Detection and management of retroperitoneal cystic lesions: A case report and review of the literature

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Abstract. The identification of cystic lesions within the retroperitoneal space is a rare event that poses clinicians the challenge of a difficult diagnosis and disease management. Retroperitoneal cystic lesions account for a group of lesions that range from common benign lesions (e.g., lymphoceles developing as a surgical complication) to rare aggressive malignant neoplasms. Currently, in the majority of cases, image-guided procedures allow for a pathological diagnosis to be achieved in these challenging lesions, thus offering the chance of an appropriate treatment; however, the overall clinical assessment of retroperitoneal cysts is highly demanding. The present study reports the management of a representative clinical case, presenting with a voluminous cystic mass able to dislocate cave vein, whose diagnosis was preceded by a deep vein thrombosis. Computed tomography-scan and ultrasound guided percutaneous drainage were performed to achieve the diagnosis. Following the discussion of the current case report, a review of the pathological and radiological characteristics of retroperitoneal cystic lesions is presented.

Introduction

The present review will discuss the cystic lesions of the retroperitoneum, an uncommon and heterogeneous group of lesions that originate behind the retroperitoneum. Lesions that occur in the retroperitoneal space are divided into solid masses and cystic lesions, as previously described, and classified (1,2). The precise incidence of these lesions is difficult to define, as the neoplastic lesions are of rare occurrence and the non-neoplastic lesions, such as postsurgical lymphoceles, are more frequent (1,2). Even if rarely identified in the retroperitoneal space (1,2), cystic lesions are highly challenging regarding the clinical presentation, the diagnostic and the choice of therapeutic approaches (3). Similar masses may be discovered during routinely performed examinations, including abdominal sonography, or may present with symptoms associated with compression of other bodily structures. Computed tomography (CT) scan and Nuclear Magnetic Resonance (NMR) represent the standard imaging approaches to evaluate these lesions (1). Due to anatomical complexity of the retroperitoneal space, the diagnostic procedures may include ultrasound-guided drainage or surgical removal. To introduce the clinical diagnostic approach and management, the present study will discuss a representative patient who presented with a cystic retroperitoneal mass.

Case report

A 68-year-old man was admitted to the Emergency Department of San Luigi Hospital (Orbassano, Italy) in December 2014 with abdominal discomfort, nausea, vomiting and oedema of the left inferior leg. The patient had a past medical history of hypertension, diabetes mellitus, hepatic steatosis and colelithiasis, with a recent (~three months prior to admission) diagnosis and treatment for a deep venous thrombosis of the left leg. No previous history of trauma or pancreatitis was reported. No significant abnormalities were observed in blood tests (normal complete blood count; normal renal and hepatic functions; normal pancreatic enzyme and lactate dehydrogenase levels). As part of the original examination, an abdominal ultrasound was performed revealing a voluminous cystic lesion (maximum diameter, 14 cm) in the abdomen. The patient was transferred to the Division of Internal Medicine (San Luigi Hospital, Orbassano, Turin, Italy) for appropriate diagnosis and treatment. A computed tomography (CT) scan was performed, which confirmed the presence of a voluminous retroperitoneal cystic lesion (diameter, 15x7.5 cm) in the perivascular retroperitoneum, occupying the space between the aorta and inferior vena cava, causing its compression and lateral deviation (Fig. 1A). Three-dimensional rendering of the CT scan image allowed the extension of the lesion and its interaction

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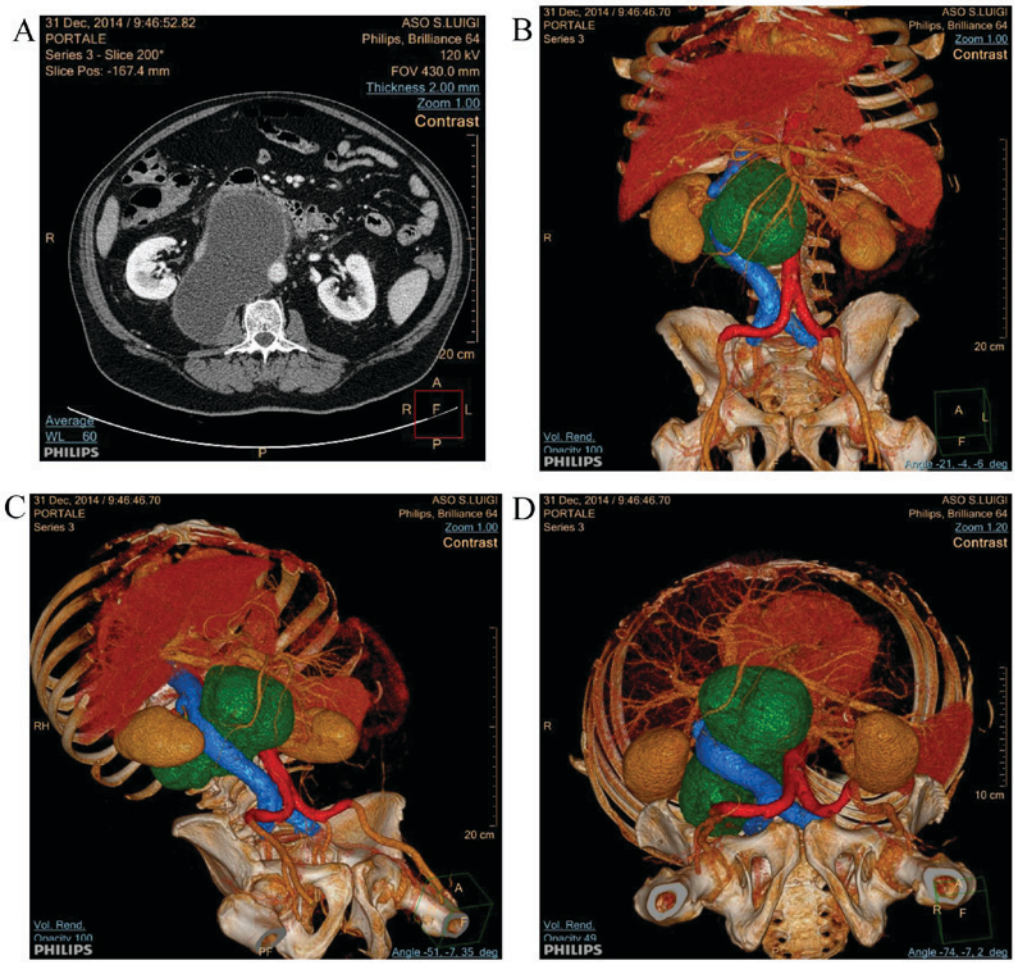

Figure 1. Retroperitoneal lesion. (A) Computed tomography scan; (B-D): Three-dimensional rendering of the retroperitoneal lesion (green) at different angles, showing clear dislocation of the vena cava.

with vessels to be described more clearly (Fig. 1B-D). The lesion appeared isolated from the pancreas and the posterior pararenal space, where it almost reached the psoas muscle. No other pathological repertoires were found at the CT scan. Based on the CT scan findings, the patient underwent ultrasound-guided drainage of the lesion. A total of 800 ml of clear liquid was removed, causing a marked improvement in the patient's level of discomfort. The liquid was examined to assess the levels of amylase and lipase, to perform microbiological analysis and to exclude the presence of neoplastic cells. All tests were found to be negative. In the absence of any CT scan elements suggestive of the neoplastic origin of the cystic lesion, and due to the lack of any significant abnormalities in the liquid examinations, the patient was discharged and a close follow-up of the retroperitoneal space was performed by abdominal ultrasound and CT. After a 3-month follow-up period, the patient did not present with any signs of relapse (the abdominal CT confirmed the absence/disappearance of any lesions), supporting the non-neoplastic origin of the cystic lesion.

Discussion

The present case prompted a review of the diagnostic approaches and clinical management of retroperitoneal cystic lesions. In order to describe these lesions, we here summarize the most comprehensive classification and review published by Dr Yang and colleagues (1). These masses arise within the retroperitoneal space, which is a complex region located behind the peritoneum (1,4,5). This region houses few organs (such as the adrenal glands and kidneys, portions of the duodenum, pancreas and colon, and the esophagus), major vessels (the aorta and inferior cava vein), deep lymphatic vessels and structures, ligaments and fatty tissues (6). Among those diseases that originate in the retroperitoneal space, neoplasms are uncommon (2). Although they are rare, retroperitoneal masses are a challenging dilemma to clinicians, either due to the lack of specific symptoms or the difficult diagnostic approach. Almost 80% of retroperitoneal masses display malignant features, but no clear diagnostic flow charts have been proposed thus far. As reported in the present clinical case, neither radiological imaging or drainage are able to clearly rule out a malignant nature, imposing the challenging decision to propose surgical diagnostic investigations of the lesion vs. an appropriate radiological follow-up. Following on from the present case report, the current study reviews the biological, clinical and radiological features of retroperitoneal cystic lesions.

As reviewed and classified elsewhere (1), benign neoplastic lesions include neoplasms with biologically benign behavior, including cystic lymphangioma, cystic teratoma,

mucinous cystadenoma, pseudomyxoma retroperitonei, cystic mesothelioma, tailgut cysts, epidermoid cysts and bronchogenic cysts. Cystic lymphangiomas are generally benign congenital malformations characterized by abnormal lymphatic tissues unable to develop normal lymphatic vessel communications (7). Cystic lymphangiomas are more common in men and can occur at any age, even though ~90% are found in children <2 years of age (7-10). Frequently, these lesions involve the head and the neck (11), while they are unusual in retroperitoneal locations (1,12-15). When they develop during the first two trimesters of pregnancy, cystic lymphangiomas are associated with genetic disorders such as Noonan syndrome (16) and chromosome 21 trisomy (17). By contrast, acquired forms may result from trauma, inflammation or lymphatic obstruction. Clinically, most cystic lymphangiomas result only in a soft, slow-growing mass, but they can eventually compress their surrounding structures, causing significant clinical consequences (1,18). Generally, cystic lymphangiomas are unilocular or multilocular cysts that contain a clear or milky fluid, with a single flattened endothelial layer lining them. Upon NMR, cystic lymphangioma typically demonstrates low T1 and high T2 signal intensity, with no significant enhancement on post-contrast images (1,19). Wall calcifications are rare.

A cystic teratoma is a neoplasm composed of different tissues that are not native to the region where it is generated. The neoplasm is composed of tissues that are derived from three germinal layers: lThe endoderm, the mesoderm and the ectoderm (20-22). These lesions can be classified as mature (benign) or immature (malignant), with cystic lesions being more likely to be benign and solid lesions generally associated with an immature and malignant behavior. Cystic teratomas generally arise within the gonadal and sacrococcygeal regions of adults and children, while they are much more infrequent at the retroperitoneum (23). The majority of cases are asymptomatic or associated with non-specific manifestations. The definitive diagnosis requires surgical excision of these lesions, with a curative intent in the case of mature (benign) teratoma (24). At the histopathological analysis, teratomas are easily recognized due to the mixture of mature components, including bone, squamous epithelium, glandular epithelium, stroma and muscle cells. At CT scan, a mature teratoma of the retroperitoneum manifests as a well circumscribed mass containing a fluid component, adipose tissue and calcifications (25). The presence of hypo-attenuating fat tissues within the cyst is considered highly suggestive of a cystic teratoma.

Mucinous cystadenomas are homogenous and well-defined unilocular cysts found in women with normal ovaries (26-29). The pathogenesis is unclear, although it has been suggested that these lesions arise from invagination of the peritoneum, with consequent mucinous metaplasia and cyst formation. The mucinous cystadenoma cysts are lined by a single layer of tall columnar epithelial cells, with pale cytoplasm and basal nuclei (30-32). Notably, even if benign per se, these lesions could transform into malignant cystadenocarcinoma (33-36). Upon CT scan, mucinous cystadenoma does not display specific characteristics over the other cystic retroperitoneal masses (37). Due to the potential differential diagnosis with other ovarian lesions, to rule out malignant lesions, exploratory laparotomy with complete excision of the cysts should always be proposed (38).

Pseudomyxoma retroperitonei is a rare clinical condition that is often associated with the development of mucinous ascites as the consequence of a rupture of mucinous lesions (39,40). These lesions generally originate from the appendix and ovary, and, more rarely, from other primary sites, including the colon, stomach, pancreas and urachus (41). Pseudomyxoma of the retroperitoneum, also known as pseudomyxoma retroperitonei and pseudomyxoma extraperitonei, is extremely rare (42,43). Clinically, pseudomyxoma retroperitonei usually presents with abdominal or lumbar pain and the presence of a palpable mass. Occasionally, the formation of abscess, with a high fever, or discharge is possible and weight loss can also be observed. At CT, pseudomyxoma retroperitonei appears as masses that are usually multicystic and are characterized by the presence of septa or thick walls. Calcifications, either single spot or curvilinear, may be discovered (1).

Although the name evokes an image of malignant cancer, cystic mesotheliomas are mostly benign neoplasms that originate in the serous lining of the pleural, pericardial or peritoneal spaces (44). Peritoneal mesotheliomas affect mainly young women, and are characterized by cysts of variable size and number, with a single layer of benign mesothelial cells. With regard to causative factors, this lesion appears to be unrelated to asbestos exposure. The life expectancy of affected patients is normal due to the low occurrence of malignant transformation (45-47). The radiological appearance may be indistinguishable from lymphangiomas and other retroperitoneal cysts, with the lesions generally appearing as thin-walled multilocular cysts (48,49).

Tailgut cysts are rare congenital malformations that may present in the presacral space. The tailgut normally regresses by the 6th week of gestation, but if the mucous-secreting remnants fail to regress, a tailgut cyst is formed. These lesions are more frequently identified in middle-aged women (50), are generally asymptomatic and are only occasionally associated with symptoms due to compression (51,52). The major complication of tailgut cysts is the infection of the cysts themselves, leading to a condition that mimics perianal or pelvic abscesses (53). During pathological examination, tailgut cysts are typically lined by different types of epithelium, including columnar, transitional and squamous epithelium. The identification of glandular or transitional epithelium aids in the differential diagnosis with epidermoid and dermoid cysts. These lesions are mostly benign, but certain cases of malignant transformation have been reported (54). CT examination shows a well-defined multicystic mass, with values of density varying from that of water to that of soft tissues (55). On NMR, a tailgut cyst typically demonstrates low signal intensity on T1-weighted images and high signal intensity on T2-weighted images (56).

Epidermoid cysts are frequently occurring benign cutaneous tumors, however, they also rarely present as retroperitoneal cysts (57). One case has even been reported in the round ligament (58). At the histological analysis, the hallmark of epidermoid cysts is the presence of a squamous epithelium, with a mixture of desquamated debris, cholesterol, keratin and water. Upon CT scan, these lesions appear as unilocular cysts. The location in the presacral space can facilitate the differentiation from other pelvic masses (59). Notably, these lesions can be

better identified by MRI as hypo-intense on T1-weighted imaging and hyper-intense on T2-weighted imaging.

The bronchogenic cyst is a spherical cyst that originates as an embryonic out-pouching of the foregut or trachea during the fifth week of gestation. The cyst is generally found in the mediastinum or lungs and is usually asymptomatic. The major risk associated with these lesions is infection. However, it should be noted that these lesions may migrate to an atypical location. The occurrence of such cysts inside the retroperitoneal space is extremely rare, with a consequent highly challenging differential diagnosis (60-62). Upon histopathological analysis, bronchogenic cysts are mainly unilocular or oligolocular, with a pseudostratified ciliated columnar epithelial lining, and mucoid material, bronchial glands, smooth muscle and cartilage. Upon CT scan, bronchogenic cysts usually present as spherical lesions, with well-circumscribed smooth or lobulated borders. These lesions lack enhancement following intravenous contrast administration, while the occurrence of hyperattenuation should suggest concomitant hemorrhage or proteinaceous secretions inside the lesions (63). On MRI, bronchogenic cysts usually display an intermediate to high signal intensity on T1-weighted images and an high signal intensity on T2-weighted images (64,65). Even if generally asymptomatic, these lesions could eventually transform into malignant lesions (66), and should therefore always be removed (60).

Malignant neoplastic cysts include neurilemmoma, paraganglioma (only rarely cystic) and perianal mucinous carcinoma. Neurilemmoma is mostly a benign encapsulated tumor of the nerve sheath. This tumor is rarely found in the retroperitoneum, where it represents 0.3-3% of all Schwannomas. This disease presentation peaks at the fifth to sixth decades and can occur as part of neurofibromatosis type 2. While it is commonly a solid tumor, neurilemmoma can also undergo cystic degeneration, therefore posing as a cystic lesion (67-69). The cellular origin of this tumor is the Schwann cells, which originate from the neural crest. The lesions are generally well encapsulated, eccentric from their parent nerve, with a unique histological presentation that is characterized by Antoni A and B cells, and positivity for the S-100 antigen. Up to 60% of retroperitoneal Schwannomas display cystic degeneration, while 1% of retroperitoneal Schwannomas can behave with malignant features and be associated with cystic degeneration. Hemorrhage can occur in 5% of the cases, while calcification is rare. Upon CT scan, the lesions can be isodense to hypodense, with contrast enhancement (70,71).

Paragangliomas are rare neuroendocrine tumors originating from the autonomic ganglia, with pathological features indistinguishable from pheochromocytomas (72,73). Generally, these lesions are associated with hormone secretion (catecholamines), with a high rate of malignant behavior (up to 25%) (74,75). The occurrence of paraganglioma peaks at the third to fifth decades, with a higher female incidence. Clinically, these lesions may be totally asymptomatic, particularly if non-functional, or occur with abdominal pain, nausea, emesis, abdominal distension and weight loss. By contrast, secreting forms may occur with paroxysmal hypertension, palpitations and profuse sweating. Paragangliomas are mostly benign tumors with an overall good prognosis, but almost one-third of cases can be locally invasive and metastatic. Upon CT scan, paragangliomas are well-circumscribed masses, with contrast enhancement due to increased vascularization. Upon MRI, paragangliomas are hypointense or isointense to the liver parenchyma on T1-weighted images and markedly hyperintense on T2-weighted images (76,77). In certain cases, scintigraphy with iodine-123-labeled metaiodobenzylguanidine can facilitate the diagnosis due to its superior specificity compared with CT and MRI imaging (78).

Perianal mucinous carcinoma is a rare carcinoma characterized by abundant mucin production (79,80). Perianal involvement constitutes ~2% of colorectal cancer and is more prevalent in middle-aged men. Notably, mucinous adenocarcinoma appears to either cause fistulation or be a potential consequence of a chronic fistula (81,82). At the pathological examination, these lesions are characterized by well-differentiated neoplastic glands associated with large lakes of mucin. On CT scan, perianal mucinous adenocarcinoma typically presents as a multiloculated cystic mass, with the possible presence of septal calcifications. Upon MRI, these lesions appears as masses filled with a markedly hyperintense content on T2-weighted images (83,84).

Non-neoplastic lesions are a group of retroperitoneal lesions composed of pancreatic pseudocysts, non-pancreatic pseudocysts, lymphoceles, urinoma and hematoma. Pancreatic pseudocysts are well described and well known among clinicians (85,86). These lesions collect pancreatic secretions, including pancreatic amylases and lipases. The identification of these enzymes inside the cysts allows an easy diagnosis (87). The lesions commonly originate as extensions from the diseased pancreas, but could also migrate to different sites of the retroperitoneal space (88). Generally, these lesions are identified simultaneously with the diagnosis of pancreatic inflammation.

Non-pancreatic pseudocysts originate from the mesentery and/or the omentum, and are characterized by a fibrous wall (5,89,90). As an important diagnostic element to differentiate them from pancreatic pseudocysts, these lesions do not contain amylase.

Lymphoceles are a common consequence of a lymphoadenectomy and/or urological surgery (91,92). These lesions are generated due to the disruption of normal lymph flow channels, causing the accumulation of the liquid in anatomical spaces without epithelial delimitation.

Urinomas are characterized by encapsulated extravasated urine (93). As a consequence of surgery, trauma or invasive procedures, urine can extravasate and accumulate in anatomical spaces.

Blood extravasation in the retroperitoneal space in the form of a hematoma is generally a consequence of trauma (94), the rupture of aneurisms and/or anticoagulation.

Overall, the identification of retroperitoneal cystic lesions is always a challenging diagnostic dilemma. As has been reviewed in the present study, following a previously reported classification and review (63), cystic lesions of the retroperitoneal space include either non-neoplastic lesions, or benign and malignant neoplasms. CT and/or MRI are mandatory to achieve a putative diagnosis (95). However, a dilemma exists as to whether clinicians should always further investigate the lesions with biopsy and/or surgical removal. The present study also described the management of a single patient who presented with a cystic mass of the

retroperitoneum and signs/symptoms due to compression of vessels and abdominal structures. The original diagnostic approach consisted of sonography-guided drainage of the lesion. This approach allowed a reduction in the compression of the surrounding structures and the analysis of the nature of the cystic liquid. Notably, no neoplastic cells, bacteria or pancreatic enzymes were detectable. In the absence of these elements, the precise diagnosis of this lesion was only speculative. Upon consideration of the risks of surgical examination of this region, which was located between the aorta and cava, it was decided that the evolution of the residual lesion should be monitored only. Notably, after 3 and then 6 months, no relapse of the cystic lesion was observed. As time has passed, a lack of relapse has confirmed the benign nature of the cystic lesion. The present study described this clinical case and reviewed the literature to emphasize how retroperitoneal cystic lesions must be managed case by case, based on surgical removal risks, CT scan data and percutaneous interventional drainage procedures. Not all lesions should undergo invasive diagnostic procedures, and therefore, a challenging close follow-up approach may be mandatory.

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