

## Primary retroperitoneal seminoma – embryology, histopathology and treatment particularities

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### Abstract

**Introduction:** Retroperitoneal seminoma is a very rare form of cancer, with embryological origin represented by primordial germ cells from the urogenital ridges left behind during the fetal development. Extragonadal germ cell tumors can also occur in the mediastinum or the pineal gland. The aim of this paper is to outline the particularities and draw embryological, histopathological and treatment conclusions regarding extragonadal germ cell tumors. **Patient and Methods:** A 43-year-old patient without any additional pathology was admitted for anemia of unknown etiology. The clinical examination revealed through deep abdominal palpation a mass in the left flank, and normal testes. Thoraco-abdomino-pelvic computed tomography (CT) scan showed a large retroperitoneal tumor adjacent to the great vessels in the left lumbo-iliac region. The blood work revealed just a low hemoglobin and hematocrit. With the established diagnosis of retroperitoneal tumor, radical surgical removal was decided. During the surgery, we were required to dissect a large solid encapsulated tumor mass from the aorta and the common iliac artery, starting at the renal pedicle all the way to the left iliac bifurcation. The surgical access was obtained through a transperitoneal left subcostal incision prolonged pararectally. Histopathological and immunohistochemical studies revealed a seminoma of the usual type. After the histological findings, the patient's tumor markers were investigated (LDH – lactate dehydrogenase,  $\beta$ HCG – beta-human chorionic gonadotropin,  $\alpha$ FP – alpha-fetoprotein), all values being within normal ranges. In addition, the left testicle was thoroughly reexamined, clinically, through ultrasound and magnetic resonance imaging (MRI) scans, and no abnormalities were observed. After the surgery, the patient followed three courses of chemotherapy (BEP – Bleomycin, Etoposide and Cisplatin). **Results:** The CT scan done 24 months after surgery found no signs of local or distant tumor recurrence. The patient entered a follow-up schedule consisting of periodical clinical, serological and imagistic evaluations. **Conclusions:** Primary retroperitoneal seminoma is a rare entity that must be taken into account when treating a retroperitoneal tumor. It develops out of the urogenital ridge, while the testes are normal. Thorough testicular evaluation (clinical, ultrasound and serum markers) is mandatory in all retroperitoneal tumors. The histopathological analysis is crucial for an accurate diagnosis and a proper management strategy. Through radical surgery and chemotherapy, the patients that are diagnosed prior to massive visceral metastatic dissemination can be cured.

**Keywords:** primary retroperitoneal seminoma, extragonadal germ cells tumors, retroperitoneal tumor, seminoma.

### Introduction

During the 5<sup>th</sup> week of pregnancy, germ cells from the yolk sac migrate along with epithelial celomic cells and cells from the mesonephros and form in the dorsal embryonic aspect the genital ridges, which will later contribute to the genesis of primitive sex cords. Through SRY (Sex determination Region of the Y chromosome), the medial aspect of the genital ridges will transform into Sertoli cells. They will perform a tight association with primordial germ cells, association which will be maintained in the further developed testes [1, 2].

The origin of primary extragonadal germ cells tumors is still under debate, with two different main theories accepted. The first one states the fact that these tumors originate from germ cells that migrated from the yolk sac to contribute to the formation of the genital ridge, but somehow remained trapped in other tissues.

The second theory states the reverse migration of transformed gonadal cells to other locations [1, 2].

There are opinions that deny both those theories and advocate that these tumors are secondary to a regressed "burned-out" or an occult testicular tumor [1].

Extragonadal germ cell tumors (EGCTs) appear mostly on midline locations, the most common being the retroperitoneum and the mediastinum, but the localization of the tumor can vary anywhere between the coccyx to the pineal gland [1, 2].

Primary retroperitoneal seminoma represents a rare condition, less than 1–2% of the germ cell tumors (GCTs) being found in an extragonadal location [1]. The term primary describes the fact that the lesion is found in the retroperitoneum, and is associated with normal testes.

The tumor is solid, lobular, gray-white, fleshy and typically composed of uniform, round to polygonal cells with pale to clear cytoplasm, distinct cell membranes and positive reactivity for PLAP, c-Kit/CD117, OCT4, SALL4 [1, 3, 4], D2-40 [1] arranged in solid sheets that are divided by lymphocyte-bearing fibrovascular septa.

The association with metachronous tumors of the testes is very rare, but it can occur [1]. In the international literature, a case of testicular seminoma is described, in which the testicular tumor was found 22 years after the treatment of the extragonadal germ cell tumor [1].

The aim of this paper is to outline the particularities and draw embryological, histopathological and treatment conclusions regarding extragonadal germ cell tumors.

## ☒ Patient, Methods and Results

### Clinical history

A 43-year-old patient with anemia (hemoglobin – Hb 10 mg/dL) of unknown cause was referred to our Clinic after a visit at his General Practitioner who had detected a large left flank palpable mass.

The clinical examination confirmed through deep abdominal palpation the large left flank mass, with clinically normal testes.

A thoraco-abdomino-pelvic computed tomography (CT) scan was performed, and revealed a large encapsulated tumor in the left lumbo-aortic and left common iliac retroperitoneum.

The blood work showed low Hb (10.2 mg/dL), low hematocrit (35%) and a low erythrocyte count (3.2 million cells/mm<sup>3</sup>), with no other biochemical modifications.

The diagnosis of retroperitoneal tumor was established and radical surgical excision using a transperitoneal approach with a left pararectal incision prolonged sub-costally was decided.

### Surgical excision

After opening the peritoneum, the descending colon was mobilized in an anterior direction by releasing the splenocolic ligament and incising along the Toldt II fascia from the iliac bifurcation all the way to the adrenal gland. Careful dissection in front of the Gerota renal fascia was performed, until the aorta was reached. The tumor and adjacent lymphatic tissue was removed in an en-bloc manner, with the upper limit of the dissection represented by the left renal vein, medial the interaortocaval space; lateral the left ureter, posterior the psoas muscle, and inferior the bifurcation of the left common iliac artery (Figure 1).

Postoperative evolution was uneventful. The patient was discharged after five days.

### Pathological examination

The resected specimen showed a solid light yellow lobular encapsulated tumor mass of 14×10×10 cm in size without hemorrhage but with areas of necrosis on gross sectioning (Figure 2).

The excision specimen was fixed in 10% buffered formalin, embedded in paraffin and sectioned at 3 μm. The slides were dewaxed and rehydrated and stained with the usual Hematoxylin–Eosin (HE) staining for the microscopic examination and diagnosis in the Department of Pathology of “Fundeni” Clinical Institute, Bucharest, Romania. The immunohistochemistry (IHC) was performed at OncoTeam Diagnostic, Bucharest, on 3 μm sections, from 10% formalin-fixed paraffin-embedded tissues, according to the IHC method – an indirect bistadial

technique performed with a polymer based detection system [EnVision™ Dual Link System–HRP (Horseradish peroxidase), Dako, Carpinteria, CA, USA]. Tissue sections were spread on poly-L-lysine-coated slides, immersed in three changes of xylene and rehydrated using a graded series of alcohol. Antigen retrieval was performed in microwave oven. In each section, endogenous peroxidase was blocked by 20 minutes incubation in 3% hydrogen peroxide. The sections were incubated with primary antibody: anti-placental alkaline phosphatase (PLAP) (Leica, 1:40 dilution, clone 8A9), CD117 (Dako, 1:250 dilution, polyclonal), podoplanin (Dako, 1:100 dilution, clone D2-40) and Ki67 (Dako, 1:100 dilution, clone Mib-1), at room temperature, for one hour. The Dako EnVision™ Detection System–HRP was then applied for 30 minutes. Finally, the sections were incubated in 3,3'-diaminobenzidine for 5 minutes, counterstained with Mayer's Hematoxylin and mounted. Negative controls were obtained by replacing the primary antibody with non-immune serum. A testicular tissue section was used as a positive control. The slides were examined and photographed on Leica DM750 microscope.

On microscopic examination, HE-stained sections showed the typical aspect of classic seminoma: a framework of fibrous septa with lymphoid infiltrate separated solid nests of round to polygonal tumor cells with well-defined borders, clear to slightly eosinophilic cytoplasm and round nuclei, often with squared-off contours, with one to several nucleoli (Figures 3–5).

The tumor cells showed diffuse strong membranous and cytoplasmic immunoreactivity for PLAP (Figure 6) and podoplanin (Figure 7), with moderate membranous immunostaining for CD117 (Figure 8).

Clinical-imaging studies and the morphological appearance and immunohistochemical profile of the tumor were inconsistent with other possible tumor entities, such as non-Hodgkin's lymphoma, perivascular epithelioid cell tumor (PEC-oma), metastatic melanoma, clear cell renal cell carcinoma, Sertoli cell tumor, non-seminomatous germ cell tumor or prostatic adenocarcinoma. The final diagnosis was classic seminoma.

### Postoperative management and follow-up

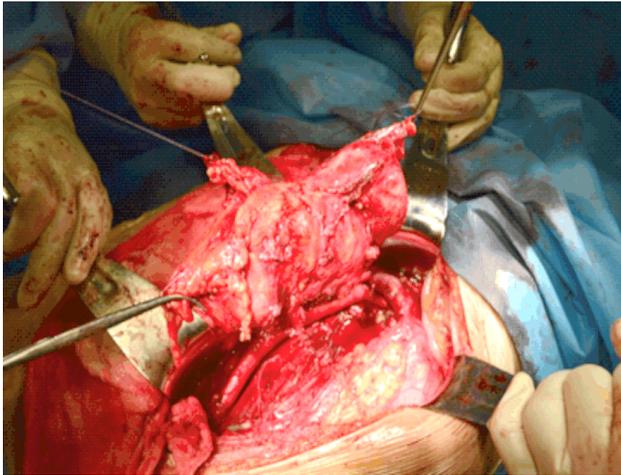
In the light of the histological findings postoperative, the patient's tumor markers were analyzed (LDH – lactate dehydrogenase, βHCG – beta-human chorionic gonadotropin, αFP – alpha-fetoprotein), all values being within normal ranges.

Also, the left testicle was thoroughly reexamined, clinically, with ultrasound and magnetic resonance imaging (MRI) scans, and again no abnormalities were observed.

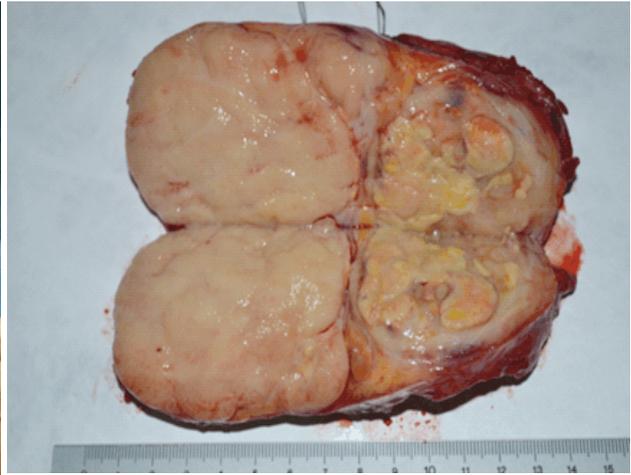
Afterwards, the patient was referred to an oncologist, who prescribed three courses of chemotherapy (BEP – Bleomycin, Etoposide and Cisplatin).

The patient entered a follow-up schedule consisting of: at every four months a simple chest radiograph, a clinical and a serological evaluation (LDH, βHCG, αFP); at every six months an abdomino-pelvic contrast-enhanced CT scan.

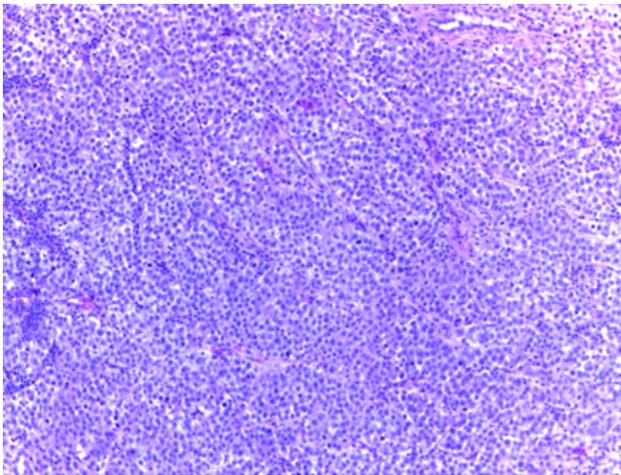
The abdominal and pelvic contrast-enhanced CT scan done 24 months after surgery found no signs of local or distant tumor recurrence.



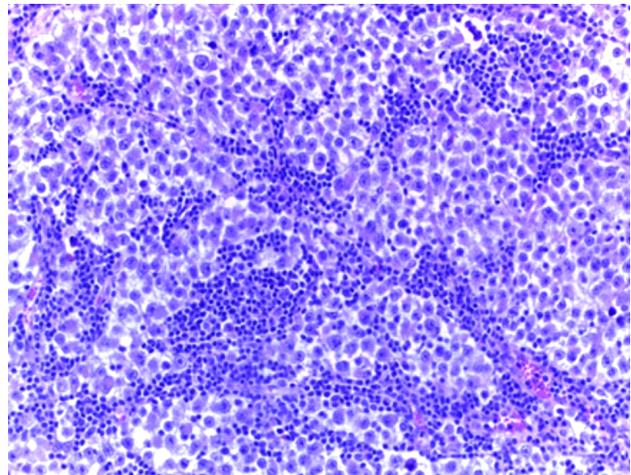
**Figure 1 – Intraoperative aspect of the tumor.**



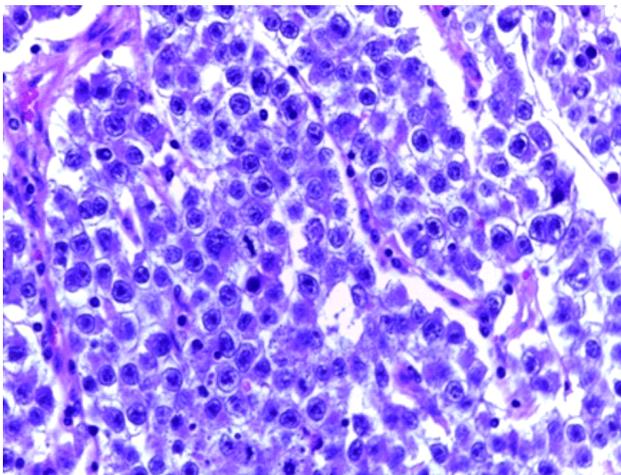
**Figure 2 – Macroscopic aspect of the tumor.**



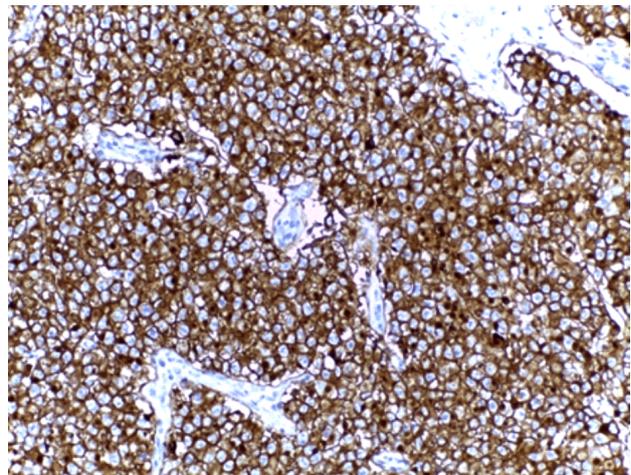
**Figure 3 – Solid sheets of seminomatous tumor cells. HE staining, ×100.**



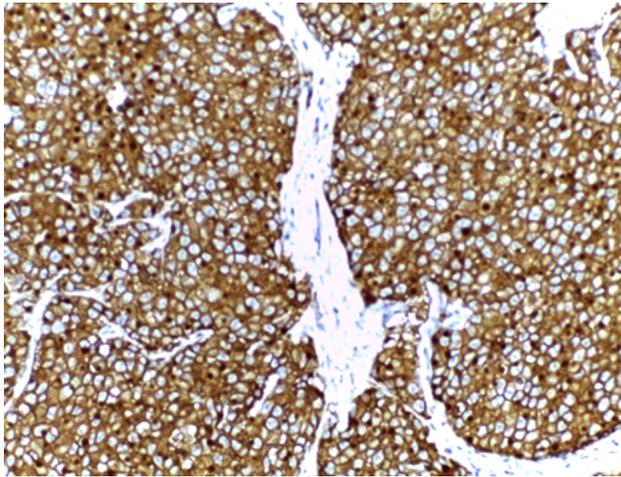
**Figure 4 – Fibrous septa with lymphoid infiltrate coursing through the tumor. HE staining, ×200.**



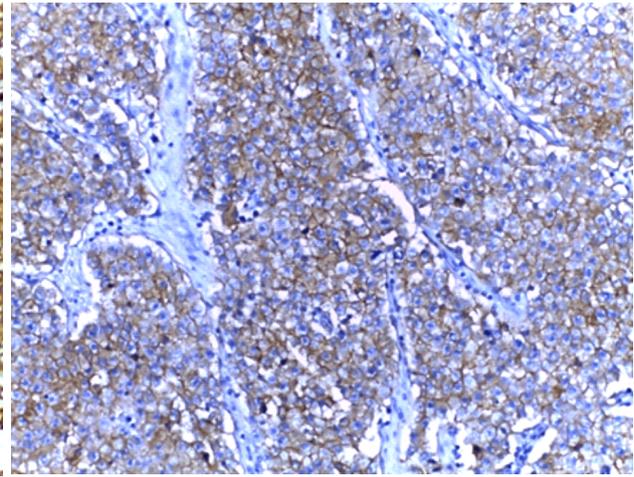
**Figure 5 – Round to polygonal tumor cells with well-defined borders, slightly eosinophilic cytoplasm and round nuclei with prominent nucleoli. HE staining, ×400.**



**Figure 6 – Diffuse strong membranous and cytoplasmic immunostaining for PLAP, ×200.**



**Figure 7 – Diffuse strong membranous and cytoplasmic immunoreactivity for podoplanin,  $\times 200$ .**



**Figure 8 – Diffuse moderate membranous immunostaining for CD117,  $\times 200$ .**

### Discussion

Primary retroperitoneal seminoma is a very rare entity in the pathology of the retroperitoneum, representing only 4.4% of all malignant primary retroperitoneal masses [1].

These tumors are usually large and palpable at diagnosis, because of their slow growth rate in a space allowing large expansion, and their poor symptomatology, both of which lead to a late presentation.

Since their clinical characteristics, lab tests and even imagistic aspects are unspecific, preoperative diagnosis and differentiation from other types of retroperitoneal tumors is often impossible. Analyzing our case, and confronting it with the literature, we identified several issues in the diagnosis and subsequent treatment of primary extragonadal germ cell tumors.

#### Precise histopathological diagnosis

Precise histopathological diagnosis of the excised retroperitoneal mass is mandatory and the corner stone of the further oncological treatment with consequences for the patient's survival.

The morphological features of the classic seminoma are well known, but its primitive retroperitoneal nature is very unusual and the histological diagnosis should be made cautiously in such cases by careful conventional morphological study and, if indicated, immunohistochemical evaluation to exclude other entities. For problematic cases, a selective panel of immunostains provides diagnostic assurance.

Placental alkaline phosphatase (PLAP) is common used as a germ cell marker. The placental fraction of alkaline phosphatase is a membrane-bound enzyme of 120 kD, normally synthesized by placental syncytiotrophoblasts, but it is also produced by many neoplasms and is expressed in lung, breast, gastrointestinal and urological tumors [5, 6]. Podoplanin is an oncofetal transmembrane mucoprotein expressed by fetal germ cells and testicular germ cell tumors and the monoclonal antibody D2-40, that labels podoplanin in a membranous staining pattern, has an excellent sensitivity for testicular and extratesticular or metastatic seminoma [5, 7, 8]. The c-Kit (CD117) is a transmembrane glycoprotein receptor tyrosine kinase and its intact signal transduction is crucial for the

development and survival of germ cells, hematopoietic stem cells, melanocytes, mast cells and interstitial cells of Cajal making it a recent favorite target of molecular therapy [5, 6]. A very sensitive and specific marker of seminoma and embryonal carcinoma is OCT4, a stem cell transcriptional regulator that maintains pluripotency in embryonic stem cells and germ cells [5, 6]. SALL4 is a nuclear transcription factor that with POU5F1, NANOG and SOX2, forms a regulatory network that maintains embryonic stem cell pluripotency and ability of self-renewal. It has been recently shown to be a sensitive and relatively specific marker for primary and metastatic gonadal and extragonadal germ cell tumors; but it may label a wider spectrum of germ cell tumor compared with OCT4 [5, 6]. The transcription factors SOX2 and SOX17 have utility in differential diagnosis, but they not be as readily available [5, 7, 8].

#### Primary versus secondary retroperitoneal germ cell tumors

A careful differentiation between primary retroperitoneal seminoma and the “burned-out” phenomenon must be made. The “burned-out” phenomenon in testicular tumors consists of an extragonadal germ cell tumor, with no current neoplasm in the testis, but with histological findings of an earlier presence of a completely regressed testicular cancer [3, 4].

This differentiation process is started with an ultrasound of the testes. Small intratesticular lesions, microlithiasis or hypoechoic atrophic testes can raise suspicion but ultimately a biopsy confirmation in order to appropriately diagnose a “burned-out” testicular tumor is needed [9, 10].

The therapeutic importance of the differentiation between a “burned-out” testicular tumor and a primary retroperitoneal germ cell tumor consists in the fact that in the first case the testicle must be excised in order to appropriately treat the patient [11, 12].

This therapeutic approach is also available if a small occult testicular tumor is found on clinical/imagistic examination. In this situation, the first step would be ipsilateral testicle removal, secondly followed by appropriate Cisplatin-based chemotherapy.

In the case of our patient, the normal aspect of both

testes, after extensive clinical, ultrasound and MRI examinations, gave us no reason to further investigate the testes with a biopsy.

Only if a testicular tumor is disproved through all investigations of the testes, the diagnosis of primary retroperitoneal seminoma can be made.

### **To remove or not the ipsilateral testicle?**

On a group of 26 patients diagnosed with primary extragonadal germ cell tumors, with testicular tumors excluded only by clinical palpation, Scholz *et al.* performed histological exams based on ipsilateral/bilateral orchiectomy or testicular biopsy. Even if only in seven patients pathological confirmation of a testicular tumor/intratubular neoplasia was found, the authors concluded that the remaining patients who had only fibrosis and scared tissue on the histological examination had a “burned-out” testicular tumor, thus recommending orchiectomy [13, 14].

Coulier *et al.* stated the need for ipsilateral orchiectomy, based on a small case series of three patients with primary retroperitoneal extragonadal germ cell tumors, because on the orchiectomy specimen in two cases an active tumor was found and in the third case a “burned-out” lesion. Of the three patients, two had a history of cryptorchidism, and associated testicular atrophy, so from the beginning their clinical and ultrasound exams could not have been considered normal [9, 10].

Anglade *et al.* described a case of primary retroperitoneal seminoma, which had an abnormal aspect of the testes on ultrasound and no proof of tumor on ipsilateral orchiectomy specimen and contralateral testicle biopsy [5, 6].

Buskirk *et al.* described his experience on a group of 12 patients treated in the Mayo Clinic for retroperitoneal primary seminoma. Two patients without clinical testicular tumor suspicion underwent ipsilateral orchiectomy, but after the microscopic examination, no histological tumor modifications were observed, and more importantly there seemed to be no effect in the retroperitoneal tumor treatment or evolution [15, 16].

Therefore, our conclusion is that ipsilateral orchiectomy is not needed if a normal testicle is found on the ultrasound. In our opinion, clinical and ultrasound examination of the testes is mandatory before surgery in all retroperitoneal masses.

### **Routine preoperative serum tumor markers determination in retroperitoneal tumors with clinically normal testes**

This case revealed to us the importance of the dosing of testicular tumor markers (LDH,  $\beta$ HCG,  $\alpha$ FP) in all retroperitoneal tumors even if the testes are clinically normal.

If the markers are elevated and the diagnosis is confirmed through biopsy, the treatment sequence could be changed, with chemotherapy as first line therapy, and surgery performed secondly only in order to remove residual masses.

In our patient’s case, the markers were determined postoperative, not at the time of the presentation, and they were within the normal ranges.

The diagnosis was made through surgery so the chemotherapy was performed in a second line manner.

$\alpha$ FP does not increase in a pure line seminoma and LDH is a rather unspecific marker, with value regarding only the prognosis and the tumor burden [7, 17, 18].

$\beta$ HCG is a marker with high specificity for seminoma, and it is of great value in monitoring the efficacy of the chemotherapy and is as well a prognostic predictor, with high values at the diagnosis being a poor outcome indicator [19, 20].

In our opinion, the testicular tumor markers should be included in the standard preoperative assessment of any retroperitoneal mass associated with normal testes, as a diagnosis of germ cell tumor can change the therapeutic approach.

### **What approach is optimal for left retroperitoneal mass excision?**

Regarding the issue of surgical approach and techniques, there are several access routes through which tumor removal can be made, each with advantages and disadvantages.

The thoraco-abdominal incision provides a wide perspective over the kidney and the renal hilum, and offers good control of the dissection especially in upper pole and hilar renal tumors in this region, but has a higher morbidity and demands longer hospitalization in the postoperative setting.

The median transperitoneal xypho-pubic incision is widely used because it provides access to the left and the right aspects of the retroperitoneum, but lacks good exposure of the left side of the retroperitoneum. In order to have a good access on the left retroperitoneal side, an extensive mobilization of the sigmoid and the descending colon is needed, usually with subsequent ligation of inferior mesenteric artery.

We decided to use a left subcostal incision prolonged paraectally, given the tumor was located on the left side, because it offers an easy and safe access to the lesion. Through descending colon mobilization, it offers a good exposure of the left lateroaortic region, without the need for inferior mesenteric artery ligation and in the postoperative setting; it provides a low morbidity and a fast recovery time for the patient.

### **Which adjuvant treatment provides better outcome (radiotherapy or chemotherapy)?**

Regarding the age of our patient (43 years old), we observe that it falls into the 34–45 years interval in which seminomatous tumors have their greatest incidence [21, 22].

Due to the histopathological diagnosis (seminoma), lack of visceral metastases, and normal values of tumor markers at diagnosis, we included our patient in the good prognosis group (*International Germ Cell Cancer Collaborative Group* – IGCCCG prognostic-based staging system) and accordingly he received three courses of Cisplatin-based chemotherapy [23, 24].

At 24 months, the patient had no signs of local or distant tumor recurrence on clinical, imagistic or serological evaluations.

We therefore recommend in this cases chemotherapy performed with a standard BEP regime as primary adjuvant treatment instead of primary radiotherapy.

## ☐ Conclusions

Primary retroperitoneal seminoma is a rare entity that must be taken into account when treating retroperitoneal tumors. It develops out of the urogenital ridge, while the testes are normal. Thorough testicular evaluation (clinical, ultrasound and serum markers) is mandatory in all retroperitoneal tumors. The histopathological and immunohistochemical exams are crucial for an accurate diagnosis and a proper management strategy. The excision of the clinical and imagistic normal ipsilateral testicle is not needed in patients with primary retroperitoneal seminomas. Through multimodal treatment (radical surgery and chemotherapy) based of the histopathological findings, most of the patients diagnosed prior to massive visceral metastatic dissemination can be cured.

## Conflict of interests

The authors declare that they have no conflict of interests.

## References

- [1] Lane RH, Stephens DH, Reiman HM. Primary retroperitoneal neoplasms: CT findings in 90 cases with clinical and pathological correlation. *AJR Am J Roentgenol*, 1989, 152(1):83–89.
- [2] Egund N, Ekelund L, Sako M, Persson B. CT of soft-tissue tumors. *AJR Am J Roentgenol*, 1981, 137(4):725–729.
- [3] Petros P, Anastasios A, Geraghty J, Macdonagh RU. Retroperitoneal seminoma with 'burned out' phenomenon in the testis. *Int J Urol*, 2005, 12(1):115–116.
- [4] Ojea Calvo A, Rodríguez Alonso A, Pérez García D, Domínguez Freire F, Alonso Rodrigo A, Rodríguez Iglesias B, Benavente Delgado J, Barros Rodríguez JM, Fiaño Valverde C, Nogueira March JL. [Extragenadal germ cell tumour with "burned-out" phenomenon in the testis]. *Actas Urol Esp*, 1999, 23(10):880–884.
- [5] Anglade RE, Chang B, Siroky MB. Primary retroperitoneal seminoma with ultrasonically abnormal testes. *Urology*, 2001, 57(4):800.
- [6] Saltzman B, Pitts WR, Vaughan ED Jr. Extragenadal retroperitoneal germ cell tumors without apparent testicular involvement. A search for the source. *Urology*, 1986, 27(6):504–507.
- [7] Klein EA. Tumor markers in testis cancer. *Urol Clin North Am*, 1993, 20(1):67–73.
- [8] Richie J, Steele G. Neoplasms of the testis. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW (eds). *Campbell–Walsh urology*. Saunders Elsevier, Philadelphia, PA, 2007, 907–908.
- [9] Comiter CV, Renshaw AA, Benson CB, Loughlin KR. Burned-out primary testicular cancer: sonographic and pathological characteristics. *J Urol*, 1996, 156(1):85–88.
- [10] Böhle A, Studer UE, Sonntag RW, Scheidegger JR. Primary or secondary extragonadal germ cell tumors? *J Urol*, 1986, 135(5):939–943.
- [11] Casella R, Rochlitz C, Sauter G, Gasser TC. ["Burned out" testicular tumor: a rare form of germ cell neoplasias]. *Schweiz Med Wochenschr*, 1999, 129(6):235–240.
- [12] Schmoll HJ. Extragenadal germ cell tumors. *Ann Oncol*, 2002, 13(Suppl 4):265–272.
- [13] Scholz M, Zehender M, Thalmann GN, Borner M, Thöni H, Studer UE. Extragenadal retroperitoneal germ cell tumor: evidence of origin in the testis. *Ann Oncol*, 2002, 13(1):121–124.
- [14] Gerl A, Clemm C, Kohl P, Niedermaier J, Schalhorn A. [Primary extragonadal germ cell tumors. Clinical manifestations, differential diagnosis and therapy]. *Med Klin (Munich)*, 1994, 89(5):240–244.
- [15] Buskirk SJ, Evans RG, Farrow GM, Earle JD. Primary retroperitoneal seminoma. *Cancer*, 1982, 49(9):1934–1936.
- [16] Tasu JP, Faye N, Eschwege P, Rocher L, Bléry M. Imaging of burned-out testis tumor: five new cases and review of the literature. *J Ultrasound Med*, 2003, 22(5):515–521.
- [17] Peyret C. Tumeurs du testicule. Synthèse et recommandations en onco-urologie. *Prog Urol*, 1993, 2:60–64.
- [18] Zagars GK, Ballo MT, Lee AK, Strom SS. Mortality after cure of testicular seminoma. *J Clin Oncol*, 2004, 22(4):640–647.
- [19] Mann K. [Tumor markers in testicular cancer]. *Urologe A*, 1990, 29(2):77–86.
- [20] Daugaard G, von der Maase H, Olsen J, Rørth M, Skakkebaek NE. Carcinoma-*in-situ* testis in patients with assumed extragonadal germ-cell tumours. *Lancet*, 1987, 2(8558):528–530.
- [21] Payombarnia SA, Safavi Sh, Azarpira N. Primary retroperitoneal seminoma: a case report. *Iranian Red Crescent Med J*, 2008, 10(2):127–130.
- [22] Inai H, Kawai K, Morishita Y, Nagata M, Noguchi M, Akaza H. Retroperitoneal extragonadal germ cell tumor in a patient with Klinefelter's syndrome. *Int J Urol*, 2005, 12(8):765–767.
- [23] International Germ Cell Cancer Collaborative Group. International Germ Cell Consensus Classification: a prognostic factor-based staging system for metastatic germ cell cancers. *J Clin Oncol*, 1997, 15(2):594–603.
- [24] Daugaard G, Rørth M, von der Maase H, Skakkebaek NE. Management of extragonadal germ-cell tumors and the significance of bilateral testicular biopsies. *Ann Oncol*, 1992, 3(4):283–289.

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