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Letter

Burned-out testicular seminoma with retroperitoneal metastasis and contralateral sertoli cell-only syndrome



Dear editor,

Spontaneous regression of testicular cancer is a rare phenomenon, which has not been completely understood. These so-called burned-out tumors typically present at metastatic stage with no testicular symptoms or clinical evidence of a primary testicular lesion and can be mistaken for primary extragonadal lesions. Choriocarcinoma is the most likely to regress without treatment, whereas a burned-out seminoma is uncommon [1]. Gonadal function is often impaired in men with testicular cancer. Approximately 25% of these men experience spermatogenic failure, such as a Sertoli cell-only syndrome with azoospermia [2]. We present the case of a patient with burned-out testicular seminoma and contralateral Sertoli cell-only pattern. Informed consent to procedures and publication was obtained from the patient before presentation of this case report.

A 52-year-old man presented with a left abdominal mass discovered by palpation in a routine physical examination performed by his general practitioner. The patient experienced no symptoms and had no relevant past medical history. Computed tomography (CT) scan showed a large retroperitoneal mass of 9.5 cm × 10.5 cm × 16 cm extending along the dorsal side of the abdominal aorta and the left common iliac artery, compressing the inferior vena cava (Fig. 1A and B). Chest CT was normal. Histological examination of one ultrasound-guided core biopsy taken from the retroperitoneal mass suggested a seminoma (Fig. 2A).

The patient was referred to our department for further diagnostic investigation. Clinical examination of the testis showed left testicular atrophy with no palpable mass. Scrotal ultrasound showed left testicular microlithiasis, but no hypoechoic lesions (Fig. 2B). The right testis was normal. Serum beta-human chorionic gonadotropin (β -hCG) and lactate dehydrogenase (LDH) were elevated at 19.7 IU/L (normally <2.6 IU/L) and 784 U/L (normally 135–225 U/L), respectively. Alpha-fetoprotein (AFP) was within normal range. Due to the possible association of microlithiasis with testicular cancer and because a regressed testicular

malignancy could not be ruled out in scrotal ultrasound, the patient underwent a left inguinal orchiectomy. Histological examination of the left testis revealed a hyaline fibrous scar with evidence of germ cell neoplasia, indicating a burned-out tumor (Fig. 2C). Biopsy of the right testicle revealed a Sertoli cell-only syndrome. The initial absence of AFP elevation and the known histology of the retroperitoneal tumor seemed to indicate a burned-out testicular seminoma.

Three weeks after surgery, the β -hCG minimally decreased to 14.9 IU/L, whereas LDH raised to 902 U/L. The chemotherapy plan of the patient included three cycles of bleomycin, etoposide, and cisplatin regimen, according to Stage IIc seminomatous germ cell tumor in good prognosis risk group [3]. At the end of the first cycle, he had a pulmonary embolism, which was treated by anticoagulants. Since bleomycin could potentially cause lung fibrosis, it was removed from the chemotherapy protocol, in order to avoid additional pulmonary complications. Another three cycles of chemotherapy with etoposide and cisplatin only were administered. After chemotherapy treatment, all testicular tumor markers were normal (β -hCG at <0.2 IU/L and LDH at 169 U/L).

Eleven weeks after the end of the treatment, abdominal CT scan showed tumor regression with residual retroperitoneal lymph nodes of 2.0 cm × 1.8 cm × 9.0 cm (Fig. 1C). Five weeks later, ^{18}F -fluorodeoxyglucose-positron emission tomography-CT showed further regression of the lesion with a maximal tumor diameter of 1.7 cm and no significant metabolic activity (Fig. 1D). Because of these findings, there was no indication for further chemotherapy. Given the lack of secondary complications, such as ureteral compression, a retroperitoneal lymph node dissection was also not indicated.

Since then, no elevation of tumor marker levels or progression of the retroperitoneal mass in CT scans has occurred. The patient remains under observation and has been recurrence free for 2 years after treatment.

<https://doi.org/10.1016/j.ajur.2021.12.001>

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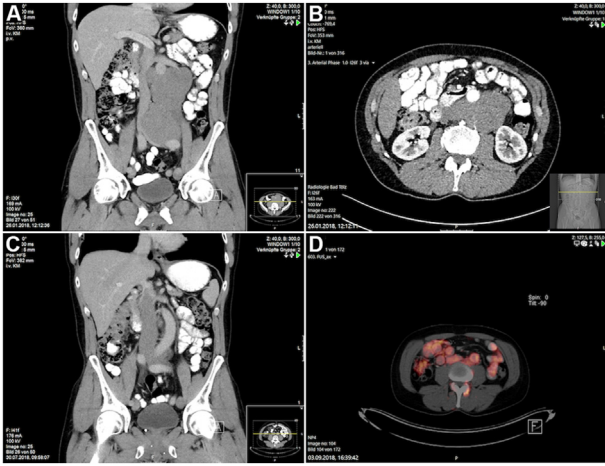


Figure 1 Abdominopelvic imaging of retroperitoneal metastasis. (A and B) Retroperitoneal mass extending along the dorsal side of the aorta compressing the inferior vena cava in abdominal CT scan, as shown in coronal and axial section view, respectively; (C) Regressed retroperitoneal mass in abdominal CT scan in coronal section view after chemotherapy; (D) The metabolic activity of the further regressed lesion in ^{18}F -fluorodeoxyglucose-positron emission tomography-CT scan in axial section view after chemotherapy. CT, computed tomography.

Spontaneous regression of tumor has been described before, such as in neuroblastoma, renal cancer, and malignant melanoma [4]. It is defined as a complete or incomplete disappearance of the tumor without therapy. The first case of burned-out testicular cancer was reported in 1927 [5]. Since then, the phenomenon is well-recognized, but not completely understood yet. Infections, fever, hormonal changes, and ischemia are some of the possible factors that have been suggested to be leading to the regression of tumor. However, immunological response in the tumor microenvironment seems to play the most important role [6].

Patients typically present with variable nonspecific symptoms at stage of metastasis. Lymph node metastases are usually located within the ipsilateral retroperitoneal lymph nodes and below the renal hilus [7] and can simulate primary neoplasms of that area arising from misplaced germ cells. Clinical examination of the testes often does not yield any specific findings, which may be the reason why

such tumors are often discovered in an advanced stage. In scrotal ultrasound, some echogenic foci or intratesticular microcalcifications can be indicative of a burned-out primary tumor [8,9]. Pathological characteristics include fibrous scarring, hematoxyphilic deposits, hemosiderin and psammoma bodies, intratubular germ cell neoplasia, and stromal calcification and extensive atrophy [8].

It is not uncommon that a metastatic lesion has different pathology from the original tumor. However, the absence of AFP elevation and the histology of the retroperitoneal tumor suggested a burned-out testicular seminoma in our case.

The distinction between burned-out testicular tumor and true primary retroperitoneal neoplasm is very important. Since the blood-testis barrier impedes the delivery of chemotherapeutic agents to the testis, primary removal of the testicular tumor is necessary, in order to avoid persistency of vital malignant cells [10].

Spermatogenesis and semen quality have been shown to be often impaired in patients with germ cell cancer [2]. One fourth of these patients experienced severe irreversible spermatogenic failure found in biopsies of the contralateral testis, including Sertoli cell-only tubules, complete spermatogenic arrest, microcalcifications, or even carcinoma *in situ*. These findings supported the theory of a testicular dysgenesis syndrome, which associates testicular cancer with impaired gonadal function [11].

Patients with germ cell tumors who receive cisplatin-based chemotherapy are at high risk of venous thromboembolic events, such as deep-vein thrombosis and pulmonary embolism [12]. Recent studies identified several risk factors for this case, including advanced stage cancer, elevated serum LDH, central venous access, and febrile neutropenia. Thromboembolic complications are significantly associated with reduced overall survival of these patients [13].

In conclusion, spontaneous regression of testicular cancer should be considered in patients who present with a retroperitoneal mass and further examinations should be performed before contemplating the diagnosis of a primary retroperitoneal germ cell tumor. The unspecific findings of clinical examination underline the importance of a radical orchiectomy in case of any abnormalities found in scrotal sonography, even if no tumor can be clearly detected, in order to avoid persistent testicular malignancy and potential source of further metastasis.

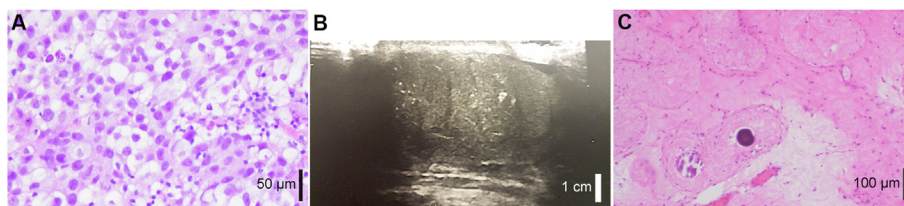


Figure 2 Histopathological and ultrasound findings. (A) Histopathology of the retroperitoneal mass showed a solid tumor consisting of large polygonal cells with mostly clear cytoplasm and prominent central nucleoli, as well as admixed lymphocytes, indicating a seminoma (hematoxylin and eosin stain). (B) Scrotal ultrasound showed left testicular microlithiasis without hypoechoic lesions. (C) Histopathology of the left testis showed focal atrophy with extensive fibrosis, multifocal calcifications, focal hemorrhage, and Leydig's cell hyperplasia (hematoxylin and eosin stain).

Author contributions

Study concept and design: Fiona-Sofia Siokou, Roman Ganzer.

Data acquisition: Fiona-Sofia Siokou.

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Drafting of manuscript: Fiona-Sofia Siokou.

Critical revision of the manuscript: Roman Ganzer.

Conflicts of interest

The authors declare no conflict of interest.

References

- [1] Tynski Z, MacLennan GT. "Burnt-out" testicular germ cell tumors. *J Urol* 2005;174:2013. <https://doi.org/10.1097/01.ju.0000183405.08748.ad>.
- [2] Berthelsen JG, Skakkebaek NE. Gonadal function in men with testis cancer. *Fertil Steril* 1983;39:68–75.
- [3] Gospodarowicz MK, Wittekind C. Urological Tumours. In: Brierley JD, Gospodarowicz MK, Wittekind C, editors. *TNM classification of malignant tumors*. 8th ed. New York: John Wiley & Sons; 2017. p195–8.
- [4] Everson TC. Spontaneous regression of cancer. *Ann N Y Acad Sci* 1964;114:721–35.
- [5] Prym P. [Spontanheilung eines bösartigen, wahrscheinlich chorionepitheliomatösen Gewächses im Hoden]. *Virchows Arch Pathol Anat* 1927;265:239–58. [Article in German].
- [6] Botseas D. Factors related to the spontaneous regression of cancer. *Hellenic J Surg* 2012;84:267–8.
- [7] 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;22:515–21.
- [8] Comiter CV, Renshaw AA, Benson CB, Loughlin KR. Burned-out primary testicular cancer: sonographic and pathological characteristics. *J Urol* 1996;156:85–9.
- [9] Bach AM, Hann LE, Hadar O, Shi W, Yoo HH, Giess CS, et al. Testicular microlithiasis: what is its association with testicular cancer? *Radiology* 2001;220:70–5.
- [10] Bart J, Hollema H, Groen H, De Vries E, Hendrikse N, Sleijfer D, et al. The distribution of drug-efflux pumps, P-gp, BCRP, MRP1 and MRP2, in the normal blood–testis barrier and in primary testicular tumours. *Eur J Cancer* 2004;40:2064–70.
- [11] Skakkebaek NE, Rajpert-De Meyts E, Main KM. Testicular dysgenesis syndrome: an increasingly common developmental disorder with environmental aspects. *Hum Reprod* 2001;16:972–8.
- [12] Piketty AC, Fléchon A, Laplanche A, Nouyrigat E, Droz JP, Théodore C, et al. The risk of thrombo-embolic events is increased in patients with germ-cell tumours and can be predicted by serum lactate dehydrogenase and body surface area. *Br J Cancer* 2005;93:909–14.
- [13] Paffenholz P, Grein K, Heidegger I, Nestler T, Grabbert M, Salem J, et al. Predictors of thrombosis in testicular cancer during platinum-based chemotherapy. *World J Urol* 2019;37:1907–16.

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