

A case of spermatic cord teratoma in low-stage testicular cancer managed by surveillance

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SUMMARY

Background A 25-year-old male presented to his local urologist with new-onset right testicular pain and swelling detected on self examination. A scrotal ultrasound scan showed a right testicular mass, suspicious for neoplasm. Serum levels of α -fetoprotein and human chorionic gonadotropin were found to be elevated at 920.2 $\mu\text{g/l}$ and 637.4 U/l, respectively. The patient underwent right inguinal orchiectomy and was diagnosed with nonseminomatous germ cell tumor of the right testis, composed of yolk sac tumor, teratoma, and embryonal carcinoma with no evidence of metastatic disease. He opted to remain under surveillance rather than undergo primary chemotherapy or retroperitoneal lymph node dissection for his clinical stage I disease. Serologic relapse at 4 months after orchiectomy was successfully treated with bleomycin, etoposide and cisplatin (BEP) chemotherapy.

Investigations Surveillance comprised regular clinic visits, measurement of serum levels of α -fetoprotein, human chorionic gonadotropin and lactate dehydrogenase, chest X-ray and CT of the abdomen and pelvis. Pathology of the testicular mass was reviewed.

Diagnosis A 1.7 cm nodule anterior to the right psoas muscle suspicious for metastatic disease that was seen on CT 16 months after orchiectomy was pathologically confirmed as recurrent mature teratoma in the spermatic cord. Additionally, one of eleven interaortocaval lymph nodes showed evidence of teratoma.

Management Bilateral nerve-sparing retroperitoneal lymph node dissection with complete excision of the right spermatic cord was performed. The patient has since remained disease-free, with normal levels of serum tumor markers and no evidence of metastasis on chest X-ray and abdominal CT.

KEYWORDS cord recurrence, nonseminomatous germ cell tumor, retroperitoneal lymph node dissection, surveillance, teratoma

CME

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THE CASE

A 25-year-old white male presented to his local urologist with new-onset testicular pain of 2 weeks' duration, and was noted on examination to have an enlarged right testicle. The remainder of his physical examination, medical history and surgical history were unremarkable. He had no history of cryptorchidism or genital trauma, and no family history of testicular cancer. A scrotal ultrasound scan performed on the day of presentation showed a solid intratesticular mass, which raised suspicion for testicular neoplasm. At presentation, levels of serum tumor markers were elevated: human chorionic gonadotrophin (hCG) level was 637.4 U/l (normal range <5 U/l) and α -fetoprotein (AFP) level was 920.2 $\mu\text{g/l}$ (normal range 1–10 $\mu\text{g/l}$). The referring urologist opted not to measure serum lactate dehydrogenase (LDH) level at this time. As testicular neoplasm was suspected, right inguinal orchiectomy with high ligation of the spermatic cord was performed 2 weeks after the onset of symptoms. Histopathology showed a 7 cm mixed germ cell tumor comprising 60% yolk sac tumor, 30% teratoma and 10% embryonal carcinoma. The tumor was confined to the testis, without vascular invasion, and all margins (including the spermatic cord) were negative. CT of the chest, abdomen and pelvis showed no sign of metastatic disease. The patient was diagnosed with stage T1N0M0S1 nonseminomatous germ cell tumor (NSGCT) of the right testis.

At 6 weeks after orchiectomy, the patient's serum tumor marker levels had normalized to hCG <0.5 U/l, AFP 8.7 $\mu\text{g/l}$, and LDH 121 U/l (normal range 100–220 U/l). The patient opted to remain under surveillance with monthly measurement of serum tumor marker levels

and chest X-rays, rather than undergo retroperitoneal lymph node dissection (RPLND) or primary chemotherapy. Four months after orchiectomy, his serum AFP level had increased to 24.8 µg/l; hCG and LDH levels had remained normal. He underwent three cycles of bleomycin, etoposide and cisplatin (BEP) chemotherapy for serologic relapse of low-risk disease. On completion of chemotherapy, the patient's serum tumor marker levels had normalized and CT of the abdomen and pelvis and chest X-ray remained negative for metastatic disease. He had one episode of febrile neutropenia, but otherwise experienced no adverse effects of chemotherapy.

The patient continued to do well; monthly measurements showed normal serum tumor marker levels, and quarterly imaging indicated remission. At 16 months after orchiectomy, a CT scan of the abdomen and pelvis revealed a 1.7 cm nodule anterior to the right psoas muscle (Figure 1). A bilateral nerve-sparing RPLND was performed 1 month later (Figure 2), which included complete excision of the spermatic cord from the origin of the testicular vein at the inferior vena cava to its distal extent in the proximal inguinal canal. Following an uncomplicated operative and postoperative course, the patient was discharged on the fourth day after surgery. His final pathology revealed a 2.2 cm mass in the right spermatic cord, consistent with mature teratoma, with negative margins and one of eleven interaortocaval lymph nodes positive for mature teratoma. The remainder of the para-aortic and paracaval nodes were negative for cancer. Seven months after RPLND, the patient was doing well with normal serum tumor marker levels. He has continued to receive follow-up with quarterly measurement of serum tumor marker levels and chest X-rays, as well as twice-yearly abdominal CT scans.

DISCUSSION OF DIAGNOSIS

Testicular tumors are the most common malignancy affecting men between the ages of 15 and 35 years, with a lifetime incidence of approximately 0.2%. Sensitive and specific serum tumor markers, predictable patterns of metastatic spread (i.e. primarily to the retroperitoneum) and effective chemotherapeutic and surgical treatment options contribute to the excellent long-term prognosis for affected patients. Testis cancers typically present with a testicular mass or enlargement or induration of the



Figure 1 CT scan of the patient's abdomen 16 months after orchiectomy. A 1.7 cm mass (arrow) superior to the right psoas muscle can be seen.

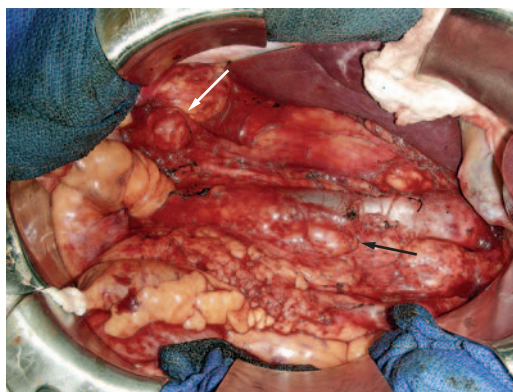


Figure 2 Intraoperative view of the retroperitoneal lymph node dissection. The image shows spermatic cord metastasis (white arrow) and interaortocaval metastasis (black arrow).

testis, and need to be distinguished from other scrotal pathologies, such as acute epididymitis, testicular torsion and benign masses. On ultrasonography, these cancers generally appear as heterogeneous intratesticular masses that prompt orchiectomy, as was the case with this patient. Diagnosis and staging of the primary disease involves inguinal orchiectomy with high ligation of the spermatic cord and preoperative measurement of serum tumor markers (i.e. AFP, hCG and LDH). Trans-scrotal biopsy is contraindicated because of the risk of tumor seeding in the scrotum. Initial radiographic studies include abdominal and pelvic CT for assessment of retroperitoneal lymph nodes, and chest X-ray to detect pulmonary metastases. Chest CT has high sensitivity for pulmonary metastases, and should be performed in patients with abnormal abdominopelvic CT scans.

Pathologic review of the orchiectomy specimen is critical for accurate disease staging. For NSGCT, lymphovascular invasion, the presence of embryonal carcinoma and the absence of yolk sac elements have been shown to be independent predictors of recurrence in the retroperitoneum.¹ More-recent studies have indicated that the proportion of embryonal carcinoma is more predictive of relapse than is simply the presence versus absence of this histopathological subtype.² The patients with the highest risk of relapse seem to be those whose tumors show lymphovascular invasion and a predominance of embryonal carcinoma. The current patient was deemed a good candidate for surveillance because his orchiectomy specimen showed no lymphovascular invasion and a low proportion of embryonal carcinoma. Risk factors for recurrence in patients with seminomas include invasion of the rete testis, tumor size >4 cm, and lymphovascular invasion.³ When there is no radiographic evidence of metastatic disease, the cancer is classified as clinical stage I. Of patients with clinical stage I NSGCT and normal postorchiectomy serum tumor marker levels, about 70% are cured by orchiectomy alone, with occult metastases present in the remainder.⁴ As CT has a 30% false-negative rate for identifying nodal metastases, RPLND is the only accurate method for staging disease in the retroperitoneum.⁵ Men with clinical stage I disease who have rising or persistently elevated postoperative serum tumor marker levels are termed to have stage IS disease, and are treated with chemotherapy for micrometastatic disease; this was the case in this patient, who exhibited serologic relapse at 4 months.

TREATMENT AND MANAGEMENT

The management options for clinical stage I NSGCT include surveillance, chemotherapy with two cycles of BEP, and RPLND; there is no clear consensus on the optimum approach, as all three carry 5-year disease-specific survival rates of 97% or more.² After factoring in the expenses associated with surgery, chemotherapy, repeated imaging and office visits, there is no significant difference in overall cost between the different options.⁶ As a result of the efficacy of cisplatin-based chemotherapy in treating germ cell tumor relapse, surveillance has become a feasible option that avoids the potential morbidity of primary chemotherapy or RPLND. Patients who opt for surveillance need to be advised on the need

for strict adherence to protocols for regular office visits, laboratory work and imaging. Primary chemotherapy or RPLND become increasingly preferable options for those patients with clinical stage I disease who have risk factors for retroperitoneal relapse.

This case illustrates the importance of regular imaging for patients on surveillance, with attention paid to common areas of metastatic spread, including paracaval, interaortocaval and para-aortic lymph nodes, as well as areas outside the retroperitoneal landing zones. The combination of serum tumor marker measurement and imaging with CT is likely to detect almost all relapses of NSGCT, making surveillance a feasible option. The current case demonstrates the importance of using both surveillance techniques, as this patient's initial relapse was detected by serum marker elevation and his second relapse was detected by imaging alone. Optimum imaging intervals for surveillance have not been determined, although a recent randomized trial, with results published in 2007, showed equal efficacy in detecting relapse for chest and abdominal CT scans performed at 3 and 12 months after orchiectomy compared with those performed at 3, 6, 9, 12, and 24 months.⁷ By contrast, physical examination, chest X-ray and measurement of serum tumor markers should be done at each quarterly office visit.

An important tenet of RPLND is complete excision of the ipsilateral spermatic cord, including testicular vein ligation at the inferior vena cava on the right or renal vein on the left. Involvement of the ipsilateral spermatic cord remnant is an uncommon occurrence that was found in 5% of patients at the time of RPLND at a tertiary cancer center, one-third of whom did not have evidence of lymphovascular invasion at orchiectomy.⁸ Four patients with NSGCT had previously presented to this center with ipsilateral paracolic recurrence that might have resulted from incomplete excision of the spermatic cord at RPLND. Paracolic recurrence has also been observed in low-stage seminoma following chemotherapy.⁹ Equally important is the high ligation of the spermatic cord at inguinal orchiectomy. In one large series of clinical stage I testicular seminoma and nonseminoma, 2% of patients on surveillance, including 4% of those with NSGCT, developed inguinal metastases.¹⁰

Patients under surveillance who relapse with elevated levels of tumor markers or metastases on radiographic survey can be treated with 3–4 cycles

of BEP chemotherapy. Whereas patients with recurrence while on surveillance have approximately a 95% 5-year disease-specific survival rate with chemotherapy, patients with small-volume retroperitoneal adenopathy and normal levels of serum markers might opt instead to undergo RPLND, with the need for chemotherapy determined by pathological findings.² The indications for postchemotherapy RPLND are still evolving, but surgery should be performed if there is radiologic evidence of residual retroperitoneal lymphadenopathy. Several series of patients undergoing resection of residual masses have shown that roughly 40% of patients have necrosis or fibrosis, 40% have teratoma, and 10–15% have viable germ cell tumor in the retroperitoneum at the time of RPLND. Patients with complete serologic and radiographic remission after chemotherapy can be safely kept under surveillance.¹¹ Some authors have argued, however, that even those individuals with residual masses less than 1 cm on CT should undergo postchemotherapy RPLND because no clinical or radiographic parameter, including size reduction, can identify those patients who have a sufficiently low risk of harboring residual cancer or teratoma.¹²

Teratoma, while histologically benign, can potentially grow to become unresectable, undergo malignant transformation, and result in late relapse.² Growing teratoma syndrome, defined as a chemorefractory metastatic mass consisting of teratoma with normal levels of serum tumor markers, is a rare entity that was seen in only 2.2% of patients who underwent RPLND at a tertiary cancer center.¹³ Some series have shown that teratoma in the orchiectomy specimen is predictive of retroperitoneal teratoma at postchemotherapy RPLND, although 28–48% of patients without teratoma in the primary tumor still had teratoma in the retroperitoneum.^{14,15} A growing retroperitoneal mass after chemotherapy in the presence of normal AFP, hCG and LDH levels should raise suspicion for teratoma and prompt surgical intervention, as in the present case.

CONCLUSIONS

The management of clinical stage I NSGCT of the testis follows evidence-based principles and is guided by well-established diagnostic tools, including orchiectomy pathology, serum tumor markers (i.e. AFP, hCG and LDH) and imaging with abdominal CT and chest radiography.

Patients affected by low-stage NSGCT have excellent long-term survival and can be managed by surveillance, adjuvant chemotherapy or RPLND. Patients on surveillance should have imaging performed at regular intervals, with attention paid to potential sites of relapse, including the retroperitoneum and the ipsilateral spermatic cord. High ligation of the spermatic cord at orchiectomy and complete excision of the spermatic cord remnant during RPLND are important principles in the surgical management of testicular cancer.

References

- 1 Freedman LS *et al.* (1987) Histopathology in the prediction of relapse of patients with stage I testicular teratoma treated by orchidectomy alone. *Lancet* **2**: 294–298
- 2 Choueiri TK *et al.* (2007) Management of clinical stage I nonseminomatous germ cell testicular cancer. *Urol Clin North Am* **34**: 137–148
- 3 Warde P *et al.* (2002) Prognostic factors for relapse in stage I seminoma managed by surveillance: a pooled analysis. *J Clin Oncol* **20**: 4448–4452
- 4 Peckham MJ *et al.* (1982) Orchidectomy alone in testicular stage I non-seminomatous germ-cell tumours. *Lancet* **2**: 678–680
- 5 Yoon GH *et al.* (2005) Retroperitoneal lymph node dissection in the treatment of low-stage nonseminomatous germ cell tumors of the testicle: an update. *Urol Oncol* **23**: 168–177
- 6 Lashley DB *et al.* (1998) A rational approach to managing stage I nonseminomatous germ cell cancer. *Urol Clin North Am* **25**: 405–423
- 7 Rustin GJ *et al.* (2007) Randomized trial of two or five computed tomography scans in the surveillance of patients with stage I nonseminomatous germ cell tumors of the testis: Medical Research Council Trial TE08, ISRCTN56475197 – the National Cancer Research Institute Testis Cancer Clinical Studies Group. *J Clin Oncol* **25**: 1310–1315
- 8 Chang SS *et al.* (2002) Paracolic recurrence: the importance of wide excision of the spermatic cord at retroperitoneal lymph node dissection. *J Urol* **167**: 94–96
- 9 Kantzavelos L *et al.* (2003) Paracolic recurrence of stage I seminomas [abstract]. *Urology* **62**: 145
- 10 Daugaard G *et al.* (2006) Inguinal metastases from testicular cancer. *BJU Int* **97**: 724–726
- 11 Debono DJ *et al.* (1997) Decision analysis for avoiding postchemotherapy surgery in patients with disseminated nonseminomatous germ cell tumors. *J Clin Oncol* **15**: 1455–1464
- 12 Oldenburg J *et al.* (2003) Postchemotherapy retroperitoneal surgery remains necessary in patients with nonseminomatous testicular cancer and minimal residual masses. *J Clin Oncol* **21**: 3310–3317
- 13 Spiess PE *et al.* (2007) Surgical management of growing teratoma syndrome: the MD Anderson Cancer Center experience. *J Urol* **177**: 1330–1334
- 14 Beck SDW *et al.* (2002) Teratoma in the orchiectomy specimen and volume of metastasis are predictors of retroperitoneal teratoma in post-chemotherapy nonseminomatous testis cancer. *J Urol* **168**: 1402–1404
- 15 Carver BS *et al.* (2006) Predicting teratoma in the retroperitoneum in men undergoing post-chemotherapy retroperitoneal lymph node dissection. *J Urol* **176**: 100–104

Competing interests

The authors declared no competing interests.