ORIGINAL ARTICLE

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Renal involvement in primary retroperitoneal tumors

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Abstract: *Retroperitoneal tumors grow quietly and are generally large in size, more than half of them being larger than 20 cm at the time of diagnosis. They usually present several therapeutic challenges because of their rarity, relative late presentation and anatomical location, often in close relationship with several important structures in the retroperitoneal space. Due to intimate relationships with vital organs in retroperitoneum, extensive surgery with en bloc resection of the involved organ is often required, most frequently the kidneys, followed by colon, pancreas and spleen. Malignant tumors have a poor prognosis, the most significant factors regarding survival rates being delayed diagnosis, high histological grade, inoperability due to invasion into vital organs, and a positive surgical border.*

Keywords: *primary retroperitoneal tumors, renal involvement, therapeutic management*

INTRODUCTION

The retroperitoneum is one of the largest spaces in the body, located behind the abdominal cavity, between the posterior leaf of the parietal peritoneum and the lumbar muscles fascia. It is delimited superiorly by the diaphragm and extending inferiorly to the pelvic floor, reaching the external borders of the lumbar muscles laterally [1]. It contains connective tissue, kidneys, adrenals, ureter, aorta with its branches, inferior vena cava with its tributaries, a portion of the duoden and pancreas, a part of the descending and ascending colon and lymph nodes. At the kidneys level, the retroperitoneum is divided into three spaces by the anterior and posterior renal fascia, as follows: anterior pararenal space, perirenal space and posterior pararenal space [2]. Primary retroperitoneal tumors represent a rare, but interesting group of neoplasms. Even though they are located in the same space, tumors of the kidneys, adrenals and pancreas, tumors originating from the organs situated partially in the retroperitoneum and retroperitoneum metastasis do not fall into this category. Primary retroperitoneal tumors do not originate from any retroperitoneal organ (parenchymatous or not), but develop from the actual retroperitoneal tissue (lymphatic, nervous, vascular, support muscle, connective, or fibroareolar tissue) or from embryonic rests of the urogenital ridge (wolffian or müllerian ducts, germ cells, primitive notochord) [3-6].

The retroperitoneum can host a wide spectrum of pathologies. Primary retroperitoneal tumors are a rare entity, having a reported incidence of 0.3-3.0%. More than half of the retroperitoneal masses are malignant (70-85%), leaving a percentage of 15-25% of the tumors to be benign. The majority of the tumors are of mesenchymal origin (75%), followed by the neural origin (24%), and last from embryonic

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rests (less than 1%) [7].

The retroperitoneum represents the second most common site of origin of malignant mesenchymal tumours after the lower extremities [7, 8]. Liposarcomas (70%) and leiomyosarcomas (15%) are the two most frequent histological subtypes of sarcomas. 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 intra-abdominal viscera attached to it, thus becoming intraperitoneal by direct, and not metastatic, invasion.

Benign tumors are often an incidental finding during an investigation for unrelated symptoms. The most common primary benign pathologies encountered in the retroperitoneum include benign neurogenic tumours (schwannomas, neurofibromas), paragon-gliomas (functional or non-functional), fibromatosis and retroperitoneal lipomas [9, 10].

Due to the inaccessibility of the region and since these tumours often give none or non-specific symptoms until they have reached a substantial size, they are usually large at presentation [11]. They grow silent and aggressively and usually invade the surrounding structures. In primary retroperitoneal tumors lympha-denopathy and distant metastases are a rare entity. More than half of the retroperitoneal tumors are larger than 20 cm in diameter at the time of diagnosis, the retroperitoneum space being “adaptable”.

The urologist has a crucial role in diagnosing and treating these tumors, because they are usually found in the anatomical region commonly used for surgical access in many major urological surgeries. However, in certain cases, a multidisciplinary approach should not be avoided.

Retroperitoneal tumors occurs frequently in the 5th and 6th decade, being found more often in female than in male patients [12, 13]. Certain histological types, such as embryonal rhabdomyosarcoma, terato-ma and neuroblastoma, are commonly found in younger patients. Patients with primary retro-peritoneal masses usually present with abdominal swelling and pain, early satiety, abdominal discomfort, most having a palpable abdominal mass. Many benign tumors are discovered as an incidental finding during imaging for unrelated symptoms [14, 15]. Pain can vary in intensity and severity and can also be located in the lumbar, inguinal or gluteal region. General symptoms such as asthenia, anorexia, weight loss or prolonged fever may be present. A study found out that out of the total number of patients, 44% had on admission gastro-intestinal symptoms such as: vomiting, abdo-minal distention, bloating, constipation, dyspepsia, gastrointestinal bleeding or intestinal blockage. Neurological symptoms (lower limb weakness, sensory loss of the obturator, femoral cutaneous or sciatic nerve, radiculitis, sciatica and sphincter dysfunctions) were also found in 3 out of the total 27 patients, and 10% showed signs of venous compression (edema, varicocele, ascites and genital swelling).

Retroperitoneal masses are usually diagnosed by clinical examination associated with blood tests and imaging studies (CT, MRI, abdominal ultrasono-graphy). The imaging test of choice in the evaluation and staging of primary retroperitoneal masses is contrast-enhanced computed tomography of the thorax, abdominal and pelvic regions. It can distinguish between different densities which suggest the nature of the mass, defines the shape and size of the tumor, can discover enlarged lymph nodes and can assess the involvement of the neighboring organs [16, 17]. It can also be used to perform CT-guided biopsies. It can detect the presence or absence of pulmonary, bone, hepatic or peritoneal metastases and local or regional recurrence in patients who have already been treated [18].

It is important to confirm that the tumor is located within the retroperitoneal space and to exclude the possibility that the tumor originates from a retroperitoneal organ. Anterior displacement of the retroperitoneal organs is a strong indicator that the mass has a retroperitoneal origin. The migration of the large vessels can be helpful as well [19, 20].

Ultrasound is a fast, easy to use, repeatable method. It can reveal whether the mass is cystic or not, it can determine its volume, topography and can assess the condition of the inferior vena cava. The main

disadvantage is that it is a subjective method, dependent on the doctor's experience [19].

If after the results of the imaging studies the diagnosis remains uncertain, an exploratory laparotomy or laparoscopy remains a last diagnostic resource.

THERAPEUTIC MANAGEMENT

Complete surgical resection is the treatment of choice for primary retroperitoneal tumors, but local recurrence occurs in the majority of the patients, being responsible for more than 75% of sarcoma-related deaths. Complete surgical ablation is not always possible, because of its invasion in vital structures. Despite the possibility of performing large organ resections, the possibility of a residual tumor is very high.

Macroscopic excision, tumour grade, multifocality and histological subtype are the main prognostic factors that dictate local recurrence and overall survival rates [21-23]. Local recurrence rates are higher and occurs at an earlier interval in high-grade tumors compared with low-grade ones. The possibility of obtaining negative margins is remarkably lower at the time of local recurrence and each successive operation is more difficult than the last. In the presence of a positive surgical border following the resection of a malignant retroperitoneal tumor, the 5-year survival rate decreases to 28%.

The most significant factors regarding survival rates are delayed diagnosis, high histological grade, inoperability due to invasion into vital organs, and a positive surgical border. For patients with high-grade tumors, the mean life expectancy is approximately 20 months, increasing to 80 months in patients with low-grade retroperitoneal masses.

A study found that tumors larger than 10 cm generally had distant metastasis at the time of diagnosis [24]. The risk of local recurrence is more important than the risk of metastasis regarding the progression of malignant primitive retroperitoneal tumors [25].

Due to the fact that a radical surgery is needed and that the tumor is usually large in size, an access route that allows a wide exposure for procedures is required. Midline laparotomy is the acces route of choice, allowing simultaneous examination of the abdominal and pelvic viscera, enabling management of the large vascular trunks, additional visceral surgery and the incision can be extended for access in the thoracic cavity. Chevron incision is usually used to remove large tumors with the invasion of inferior vena cava and lombotomy should be used to remove small retroperitoneal masses [26].

Because of the high risk of local recurrence, a strict follow-up with CT or MRI testing is necessary every six months for 2 or 3 years [27, 28]. Since primary retropritoneal tumors have such high rates of local recurrence, adjuvant therapy is recommended.

The use of high-dose therapy, in an attempt to lower the rate of local recurrence, is limited because these tumors are often adjacent to radiosensitive structures with low radiation tolerance (such as kidneys and intestines). The doze usually used is about 60 Gy, studies found that therate of local recurrence is 67% with doses below 50 Gy but only 17% at doses equal to or higher than 50 Gy [27]. Lymphomas, rhabdo-myosarcomas, neuroblastomas and undifferentiated sarcomas seem to have good results with radiotherapy.

The use of chemotherapy in retroperitoneal tumors is controversial, having a similar response index with other therapeutic regimen and equally poor in single drug therapy or in combination [18]. The most commonly used drug, both in single drug therapy or in combination (adriamycin – dacarbazine, or cyclophos-phamide – vincristine – adriamycin – dacarbazine), is Adriamycin. This drug is also used for metastatic disease, as a palliative form of treatment [28, 29].

If a tumor is considered unresectable or the patient has distant metastases, a core needle biopsy may be indicated to confirm the diagnosis and to enable consideration of alternative therapy.

Palliative surgery (incomplete resection for unresectable tumor) should be considered for symptom control and may improve quality of life [28].

DISCUSSION

Due to the fact that kidneys and ureteres are retroperitoneal organs, they are usually involved by retroperitoneal masses, either by extrinsec compression or direct invasion. If the tumor is left unchecked, it will grow to cause secondary hidronephrosis and renal parenchymal destruction that will lead to chronic kidney disease with severe hydroelectrolytic imbalance and serious consequences. Resistant hypertension [30] with dyselectrolytemia [31, 32], secondary heart failure [33] and cardiac arrhythmias [34] may be the result of compromised renal arteries by extrinsec compression caused by the retroperitoneal masses [9].

Urological manifestations, caused by possible urinary tract involvement (displacement, compression and invasion) at any level (kidneys, ureter, and bladder) were not as frequent, only 25% of the patients presented chronic lower back pain, or acute renal and ureteral colic. Hematuria, polakiuria, dysuria or urinary retention usually occur in tumors located in the pelvic region, near the bladder [13]. Hematuria may also appear if the retroperitoneal mass invades the ureters or the pyelocaliceal system [35].

In terms of treatment, the complete surgical resection of the tumor en bloc with the involved organs is the gold standard. It can vary from segmental ureterectomy, followed by a surgical repair of the defect, to radical nephrectomy. In cases with extrinsec compression of the ureter and secondary hidronephrosis, with no signs of invasion, an internal (ureteral stent) or external (percutaneous nephrostomy) renal drainage method can be used, until the tumor can be surgically removed. More than 83% of the patients require resection of neighboring organs, most frequently the kidneys, followed by colon, pancreas and spleen, for achieving a negative margin [27].

If the ureteral defect after extensive surgical removal of the retroperitoneal mass is proximal to the ureterovesical junction and it is not large in size, a ureteroneocystostomy or a primary anastomosis of the ureter (ureteroureterostomy) is usually preferred. When ureteroureterostomy or ureteroneocystostomy cannot be performed, the psoas hitch ureteral reimplantation is the best approach. For defects in the middle third of the ureter after partial ureterectomy, the optimal approach is ureteroureterostomy, but if it cannot provide a tension free anastomosis, a Boari flap is an optimal, but complex approach. The optimal procedure for repair of an upper ureteral injury is a ureteroureterostomy, if it can be performed without tension. A nephropexy with fixation to the psoas tendon can provide a tension-free anastomosis. When a tension-free anastomosis cannot be achieved, even after kidney mobilization, autotransplantation, ileal or appendiceal interposition graft, nephrostomy or a cutaneous ureterostomy can be performed. The ureteral anastomosis following any type of primary repair is typically stented.

In advanced cases, with inoperable tumor and secondary ureterohydronephrosis, an urgent drainage of the obstructed kidney should be used [36]. This can be achieved either by internal drainage using a double J ureteral stent [17] or by using a percutaneous nephrostomy. A nephrostomy deteriorates the patient's quality of life and leads to frequent infections, blockage of tubes or bleeding. Ureteral stenting, on the other hand, can be associated with irritative bladder symptoms, blockage, sepsis and a high failure rate, which ultimately leads to a nephrostomy tube [28].

Wrona AJ et al wanted to offer a better solution than ureteral stenting and nephrostomy for kidney drainage. In their study, they presented a subcutaneous pyelovesical bypass as a solution for ureteric obstruction (detour bypass). A detour bypass is made of two coaxial tubes, a 27F porous polytetrafluoro-ethylene (PTFE) outer tubeand an inner 17F silicone tube extending beyond the PTFE, with perforations on both ends and a radio-opaque ring on the proximal end (for an accurate placement of the proximal end of the stent). The detour is placed subcutaneously, using a tunneling device, and the distal end of the tube is placed into the dome of the bladder by a small incison. They concluded that this method is a safe, minimally invasive and highly effective alternative in patients with ureteral obstruction caused by both malignant and benign

diseases and that the potential complications (infection, encrustation) may be easily and efficiently managed [37].

Andrea Montenegro et al presented a case of a 65 year-old female with a large retroperitoneal liposarcoma, in whom, due to the fact that it was very adherent to the left kidney, a complete resection of the tumor with concomitant left nephrectomy was practiced.

In a case report by Mariko Tanaka et al, they introduced the case of a 60 year old female who presented with abdominal distension. The CT revealed a large retroperitoneal tumor which proved to be a dedifferentiated liposarcoma at biopsy. Due to the fact that the tumor invaded the duodenum, head of the pancreas, right kidney, inferior vena cava and the aorta below the left renal artery, an extensive surgical removal of the tumor was performed, with en bloc resection of the right kidney, duodenum, head of the pancreas, a portion of the inferior vena cava and abdominal aorta, with concomitant vascular reconstruction [38].

In their study, Rodriguez et al found out that sarcomas, mainly liposarcomas, followed closely by leiomyosarcomas, were the most common type of primary retroperitoneal tumors. More than half of the patients included in the study presented at admission pain of varying severity and location (mainly abdominal and lumbar) and general symptoms such as asthenia, anorexia, weight loss or prolonged fever. Gastrointestinal manifestations (vomiting, abdominal distention, bloating, constipation, dyspepsia or intestinal blockage), due to compression/invasion of the gastrointestinal tract, were present in 44% of cases. Renal involvement was not as frequent, only one quarter of patients had urological symptoms, such as lower back pain, but also dysuria, polakiuria and urge [13].

Pereira et al reported the case of a 48-year-old male who presented for pain and right abdominal swelling. Clinical investigation revealed a right varicocele and imaging studies found a solitary hydronephrotic right kidney (personal history of left renal agenesis). Contrast enhanced computed tomography showed a retroperitoneal mass and a right hydronephrotic kidney. The particularity of this case was the presence of a solitary right kidney with left renal agenesis, with the possibility that the patient will become anephric after extensive surgery. Ultrasonography-guided biopsy was performed that confirmed a well-differentiated liposarcoma. Surgical excision of the retroperitoneal sarcoma was performed, sparring the right kidney, but the patient unfortunately died during chemotherapy [39-42].

Another case reported by the previous team presented with hypertension, anorexia, and weight loss (10 kg in 2 months). This patient had a solitary right kidney following a left radical nephrectomy subsequent to renal cell carcinoma. A right retroperitoneal mass was found during the study of his hypertension, which had a compressing effect on the right renal artery. Surgical excision of the mass was performed, but the patient died of local recurrence.

MRI of an 84-year-old male, who presented with complaints of pain and a palpable right lumbar mass, revealed a large retroperitoneal tumor invading the right kidney. Extensive surgical excision was made, with concomitant right nephrectomy.

Kazim et al stated that the location of intra-abdominal organs can shift in the presence of retroperitoneal tumors, due to the mass effect, with the kidneys being the most common viscera with an altered intra-abdominal location. In their series, they reported one retroperitoneal tumor, measuring 30 cm in diameter that pushed the left kidney to the right anterolateral direction. Since the left kidney was completely engulfed by the mass, the patient underwent extensive surgical excision of the mass and a left nephrectomy [43].

CONCLUSIONS

The retroperitoneum can host a wide variety of pathologies, including benign and malignant tumors. Primary retroperitoneal tumors are rare, almost all of them being malignant. Retroperitoneal masses grow silently, presenting late, usually invading neighboring structures at time of diagnosis. Contrast-enhanced computed tomography is the best way to evaluate this

kind of tumors. Complete surgical resection is the only potential curative treatment modality for retroperitoneal masses, but the characteristics of retroperitoneal tumors (size, proximity to abdominal organs and structures, proximity to large retroperitoneal vessels) make surgical treatment a real challenge for surgeons. The efficiency of pre-operative and post-operative radiotherapy and chemotherapy is still a controversial issue, complete surgical excision with negative margins remains the gold standard procedure.

References:

1. Ackerman LV. Tumors of retroperitoneum, mesentery and peritoneum. En "Atlas of tumor pathology". Armed Forces Institute of Pathology. Washington D.C, Sec 6, fasc. 23 y 24. 136. 1954.

2. Tirkes T, Sandrasegaran K, Patel AA, Hollar MA, Tejada JG, Tann M, et al. Peritoneal and retroperitoneal anatomy and its relevance for cross-sectional imaging. Radiographics 2012;32(2):437–51

3. Bratu O, Mischianu D, Spinu D, Barla R, Hoara P, Constantinoiu S. Paraneoplastic syndrome in primitive retroperitoneal tumours.Chirurgia (Bucur). 2013;108(1):26-31.

4. Bratu OG, Marcu RD, Socea B, Neagu TP, Diaconu CC, Scarneciu I, Turcu FL, Radavoi GD, Bratila E, Berceanu C, Spinu AD. Immunohistochemistry particularities of retroperitoneal tumors. Rev Chim (Bucharest). 2018, vol. 69, nr. 7, pag. 1813-1816.

5. Bratu OG, Cherciu AI, Bumbu A, Lupu S, Marcu DR, Ionita Radu F, Manea M, Furau C, Diaconu CC, Mischianu DLD. Retroperitoneal tumours - treatment and prognosis of tumour recurrence. Rev Chim (Bucharest). 2019; 70(1): 190-194.

6. Tambo M, Fujimoto K, Miyake M, Hoshiyama F, Matsushita C, Hirao Y. Clinicopathological review of 46 primary retroperitoneal tumors. Int J Urol, 2007; 14(9):785-8.

7. Rajiah P, Sinha R, Cuevas C, Dubinsky TJ, Bush WH Jr, Kolokythas O. Imaging of uncommon retroperitoneal masses, Radiographics. 2011;31(4):949–76.

8. Weiss SW, Goldblum JR. Enzinger and Weiss's Soft Tissue Tumors. 4th edn. St Louis, Missouri, US: Mosby; 2001.

9. Van Roggen JF, Hogendoorn PC. Soft tissue tumours of the retroperitoneum. Sarcoma. 2000;4:17–26.

10. Clark MA, Fisher C, Judson I, Thomas JM. Soft-tissue sarcomas in adults. N Engl J Med. 2005;353:701–711.

11. Strauss DC, Hayes AJ, Thway K, et al. Surgical management of primary retroperitoneal sarcoma. Br J Surg. 2010;97:698–706.

12. Dirk C Strauss, Andrew J Hayes, and J Meirion Thomas; Retroperitoneal tumours: review of management, , Ann R Coll Surg Engl. 2011; 93(4): 275–280.

13. Virseda Rodríguez JA, Moreno MJD, Navarro HP, et al. Primary retroperitoneal tumors: review of our 10-year case series. Arch Esp Urol. 2010; 63(1):13-22.

14. Hueman MT, Herman JM, Ahuja N. Management of retroperitoneal sarcomas. SurgClin North Am. 2008;88:583–597.

15. Hughes MJ, Thomas JM, Fisher C, Moskovic EC. Imaging features of retroperitoneal and pelvic schwannomas. ClinRadiol. 2005;60:886–893.

16. Marcu RD, Spinu AD, Socea B, Bodean O, Diaconu CC, Vasilescu F, Neagu T, Bratu O. Castleman`s disease-clinical, histological and therapeutic features. Rev Chim (Bucharest). 2018; 69 (4): 823-830.

17. Spinu AD, Marcu RD, Socea B, Diaconu CC, Scarneciu I, Scarneciu C, Bodean OM, Dragomirescu RIF, Stanescu AMA, Mischianu DLD, Bratu OG. Ureteral JJ Stent – Which one is better?. Rev Chim (Bucharest). 2018; 69(8): 2061-2063.

18. Ferrero Doria R, Moreno Pérez F, Huertas Valero E, García Víctor F, GassóMatoses M, Calatrava Gadea S, Díaz Calleja E. Liposarcoma retroperitoneal calcificado. ActasUrol Esp. 2004; 28 (3): 234-237.

19. Lee JKT, Hiken JN, Semelka RC. Retroperitoneum. In: Computed Body Tomography with MRI Correlation, 3rd edn, Lee JKT, Sagel SS, Stanley RJ, Heiken JP (Eds.). Philadelphia, PA: Lippincott-Raven, 1996. : 1023–86.

20. Nishino M, Hayakawa K, Minami M, Yamamoto A, Ueda H, Takasu K. Primary retroperitoneal neoplasms: CT and MR imaging findings with anatomic and pathologic diagnostic clue. Radiographics 2003;23(1):45–57.

21. Neuhaus SJ, Barry P, Clark MA, et al. Surgical management of primary and recurrent retroperitoneal liposarcoma. Br J Surg. 2005;92:246–252.

22. Bonvalot S, Rivoire M, Castaing M, et al. Primary retroperitoneal sarcomas: multivariate analysis of surgical factors associated with local control. J Clin Oncol. 2009;27:31–37.

23. Lehnert T, Cardona S, Hinz U, et al. Primary and locally recurrent retroperitoneal soft-tissue sarcoma: local control and survival. Eur J Surg Oncol. 2009;35:986–993.

24. Jagues DP, Coit DG, Hajdu SI, Brennan MF. Management of primary and recurrent soft-tissue sarcoma of the retroperitoneum. Ann Surg. 1990;212:51–9.

25. Constantinoiu S, Barla R, Iosif C, Cociu L, Gindea C, Hoara P, Bratu O, Ruşitoru L. Difficulties in diagnosis and surgical treatment of a giant retroperitoneal lipoma. Chirurgia (Bucur). 2009;104(3): 363-367.

26. Xu YH, Guo KJ, Guo RX, Ge CL, Tian YL, He SG. Surgical

management of 143 patients with adult primary retroperitoneal tumor. World J Gastroenterol. 2007; 13(18):2619-21.

27. Nitipir C, Niculae D, Orlov C, et al., Update on radionuclide therapy in oncology, Oncology Letters. 2017;14(6): 7011-7015.

28. An JY, Heo JS, Noh JH, Sohn TS, Nam SJ, Choi SH, Joh JW, Kim SJ. Primary malignant retroperitoneal tumors: analysis of a single institutional experience. Eur J Surg Oncol. 2007; 33(3):376-82.

29. Ciuhu AN, Rahnea Niţă RA, Popescu M, Badiu CD, Pantea Stoian AM, Lupuliasa D, Gherghiceanu F, Diaconu CC, Rahnea Niţă G. Evidence of strong opioid therapy for palliation of breathlesness in cancer patients. Farmacia 2017;65(2):173-178.

30. Diaconu CC, Drăgoi CM, Bratu OG, Neagu TP, Pantea Stoian A, Cobelschi PC, Nicolae AC, Iancu MA, Hainăroșie R, Stănescu AMA, Socea B. New approaches and perspectives for the pharmacological treatment of arterial hypertension. Farmacia. 2018; 66(3): 408-415.

31. Diaconu CC, Stanescu AMA, Pantea Stoian A, Tincu RC, Cobilinschi C, Dragomirescu RIF, Socea B, Spinu DA, Marcu D, Socea LI, Bratu OG. Hyperkalemia and cardiovascular diseases: new molecules for the treatment. Rev Chim (Bucharest). 2018 ; 69(6): 1367-1370.

32. Diaconu CC, Manea M, Iancu A, Stănescu A, Socea B, Spinu DA, Marcu D, Bratu OG. Hyponatremia in patients with heart failure: a prognostic marker. Rev Chim (Bucharest). 2018; 69(5): 1071-1074.

33. Manea M, Marcu D, Pantea Stoian A, Gaman MA, Gaman AM, Socea B, Neagu TP, Stanescu AMA, Bratu OG, Diaconu CC. Heart failure with preserved ejection fraction and atrial fibrillation. A review. Rev Chim (Bucharest). 2018, 69(11): 4180-4184.

34. Țica OA, Țica O, Antal L, Hatos A, Popescu MI, Pantea Stoian A, Bratu OG, Găman MA, Pițuru SM, Diaconu CC. Modern oral anticoagulant treatment in patients with atrial fibrillation and heart failure: insights from the clinical practice. Farmacia, 2018, 66(6): 972-976.

35. Diaconu CC, Arsene D, Bălăceanu A, Bartoş D. A rare tumor revealed by abdominal trauma: case presentation. Romanian Journal of Morphology and Embryology 2014; 55(3): 973-976.

36. Radulescu A, Madan V, Aungurenci A, Bratu O, Farcas C, Dinu M, Mischianu D. Antibiotic resistant urinary tract infections in an urology ward. Romanian Journal of Military Medicine. 2015, 118(3): 20-22.

37. Ahmad I, Saeed Pansota M, Tariq M, Shahzad Saleem M, Ali Tabassum S, Hussain A. Comparison between double J (DJ) Ureteral stenting and percutaneous nephrostomy (PCN) in obstructive uropathy. Pak J Med Sci. 2013; 29: 725-729.

38. Wrona AJ, Zgajewski J, Kopeć N, Chodor D, Kopcza P, Klekot S. Subcutaneous pyelovesical bypass - Detour bypass - as a solution for ureteric obstruction.Cent European J Urol. 2017;70(4):429-433.

39. Tanaka M, Kawahara T, Nishikosh T, et al. Successful surgical treatment for huge retroperitoneal liposarcoma involving the pancreas, right kidney, abdominal aorta and inferior vena cava. Journal of Surgical Case Reports, 2017; 2017(11):rjx200.

40. Argüelles Salido E, Congregado Ruiz CB, Medina López RA, Pascual del Pobil Moreno JL. Histiocitoma maligno fibroso retroperitoneal. ActasUrol Esp. 2004; 28(8): 624-6.

41. Azpiazu Arnaiz P, Muro Bidaurre I, de Frutos Gamero A, Castro Esnal E, Martín López A, Asensio Gallego JI, Ribera Gargayo JR. Tumores retroperitoneales. Liposarcomamixoide retroperitoneal. Presentación de un nuevo caso. Arch Esp Urol. 2000; 53(2):170-3

42. Pereira BJ, Borges R, Leão R, Grenha V, Coelho H, Brandão A, Temido P. Retroperitoneum beyond the kidney: retroperitoneal sarcomas in a urology department. UroToday Int J. 2012; 5(4) : art35

43. Gemici K, Buldu İ, Acar Türker, et al. Management of patients with retroperitoneal tumors and a review of the literature; World J Surg Oncol. 2015; 13: 143.