PRIMARY RETROPERITONEAL TUMORS: REVIEW OF OUR 10-YEAR CASE SERIES

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Summary.- OBJECTIVES: To investigate our case series of patients with primary retroperitoneal tumors over the past 10 years, analyzing clinical symptoms, diagnostic tests, tumor pathology, surgical data, concomitant cancer treatments, recurrence and survival rates.

METHODS: Retrospective analysis of 37 patients with primary retroperitoneal tumors diagnosed at our hospital over the past 10 years.

RESULTS: Computed tomography (CT) was the imaging technique used most often and the most accurate. Tumors were malignant in 83% of patients and benign in 17%. Complete tumor resection was performed in 73% of cases; the most common approach was midline laparotomy. Neighboring organs were also removed in 51.8% of cases in which radical resection was performed. The recurrence rate was 45% in patients who underwent surgery. Median time to onset of recurrence following open surgery was 23 months. Repeat resection was performed in 66% of cases with recurrence. Five-year survival following total resection of malignant tumors was 44%. The mean patient survival after repeat resection was 9.8 months.

CONCLUSIONS: Primary retroperitoneal tumors are rare and usually malignant. Surgery is the treatment of choice and complete tumor resection is the main factor that determines prognosis.

Keywords: Primary retroperitoneal tumors. Retroperitoneum. Surgery.

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The retroperitoneal space is the area located behind the abdominal cavity, between the posterior parietal peritoneum and the fascia that covers the muscles of the lumbar region, extending from the inferior aspect of the diaphragm superiorly, to the pelvic floor inferiorly, reaching the external borders of the lumbar muscles laterally. Anteriorly, the retroperitoneal space is closed by the posterior leaf of the peritoneum by which it contacts the posterior surface of the liver, a portion of the duodenum and pancreas, and part of the ascending and descending colon (1).

Primary retroperitoneal tumors represent a rare, but varied and interesting group of neoplasms (2-4). Kidney, adrenal, and pancreatic tumors and malignant lymphoproliferative processes in general do not fall into this category, even though they are located in the same space (5). In other words, primary retroperitoneal tumors do not originate in any retroperitoneal organ, whether parenchymatous or not, but arise from actual tissues in the same space or from embryonic rests found therein.

The urologist plays a key role in the diagnosis and treatment of these tumors because they are usually found in the anatomical region commonly used for surgical access in many major urological surgeries of varying nature. However, on certain occasions, a multidisciplinary approach should be considered in order to treat these patients appropriately.

Historically, Lobstein in 1820 and Witzel (2) used the term retroperitoneal tumors to refer to these neoformations, thus replacing earlier terms that related these tumors to the renoureteral system (i.e., pararenal, perirenal, paranephritic, juxtaperitoneal, or subperitoneal).

A retrospective analysis was conducted of patients seen by both the General Surgery Department and the Urology Department at the Hospital and University Complex of Albacete and diagnosed with primary retroperitoneal tumors between 1997 and 2008.

The following patient data were analyzed: sex, age, clinical symptoms at diagnosis, additional tests, and surgical data (e.g., type of incision, need to excise neighboring organs, total or partial removal of the mass, and postoperative complications). The anatomical pathology data, use of chemotherapy or radiotherapy, and patient survival are also reported.

The study included a total of 37 patients with primary retroperitoneal tumors diagnosed in the Hospital Complex of Albacete between January 1997 and September 2008. Of these patients, 22 were seen by the Urology Department (60%) and 15 by the General Surgery Department (40%). The mean patient age was 58.70 years (range, 26-80); 16 were men (43%) and 21 women (57%).

The clinical manifestations included pain of varying severity and location, mainly in the abdominal, lumbar, inguinal, or gluteal area (60% of patients), palpation of an abdominal mass (28%), and general symptoms, such as asthenia, anorexia, weight loss or prolonged fever (54%). Gastrointestinal symptoms (vomiting, abdominal distention, bloating, constipation, dyspepsia or intestinal blockage) were present in 44% of patients; 3 patients presented neurological symptoms, such as lower limb weakness and sensory loss of the obturator, femoral cutaneous or sciatic nerve. Urological symptoms (mainly lower back pain, but also dysuria, pollakiuria and urge) were observed in 25% of patients. Signs of venous compression (edema and genital swelling) were present in 44% of patients; 3 patients presented neurological symptoms, such as lower limb weakness and sensory loss of the obturator, femoral cutaneous or sciatic nerve. Urological symptoms (mainly lower back pain, but also dysuria, pollakiuria and urge) were observed in 25% of patients. Signs of venous compression (edema and genital swelling) were present in 25% of patients. Signs of venous compression (edema and genital swelling) were present in 25% of patients.

The tumors were diagnosed by plain chest and abdominal x-rays, abdominal ultrasound, intravenous urography, computed tomography (CT), magnetic resonance imaging (MRI) and arteriography (only occasionally in earlier cases). CT was used most often and demonstrated the highest diagnostic yield.
Pathology confirmed that 83% of tumors were malignant (13 liposarcomas, 4 malignant fibrous histiocytomas, 7 leiomyosarcomas, 6 fibrosarcomas, and 1 chondrosarcoma) and 17% were benign (2 cystic lymphangiomas, 2 urogenital cysts, 1 neuroblastoma, and 1 neurofibroma).

Complete resection of the mass was performed in 27 patients (73%), partial tumorectomy in 2 (5.5%), open biopsy of the mass in 6 (16%) with tumors considered irresectable, and punch biopsy in 2 (5.5%) with inoperable tumors.

The xiphopubic midline laparotomy approach was used in 65% of cases, subcostal laparotomy in 18%, chevron incision in 9%, thoracoabdominal incision in 5%, and lumbotomy in 3%.

In 14 cases (51.8%) in which radical resection was performed, adjacent organs were also removed: 7 nephrectomies (50%), 3 suprarenalctomy (21%), 2 cystectomies (14%), 1 duodenal resection (7%), 1 caudal pancreactectomy (7%), 3 splenectomies (21%), 1 hysterectomy and bilateral salpingooophorectomy (7%), 2 hemicolecotomies (14%), and 1 total pelvic exenteration (7%).

Postoperative complications were observed in 18% of patients and included bleeding, respiratory infection, wound complications, and persistent paralytic ileus. Postsurgical mortality was 2.75%.

Chemotherapy was used as adjuvant therapy in 4 patients following complete resection of the tumor with therapeutic regimens such as CYVADIC (cyclophosphamide, vincristine, doxorubicin) and MAID (doxorubicin, ifosfamide). Doxorubicin was used as palliative therapy in 4 patients. Postsurgical radiation therapy was administered to 11 patients with a total dose of 50-55 grays.

The recurrence rate in patients who underwent complete resection of the tumor was 45%. The mean time to recurrence following open surgery was 23 months (range, 7-57). The recurrence site was local (9 patients), paratesticular (1), intestinal (1), and adrenal and pulmonary metastasis (1). Repeated resection of recurrent tumors was performed in 66% of patients, with total resection performed in patients with local recurrences and radical orchietomy, intestinal resection, adrenalectomy and pulmonary segmentectomy in the others, respectively.

Five-year survival following complete resection of malignant tumors was 44%. The 2 patients who had undergone incomplete resections did not live longer than 5 months after diagnosis. The mean survival was 5.6 months (range, 1-14) in patients considered inoperable and 9.8 months (range, 1-18) in patients who had undergone repeated resection. In patients with benign tumors, 5-year survival was 83%. One patient died during surgery from hypovolemic shock secondary to massive bleeding of a retroperitoneal neurofibroma.

**DISCUSSION**

Primary retroperitoneal tumors are defined as solid or cystic tumors, whether benign or malignant, that develop in the retroperitoneal space and arise from lymphatic, nervous, vascular, support muscle, connective, or fibroareolar tissue independent of the organs and large vessels in the space (eg, kidneys, adrenal glands and retroperitoneal areas of the pancreas, colon or duodenum) (2-7). Primary retroperitoneal tumors also include tumors caused by embryonic rests of the urogenital ridge (wolffian or müllerian ducts, germ cells) and the primitive notochord (8) and those arising from the neural crest, such as paragangliomas in the organ of Zuckerkandl or at other sites, and retroperitoneal extra-adrenal neuroblastomas (9).

The classification of primary retroperitoneal tumors remains essentially similar to the traditional classification proposed by Ackerman in 1954 (1,10), and only the reference to malignant fibrohistiocytoma (classically considered a pleomorphic liposarcoma) has changed (11) (Table I).

The most common tumors are sarcomas (83.7% of our series), mainly liposarcoma (6-20%) and leiomyosarcoma (8-10%). These tumors present as hard abdominal masses with an irregular surface; they are surrounded by a capsule that is rapidly outgrown by tumor growth and infiltrate the posterior parietal peritoneum and the infra-abdominal viscera attached to it (eg, ascending and descending colon, mesentery), thus secondarily becoming intraperitoneal by direct, and not metastatic, invasion. At present, tumor exteriorization through weak points or routes such as the lumbar triangle, inguinal tract or obturator canal, during tumor spread is extremely rare.

Primary retroperitoneal tumors are uncommon and account for only 0.2% to 0.6% of all neoplasms (12). No gender-related differences in incidence are observed, although our series included more women than men (57% vs. 43%). Most tumors are diagnosed between the sixth and the seventh decade of life (2,8). However, certain histological types (embryonal rhabdomyosarcoma, teratoma and neuroblomastoma) are more common in childhood (13). Retroperitoneal...
tumors are malignant in 85% of cases; of these, nearly 50% are sarcomas (2,8,9).

Late diagnosis of primary retroperitoneal tumors is common because the retroperitoneum space is “adaptable” and the tumors remain asymptomatic for some time (2,8,14-18). In fact, Melicow has described that the retroperitoneal space can be clinically “silent” (4). The first, although late, symptom is usually the appearance of a visible and palpable mass (4,13-16) (Figure 1A). In other patients, the symptoms arise from compression or invasion of neighboring organs (14-16,21-24) and various types and sites of pain may be present in half the cases (22). Digestive symptoms (nonspecific abdominal pain, nausea, vomiting, gastrointestinal bleeding, constipation, jaundice, etc) are present in up to 60% of cases (23). Neurological symptoms (radiculitis, sciatica, and sensory, motor and sphincter dysfunctions) are also observed. The sign of Hesse manifests as temperature, pilomotor and sudomotor changes in the legs caused by compression of the paravertebral sympathetic chain (25). Urological symptoms are caused by possible urinary tract involvement at any level (kidneys, ureter, bladder) manifested as chronic lower back pain or acute renal and ureteral colic. Urinary symptoms (hematuria, dysuria, pollakiuria or urinary retention) are more common in pelvic tumors near the bladder (12). Compression of large vessels may cause ascites, edema and varicose veins in the legs as well as varicoce-

<table>
<thead>
<tr>
<th>Tissue of Origin</th>
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<td>Chemoctoma</td>
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<td>Ependymoma extra-adrenal</td>
<td>Malignant non-chromaffin paraganglioma</td>
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<td><strong>Embryonic rests and notochord</strong></td>
<td>Benign teratomas</td>
<td>Malignant teratomas</td>
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le in men (2,12) and edema of the external genitalia in women. General symptoms with nonspecific abnormalities (eg, weight loss, asthenia, anorexia and/or prolonged fever) often appear (8). Hypertension may result from compromise of the renal vessels and intermittent claudication from compression of the iliac veins. Acute abdominal symptoms with hemorrhagic shock (Wunderlich) may sometimes be present.

Retroperitoneal tumors are usually diagnosed by imaging tests (2,6), along with the clinical examination and laboratory parameters (catecholamines, testicular tumor markers, etc). The radiological examination of the retroperitoneal space is currently based on the use of CT, MRI and abdominal sonography. In the past, indirect images revealed the mass effect on retroperitoneal structures (kidney and urinary tract) or intraperitoneal structures (stomach, duodenum, colon), which converted the retroperitoneal space into a “blind” space with the ureter as the only indicator (19,20). Current imaging studies confirm the retroperitoneal location of the palpable mass and establish the anatomical and surgical relationships to the abdominal viscera and retroperitoneal organs (diagnosis of tumor spread).

A plain x-ray of the abdomen often shows signs that suggest a retroperitoneal mass: increased density, displacement or alteration of the renal shadow, displacement of intestinal gases, possible presence of calcifications, and blurred psoas line (inconsistent sign) (2,26). In a chest x-ray, the diaphragm may appear to be elevated and would allow the presence of pulmonary metastases to be assessed (10,26). Before CT and MRI were available, intravenous urography was used most often to diagnose primary retroperitoneal tumors (2), as the technique commonly revealed abnormalities. This exploration may reveal a rejected, compressed or turned kidney, and occasionally the kidney may have crossed the midline into a pelvic position (Figure 2). Large masses can cause caliceal dilatation or functional impairment. The ureter may also be displaced, compressed or dilated; when it is not visible, ascending pyelography may be necessary. In many cases, the bladder tends to be compressed and rejected when tumors extend into the pelvic space (12,27).

The main advantage of an ultrasound is that it can reveal whether the mass is cystic (urogenital tumors of mesodermal origin, enterocystic, cystic lymphangioma, etc.) or solid, as well as determine its volume, topography and the condition of the abdominal vena cava (28).

CT screening is the most important imaging test for the retroperitoneum and is superior to other screening tools in defining the characteristics of the mass and the condition of neighboring organs and structures (abdominal cava, kidneys, pancreas, psoas, etc). The technique is considered most optimal for diagnosis and preoperative staging of primary retroperitoneal tumors (29,30). Moreover, it distinguishes different densities which suggest the nature of the tumor (fat content), clearly defines the shape and the size of the mass, identifies the entrapment or infiltration of surrounding tissue and organs, and reveals any enlarged lymph nodes (27) (Figure 3). CT-guided biopsies are possible, although the procedure is debatable, particularly in adults for whom...
the primary therapeutic indication is surgical excision (3), and many authors reserve punch biopsy for cases of persistent diagnostic uncertainty with lymphoma (in particular, non-Hodgkin’s) or metastasis (10). CT can also be used to detect pulmonary, bone, hepatic or peritoneal metastases and local or regional recurrence in patients who have already been treated (28).

The main advantage of magnetic resonance imaging (MRI) is that the tumor can be studied in all planes of the space; furthermore, MRI provides a new preoperative interpretation of the anatomy, structure and vascularization of the tumor (8). The technique is extremely useful in diagnosing extra-adrenal pheochromocytoma (paraganglioma) (9).

Currently, studies of the vascular structure (cavography and arteriography) have been replaced by three-dimensional CT reconstruction and MRI to assess the irrigation of a mass prior to surgery (13). Digital subtraction angiography is also useful (Figure 4).

Laparoscopy is the last diagnostic resource available before proceeding with an exploratory laparotomy for guided biopsies prior to surgery (31).

Surgical ablation of the entire lesion is the treatment of choice for retroperitoneal tumors (24), but is not always feasible because infiltration affects vital structures (2,30). Despite the possibility of performing large organ resections (stomach, kidneys, spleen, tail of pancreas, duodenum, colon, abdominal cava, etc) and in which case the tumor would be considered a residual tumor, rather than recurrence. In our series, complete macroscopic removal without violating the tumor capsule was possible in 73% of patients; visceral removal was necessary in 51.8% (half of these were nephrectomies). Despite the surgery, complete resection is only achieved in 38% to 70% of patients and depends on multiple variables.

The importance of the complete resection is directly related to the possibility of survival (30). In favorable cases, five-year survival could be as high as 50% to 74%. Criteria for radical surgery and the usually large size of the masses require an access route that permits wide exposure for procedures (2). Midline laparotomy allows simultaneous examination of the abdominal and pelvic viscera, facilitates management of the large vascular trunks, and permits additional visceral surgery which may be necessary when there is local and regional involvement (Figures 1B and 5). Midline laparotomy also allows the incision to be extended to access the thoracic cavity (3,11,17,24 ). The chevron or bilateral subcostal incision is commonly used to remove large tumors with vena cava involvement (2). Lumbotomy and subcostal incisions should only be used for smaller masses located at the inferior half of the kidneys (13). The thoracoabdominal incision is ideal for the complete resection of large masses in the retroperitoneal space. The main advantage of this incision is that it exposes the crural area on both sides, the celiac trunk, the superior mesenteric artery, and the adrenal glands (9,24,29,32).

**FIGURE 2.** Intravascular sonography. A) Peritumoral calcifications, B) Displaced, malrotated right kidney and displaced right ureter, C) Medialization of right ureter.
The progression of malignant primitive retroperitoneal tumors (more than 80% at diagnosis) is determined by the risk of local recurrence rather than the risk of metastasis (3,8). En-bloc tumor resection with a margin of normal tissue is recommended; for this reason, a high percentage of patients (up to 83%) require resection of neighboring organs (9), such as the kidneys (32%-46%), adrenal gland (18%), spleen (10%), colon (25%), and pancreas (15%), according to the series (2-17) (Figure 5A). For this reason, gastrointestinal and vascular surgery skills plus urological skills (or a multidisciplinary approach) are necessary in the radical treatment of such tumors. With different variables, complete resections are achieved in 38% to 73% of patients, according to the author (2-17). Postoperative mortality has decreased to 2% because of improved surgical technique and postoperative intensive care.

Mean survival following complete resection is around 60 months (2,5,33) and 5-year survival is between 40% and 74% in patients who have undergone complete resection [2,3,10,17], 8% to 35% in partial resection (8,9,12,30), and 3% to 15% in unresectable tumors (2-4,5,7-18).

All retroperitoneal sarcoma series report high local recurrence rates (40%-82%). Mean time to recurrence is 15 to 24 months (2-4,5,7-18). Hence, strict follow-up with CT or MRI testing to detect recurrences is necessary every six months for 2 or 3 years (27,29,34). Repeated resections may be very useful, not only from the symptomatic and palliative point of view, but also in terms of survival (2,9,10). The overall mean survival of repeated resection patients is 24 months, ranging between 15 and 30 months depending on the histological grade (2-4,5,7-18).
Because local recurrence is common, adjuvant therapy is recommended. The role of radiotherapy and chemotherapy as adjuvant therapies in the management of retroperitoneal tumors is disputed. In general, these therapies may increase disease-free survival when compared with patients who do not receive them, but no increase in overall survival has been demonstrated (2,30). The use of high-dose radiotherapy is limited because the kidneys as well as the intestine are found within the field of radiation (12). The most commonly used dose is 6000 cGy (2,12). The relationship between the response obtained and the dose used appears to be important; the rate of local recurrence is 67% with doses below 5000 cGy but only 17% at doses equal to or higher than 5000 cGy (3). The association of chemotherapy with various applications of radiotherapy may obtain better local and systemic progress (9,30). Adjuvant radiotherapy is mainly indicated in cases with unresectable residual tumors. In addition to lymphomas, good results may be obtained in some types of retroperitoneal tumors such as rhabdomyosarcoma, neuroblastoma and undifferentiated sarcomas.

The role of adjuvant chemotherapy in these tumors is also controversial (30). Multiple variants have been used, with single drugs or combination drugs, and the response index is similar to any other therapeutic regimen and equally poor (12). Adriamycin is the most commonly used drug in monotherapy regimens, but is also used in combination regimens with DTIC (adriamycin-dacarbazine) or CYVADIC (cyclophosphamide, vincristine, adriamycin and DTIC) (9). Adriamycin is also used palliatively for metastatic tumors (3).

CONCLUSIONS

The characteristics of retroperitoneal tumors (eg, size, proximity to abdominal organs and structures, proximity to large retroperitoneal vessels) make...
surgical treatment a real challenge for surgeons, who must have general surgical experience and skills or resort to a multidisciplinary approach whenever deemed necessary for the patient’s welfare. Surgical radicality is directly related to recurrences and particularly to residual tumors and survival results. In our hospital setting, 60% of patients were treated by the Urology Department and the remaining 40% by the General Surgery Department, as it is not clearly established which department should treat this type of condition.

REFERENCES AND RECOMMENDED READINGS

(*of special interest, **of outstanding interest)


