinoma and epithelioid angiosarcoma immunohistochemistry was applied. The results excluded the presence of carcinoma as well as the possibility of other, less likely diagnoses including metastatic large cell lymphoma and malignant melanoma.

Lymphangioleiomyomatosis (LAM) is a relatively rare condition that represents an hamartomatous proliferation of muscle cells causing gradual obstruction of small airways, lymphatics and vasculature. It most commonly occurs in the lungs and the mediastinum, and exclusively in reproductive age women. Cases with involvement of the retroperitoneal lymphatics, with or without subsequent development in the lungs are only rarely reported [11, 12]. Pathological examination in conjunction with immunohistochemistry is essential for the establishment of the diagnosis in most cases of abdominal LAM. The proliferated smooth muscle cells are arranged in short fascicles around narrow, branching, endothelium-lined spaces. There is positive staining for muscle-specific actin, desmin and HMB-45 in all proliferating cells. In our case both a uterine leiomyoma and an angiomyolipoma were also present. A relationship between LAM and angiomyolipoma has been previously suggested and explained on the basis of their common hamartomatous histogenesis. Others believe that LAM is a partial presentation of "forme fruste" of tuberous sclerosis, because they both manifest the same pulmonary lesions and may have concomitant angiomyolipomas of the kidneys [13-15]. The coexistence of a leiomyoma in our case may be an indication of smooth muscle proliferation etiologically linked to a genetic alteration also predisposing to the development of LAM and angiomyolipoma. The treatment of choice for LAM is surgical excision of the mass [16]. Lymph node irradiation has been also performed. The presence of steroid receptors on these lesions has also encouraged oophorectomy and administration of tamoxifen and progesterone as treatment options with some success [17, 18].

Our third reported case was an angiomyxoma of the minor pelvis. This neoplasm is a type of myxoma with a particular biological behavior, characterized by slow growth and frequent relapses. It was only recently described by Stepher and Rosai, who also proposed the term "aggressive angiomyxoma" [19]. These tumors are commonly located in the soft tissues of the pelvic and perineal area of women, although cases in men have also been reported [1]. They are often misinterpreted as bartholin cysts, perineal abscesses and hernias [20, 21]. CT scan, MRI or angiography are necessary for the detection of the tumor and preoperative planning [1]. When located in the deep soft tissue structures (pelvis, abdomen) they may not be diagnosed unless they reach an extremely large size since they are asymptomatic. Such cases of giant angiomyxomas of the pelvis have been previously reported [7, 22, 23]. The high rate of recurrence (> 50%) of these tumors is often due to subtotal excision of the mass. Indeed, local infiltration and ill-defined borders are common findings and indicate the importance of wide surgical margins of excision [20, 24]. The surgical margins were also infiltrated in our case. Pathological examination of the tumor revealed the typical features of angiomyxoma: loose myxomatous stroma with spindle-shaped cells, cystic degeneration and an abundance of thick-walled vessels of varying size. The absence of mitoses and staining results were essential in the differential diagnosis from other mesenchymal tumors such as embryonal rabdomyosarcoma, pseudosarcomatous vaginal fibrous polyps and tumors of fibriohistocytic or nervous origin, benign and malignant.

The fourth of our reported cases was a spindle cell hemangioendothelioma which was preoperatively considered as a possible local recurrence of a pelvic hemangiopericytoma, surgically removed one year before. Spindle cell hemangioendothelioma occurs in children and young adults, with a male predominance, and is more commonly located in the subcutaneous tissue of the distal extremities than of the pelvis [1]. According to Rosai and Ackerman, although in previous classifications it has been described as a low grade angiosarcoma and a lesion related to a vascular malformation, it is currently classified as a benign endothelial neoplasm [25]. Even when it involves an extensive area, as in our case, it does not metastasize. On the other hand, "hemangiopericytoma" is a questionable term, which has been used – and possibly misused – for the description of tumor types composed of cells with pericytic features or with a hemangiopericytoma-like pattern [25]. The biological behavior of these tumors varies significantly [25]. Our patient was a 40-year-old woman with vascular nodules in the retroperitoneal space, the pelvic cavity and the greater omentum. Microscopic examination and the results of immunohistochemistry were strongly suggestive of a vascular neoplasm of mesenchymal origin, most probably a spindle cell hemagioendothelioma. The diagnosis of hemangiopericytoma was excluded from the results of reticulin staining and the absence of nuclear atypia and mitotic activity. It is possible that the initial diagnosis of hemangiopericytoma in our case was inappropriate, and the lesion represented a local recurrence of a spindle cell hemangioendothelioma. Indeed, the latter tumor is characterized by a high rate of recurrence.

Gastrointestinal hemangiomatosis is a term referring to the extensive presence of hemangiomas throughout the gastrointestinal tract, with or without concomitant development in the skin, and may be part of a syndrome (such as blue rubber bleb nevus syndrome, Klippel-Trenaunay-Weber syndrome, Maffucci's syndrome, Osler-Weber-Rendu syndrome, Kasabach-Meritt syndrome, Hippel-Lindau syndrome, diffuse neonatal hemangiomatosis and Proteus syndrome) [26-29]. The colon is the second most common site of this lesion. Diffuse hemangiomatosis of

the colon is an extremely rare disease most commonly found in young adults, children or neonates [26, 30-32]. The intestinal wall, the mesentery, the retroperitoneum as well as solid abdominal organs such as the liver may be diffusely involved [30]. Although benign in nature, this lesion usually presents with severe rectal bleeding, which may be massive and life-threatening. Other presenting symptoms include bowel obstruction and perforation, chronic anemia due to insidious blood loss, abdominal pain or even congestive heart failure [26-30]. Some authors report an equal incidence for both sexes, while others support that men are more likely to be affected [32, 33]. Imaging techniques such as conventional radiography, barium enema or angiography often lead to non-specific findings [27, 28, 34, 35]. Three-dimensional CT colonography is a more sensitive diagnostic technique that offers, according to a recent report, significant advantages in the preoperative evaluation of colonic hemangiomatosis, but still largely depends on the presence of phleboliths, which may, as in our case, be absent [31]. On the other hand, endoscopic findings may be obscured by the presence of inflammatory changes and lead to an unwarranted biopsy, possibly resulting in profuse bleeding [31].

Colonic hemangiomas are considered of hamartomatous rather than neoplastic origin and arise from the submucosal vascular network [33]. They grossly present as polypoid masses, or have an infiltrative pattern and may be of the cavernous or capillary type [30]. Cavernous colonic hemangiomas represent the large majority (about 80%) of all reported cases, typically involve the whole intestinal wall and infiltrate the surrounding tissues or even the adjacent organs [31]. They are composed of large vascular channels filled with blood and lined by endothelial cells [31]. Degenerative changes may also be found and include calicification, hyalinization and thrombosis from inflammation and stasis [30]. The latter results in the formation of clustered pleboliths, which are considered as a pathognomonic characteristic of hemangiomas in radiography, especially when found in young patients and in uncommon locations [30].

In our case, the patient complained only of non-specific abdominal pain, without rectal bleeding which is considered the leading symptom. In addition, no pleboliths were demonstrated in abdominal radiography. Despite the infiltrative pattern of angiomatous growth of this lesion, the exclusion of a primary or secondary malignancy is easily established with pathological examination, which fails to reveal any atypia, mitotic activity or necrosis.

Conclusion

In conclusion, pathological examination in conjuction with immunohistochemistry is essential for the establishment of the final diagnosis, since the clinical presentation and diagnostic imaging findings of vascular lesions may occasionally be far from typical and lead to misdiagnosis. Differential diagnosis of vascular lesions should be thorough and careful. Most importantly, a safe distinction between a benign and a malignant vascular tumor should be made. However, in all cases surgical removal of the tumor should be performed with wide surgical margins, because of the common tendency of these lesions to recur.

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