



CASE REPORT

Seminoma Retroperitoneal Relapse 23 Years After Surgery

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ABSTRACT

Stage I seminoma is the most frequent tumour in young men. It has a very good prognosis thanks to the use of a multidisciplinary therapeutic approach including surgery, radiotherapy and systemic chemotherapy. Late (after 2 years) and very late (after 5 years) relapses are uncommon, but not impossible, even if standardized follow-up for testicular tumours lasts up to 5 years after the diagnosis. We report a case of a 67-year-old Caucasian man with metachronous bilateral testicular seminoma who developed a retroperitoneal relapse of testicular seminoma 23 years after the first

orchiectomy. Based on histological confirmation of testicular relapse, the patient underwent four cycles of systemic chemotherapy with bleomycin, etoposide and cisplatin (PEB), with no adverse reactions. He subsequently achieved complete radiological response at restaging computed tomography imaging, confirmed by the absence of glucose metabolism on positron emission tomography. In conclusion, this case report suggests the importance of longer standardized follow-up for patients treated for testicular tumours in order to detect earlier recurrence, which can be successfully treated.

Keywords: Late relapse; Retroperitoneum; Stage I seminoma

Sonia Crocetti and Laura Tassone contributed equally to this case report.

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Key Summary Points

Stage I seminoma has a very good prognosis, with a survival rate about 99%.

Standardized seminoma follow-up, including laboratory and radiological exams, lasts up to 5 years after diagnosis.

Late (> 2 years) and very late (> 5 years) relapses of testicular cancer are rare, but not impossible, especially for seminoma.

We reported a case of a Caucasian man with metachronous bilateral testicular seminoma that developed retroperitoneal seminoma relapse 23 years after first surgery, successfully treated with chemotherapy.

We suggest the necessity to personalise standardized follow-up for testicular cancers, according to risk factors (primary tumour size and rete testis invasion).

DIGITAL FEATURES

This article is published with digital features, including a summary slide, to facilitate understanding of the article. To view digital features for this article go to <https://doi.org/10.6084/m9.figshare.13603853>.

INTRODUCTION

Testicular cancers are divided into seminomatous and non-seminomatous germ cells tumours, characterized by different therapeutic strategies [1]. Stage I seminoma represents 40–45% of germ cell cancers diagnosed [2], and overall survival (OS) after a successful multidisciplinary approach is close to 99% [3]. However, 4–15% of these patients experience a recurrence after the initial treatment [4]. Seventy-five percent of tumour recurrence occurs within the first 2 years after surgery (early relapse), while

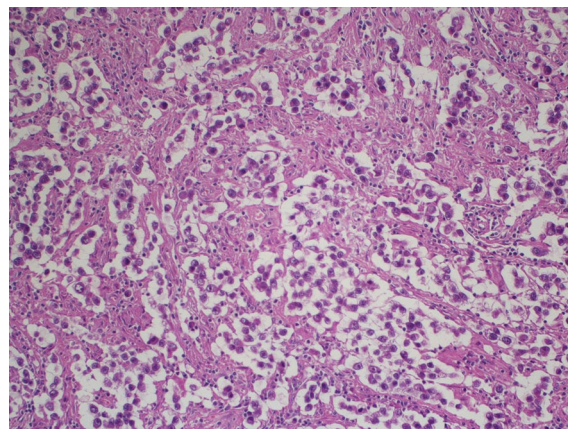


Fig. 1 Hematoxylin and eosin staining of the orchietomy specimen in 1992

late relapse (> 2 years) and very late relapse (> 5 years) are uncommon, even if the extent and pattern are similar between settings [5]. We report a case of a Caucasian man who developed retroperitoneal relapse of testicular seminoma 23 years after surgery.

CASE PRESENTATION

We present the case of a 67-year-old man with a history of right orchietomy in January 1992 for a typical seminoma limited to the testicle (stage I), with intratubular malignant germ cells (in situ seminoma) in the near parenchyma (Fig. 1). The spermatic cord was free of

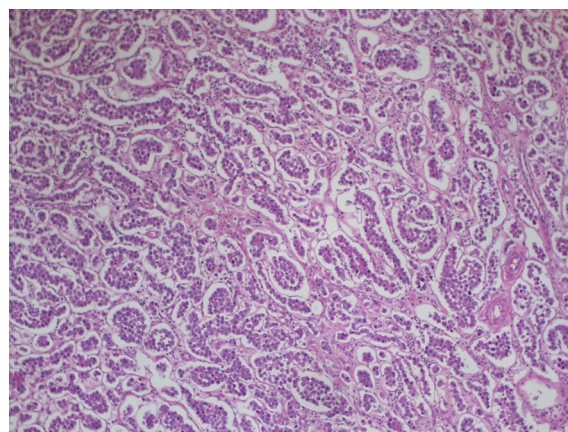


Fig. 2 Hematoxylin and eosin staining of the orchietomy specimen in 1997

neoplasia. A biopsy of the contralateral testicle showed in situ seminoma which, probably due to the young age, was monitored by regular sonography instead of removal by contralateral orchiectomy. From February to March 1992, the patient underwent radiation therapy on the inguinal and iliac bilateral lymph nodes (2540 cGy) and lumbo-aortic lymph nodes (2680 cGy), according to the guidelines of the time. In 1997, the patient underwent left orchiectomy for a palpable nodule in the left testicle, and the histological examination revealed typical testicle seminoma with infiltration of the albuginea, rete testis and spermatic cord (Fig. 2). Clinical and imaging surveillance were performed, according to international guidelines. In January 2020, the patient presented to our hospital with lumbar pain irradiating to the left leg, increasing in the last month. Nuclear magnetic resonance imaging (MRI) of the lumbosacral spine was performed and showed a large anterolateral left para-vertebral mass (9.9×8 cm), extending from L1 to L3–L4, which encased the abdominal aorta and the inferior vena cava. A staging chest and abdomen computed tomography (CT) scan confirmed the left para-aortic solid expansive mass ($10 \times 7 \times 9$ cm) (Fig. 3). Blood tests showed normal levels of alpha-fetoprotein



Fig. 3 CT scan of retroperitoneal left mass at diagnosis

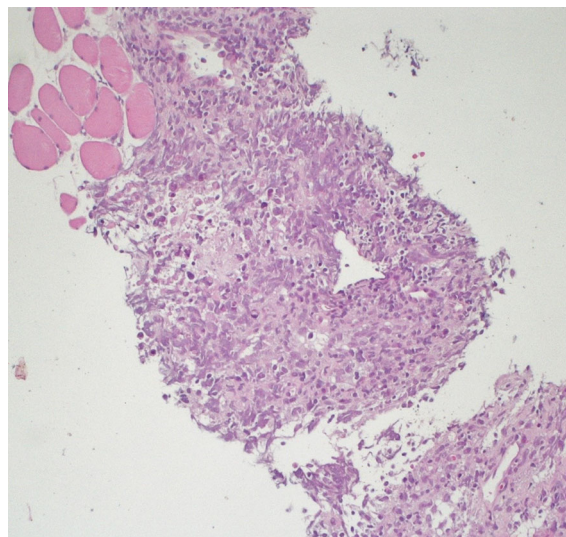


Fig. 4 Hematoxylin and eosin staining of the retroperitoneal dissected specimen

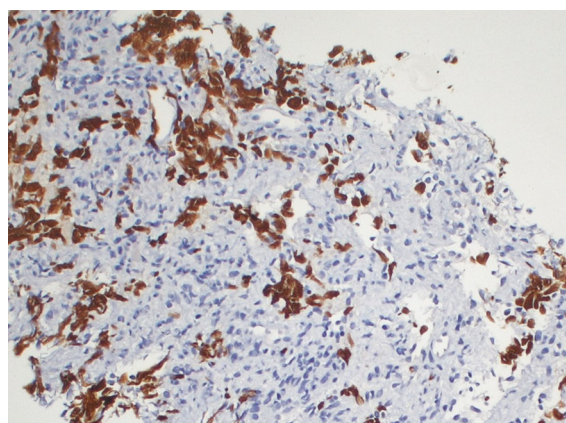


Fig. 5 Immunohistochemical staining for SALL4 of the retroperitoneal dissected specimen

(AFP) (2.4 ng/mL) and beta human chorionic gonadotropin (beta-hCG) (3 mIU/mL) and elevated levels of lactate dehydrogenase (LDH) (257 U/L). A CT scan-guided biopsy of the left retroperitoneal lesion was performed; the histological examination revealed fibro-adipose muscular striated tissue infiltrated by germinal neoplasia, type seminoma (SALL4+, OCT4+, PLAP–, CK AE1/AE3–, CD30–) (Figs. 4, 5, 6, 7). In addition, the patient underwent electrocardiography and cardiac ultrasound, which

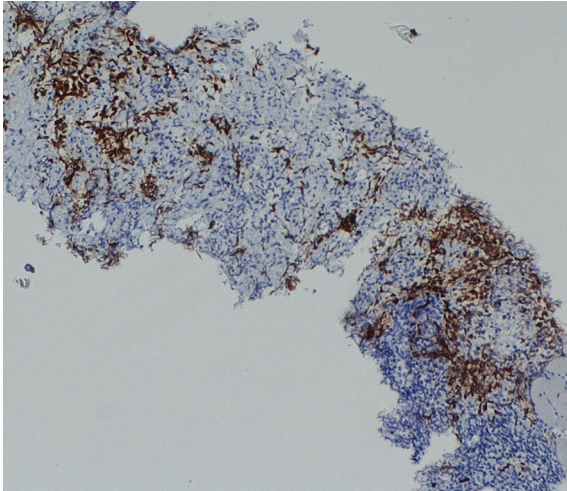


Fig. 6 Immunohistochemical staining for OCT4 of the retroperitoneal dissected specimen

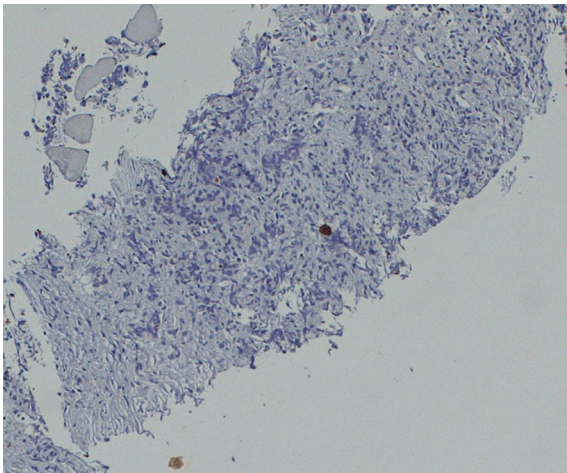


Fig. 7 Immunohistochemical staining for CKAE1/AE3 of the retroperitoneal dissected specimen

showed no alterations, and spirometry, which showed moderate restrictive respiratory failure. Therefore, after multidisciplinary discussion, chemotherapy regimens including TIP (paclitaxel, ifosfamide and cisplatin) or PEI (modified cisplatin, etoposide and ifosfamide) were proposed to the patient, who refused these options because of the hospitalization required. For this reason he was treated with four cycles of chemotherapy with bleomycin, etoposide and

cisplatin (PEB) with a modified schedule of bleomycin (only first day of treatment) due to the respiratory failure, and with the support of granulocyte colony-stimulating factor (pegfilgrastim). Chemotherapy was administered without any complications except for mild dyspnoea, occasional hiccups and dry eye sensation. There was a progressive normalisation of LDH levels, whereas AFP and beta-hCG remained within the normal range. A chest and abdominal CT scan performed after the fourth cycle of chemotherapy showed a significant reduction in the left retroperitoneal para-aortic mass, with no further extension between left renal vessels. The residual tissue remained indistinguishable from the left psoas muscle and from the longitudinal vertebral anterior ligament (Fig. 8). Fluorodeoxyglucose positron emission tomography (FDG CT-PET) was performed and showed a minimal increase in glucose metabolism (standardized uptake value: max 2.8) of the left retroperitoneal para-aortic solid residue tissue, indicating a nearly complete response to the chemotherapy. Approximately 6 weeks later, a second FDG CT-PET confirmed complete response to treatment, and the patient was started on clinical and imaging surveillance. Written informed consent was obtained for publication of the patient's clinical details.

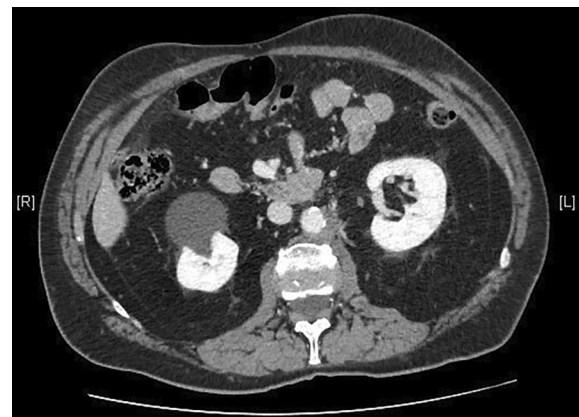


Fig. 8 CT scan of retroperitoneal left mass after four cycles of chemotherapy

DISCUSSION

Patients with stage I seminoma achieve a survival rate of about 99%, regardless of therapeutic strategy including adjuvant radiotherapy, adjuvant chemotherapy with one cycle of carboplatin, or surveillance [6]. Good prognosis post-orchietomy has been confirmed in several trials: Kamba et al. performed a Japanese multi-institutional retrospective observational study on 425 patients, showing 10-year OS of 100%, 100% and 99% in the surveillance, chemotherapy and radiotherapy groups, respectively. Conversely, the relapse-free survival rates at 10 years were 79%, 94% and 94%, respectively, in the same groups [7]. The risk of relapse is highest during the first 2 years after treatment (early relapses); the annual risk rate is > 5% for surveillance and > 1% for radiotherapy or chemotherapy. However, late relapses are very uncommon and occur more frequently in the retroperitoneal space, followed by the chest or neck [8]. They are generally detected by symptoms because they occur after the conclusion of the standard follow-up, and up to half can present with elevation of tumour markers [9, 10]. The treatment of stage I seminoma late relapse is based on the previous therapy, with good prognosis. In particular, after radiation, late relapses occur mainly outside the prior radiation field, most commonly in the pelvis, with a recurrence rate of 3–4%, and are usually responsive to cisplatin-based chemotherapy. Otherwise, late relapses after single-agent carboplatin are mostly salvaged by cisplatin chemotherapy or by radiotherapy [8, 11].

Primary tumour size greater than 4 cm and rete testis invasion represent the major prognostic factors for relapse [12]. For example, Chung et al. showed an increase in the risk of relapse at 3 years from 2% for tumour size equal to or less than 1 cm, to 25% for tumour size of 6 cm or greater [13]. AFP and beta-hCG represent the common biomarkers used in the follow-up of germ cell tumours, even if the increase in AFP is typical in late-relapsing of non-seminoma neoplasms, with levels greater than 100 U/L appearing to indicate poor prognosis [14]. On the contrary, in relapses of

seminoma, the level of LDH increases according to the volume of disease, especially in late relapses [15], as we found in our patient's blood test. Several studies have evaluated differences between early and late relapses of germ cell tumours. Fedyanin et al. showed that patients with late relapse were usually older and had more frequent pure seminoma in primary tumours. Both groups showed similar prognostic factors at the time of relapse, even though patients with late relapse showed a larger size of disease, especially in seminoma recurrence. Regarding the outcome, subjects with late relapse achieved a lower response rate after chemotherapy, 3-year progression-free survival (PFS) and 3-year OS, and prognosis seems even worse in the case of pure seminoma [15]. On the contrary, Mortensen et al. analysed 2000 cases of seminoma and revealed no significant differences in disease-specific or overall survival between early, late and very late groups, although increased time to relapse was negatively associated with survival [16]. The role of the time to relapse is not clear, and the literature data are conflicting, due to the rarity of testicular disease. Regarding advanced disease, the prognosis of patients relapsing after cisplatin-based first-line treatment is variable, with 2-year survival rates ranging from 75% (very low risk) to 6% (very high risk). In these cases, salvage treatment is based on high-dose chemotherapy or conventional-dose chemotherapy, without significant differences in OS or PFS. Considering the variability in chemotherapy response, surgery should be conducted whenever possible, especially in localized relapses and in chemotherapy-refractory patients [17, 18].

Finally, our case report underlines the importance of an individualised approach to prolong duration of follow-up in patients treated for testicular cancer, considering the patient's age and the primary risk factors (rete testis invasion and tumour size), due to the possibility of disease relapse even after many years from the initial treatment. Moreover, these patients have an increased risk for developing secondary malignant neoplasms following radiation exposure from diagnostic imaging and due to radiotherapy, which is correlated

with increased risk of developing both solid tumours, leukaemia and cardiovascular diseases [19, 20].

CONCLUSION

We reported a case of very late retroperitoneal relapse of pure seminoma successfully treated with chemotherapy. Even if there is not a standardized long follow-up for testicular cancers, our case suggests that, according to risk factors such as size of primary tumour and rete testis invasion, patients treated for testicular cancers need to be monitored longer to detect earlier recurrence and/or secondary malignant neoplasms.

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Disclosures. Sonia Crocetti, Laura Tassone, Mariangela Torniai, Chiara Pierantoni, Luciano Burattini, Alessandra Mandolesi, Maika Di Benedetto, Giovanna Mantello and Marina Scarpelli have nothing to disclose. Rossana Berardi is an Editor-in-Chief of *Oncology and Therapy* but has nothing else to disclose.

Compliance with Ethics Guidelines. Written informed consent was obtained for publication of the patient's clinical details.

Data Availability. Data sharing is not applicable to this article as no data sets were generated or analysed during the current study.

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