Journal of Cancer Science & Therapy

Case Report Open Access

Spinal Cord Compression Caused by Metastasis of a Non-Seminomatous Testicular Tumour with a Predominant Yolk Sac Component in a 26-Year-Old Man

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Abstract

Background: Pure testicular yolk sac tumours are extremely rare among adults, and there is no prior report of spinal cord compression syndrome due to yolk sac testis tumour metastasis in an adult.

Case presentation: Here we describe the case of a 26-year-old male with a testicular yolk sac tumour that was found when a vertebral metastasis caused spinal cord compression. Symptoms included lower back pain and a growing painless testicular mass. Treatment comprised emergency surgical spinal cord decompression and orchidectomy, followed by 3 cycles of bleomycin, etoposide, and platinum (BEP) chemotherapy, and then 3 cycles of etoposide and platinum and 40 Gy vertebral radiotherapy. One year later, cement leaked into the spinal duct, prompting a return of compression syndrome. Corporectomy was performed, followed by osteosynthesis. The patient's treatment was consolidated with 34 months and zoledronic acid administration. Although spinal metastasis from a yolk sac tumour is extremely rare, it must be considered in young adults with a testicular mass who exhibit pain or limb numbness. Such cases warrant rapid surgical decompression and radical orchidectomy, followed by adjuvant chemotherapy.

Conclusion: Our case is atypical due to the patient's age and the disease presentation. Spinal cord compression syndrome caused by yolk sac tumor metastasis is extremely rare in adulthood, and usually has a bad prognosis when diagnosed late.

Keywords: Yolk sac tumour; Spinal cord compression syndrome ; Adult; Cisplatin; Testicular tumour

Abbreviations: NSGCTs: Testicular Seminomas and Non-Seminomatous Germ Cell Tumours; CT: Computed Tomography; LDH: Lactate Dehydrogenase; beta-HCG: Gonadotropic Chorionic Hormone; MRI: Magnetic Resonance Imaging; ^{18}FDG-PET: 18-Fluorodeoxyglucose Positron Emission Tomography; PLAP: Phosphatase alkaline; MMO: Multidisciplinary Meeting of Oncology; BEP: Bleomycin, Etoposide, and Platinum; Gy: gray

Introduction

Testicular cancer is rare among adults (representing 0.5% of all cancers), but accounts for 21% of all neoplasms in male adolescents and young adults (15-29 years of age) and is the most common solid cancer in this age group [1]. This cancer has two histological subtypes: testicular seminomas and non-seminomatous germ cell tumours (NSGCTs). The latter group includes embryonal carcinomas, teratomas, choriocarcinomas, and yolk sac tumours. Five-year survival rates vary based on histology, being over 95% for seminomas, and below 70% for NSGCTs (<50% for yolk sac tumours) [1].

A few cases have been reported in which a primary retroperitoneal tumour shows spinal column or spinal cord invasion, usually involving paediatric patients [2,3]. To our knowledge, the literature includes no previous report of an adult patient showing spinal cord compression syndrome due to metastasis of a NSGCT with a yolk sac component. Two reported cases have involved an extragonadal yolk sac tumour: one originating from the retroperitoneum [4], and the other from the mediastinum [5].

For NSGCTs in the paediatric population, recommended therapies include an initial radical orchiectomy, followed by retroperitoneal lymph node dissection. In cases with recurrence or metastasis, cisplatin-based chemotherapy is administered, along with strengthening radiotherapy when necessary [6,7]. However, the treatment protocol is not well-defined [1]. In Europe, the current standard is metastasis-directed radiotherapy [7].

In the present case report, we describe an unusual presentation of a yolk sac testis tumour with spinal metastasis, and report the successful treatment administered in this case.

Case Presentation

On December 30, 2005, a 26-year-old man with no remarkable medical history was admitted to the emergency room of our hospital for low back pain. His general practitioner had sent him to the hospital to undergo a computed tomography (CT) scan of the lumbo-sacral

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Received March 27, 2020; **Accepted** April 17, 2020; **Published** April 24, 2020

Citation: Di Gregorio M, Pochet C, Dupont M, Nollevaux MC, Lorge F, et al. (2020) Spinal Cord Compression Caused by Metastasis of a Non-Seminomatous Testicular Tumour with a Predominant Yolk Sac Component in a 26-Year-Old Man. J Cancer Sci Ther 12: 06-09.

region. The patient had experienced major back pain for several months but had no neurological symptoms. He also had a painless scrotal mass that had been growing for 3 years, which had not been previously investigated. He had no fever and wasn't taking any medication. He was non-smoker, and his alcohol consumption was unremarkable.

Neurological examination was normal, but a positive Lasègue's sign was observed. Laboratory testing revealed an increased LDH of 1504 IU/L (normal range: 313-618 IU/L), increased alpha-foetoprotein of 80 957 ng/ml (normal range: <7 ng/ml), and normal beta-HCG of 22 mIU/L (normal range: <25 IU/ml).

The patient exhibited a 15-cm tumefaction in the right testis. This tumefaction was not erythematous, did not show ecchymosis, and was not painful or depressible upon palpation. It was not fixed to the skin, but rather to deeper tissues. Scrotal ultrasound revealed a right testicular mass exhibiting a heterogeneous echo structure with multiple small cystic components (Figure 1A). Contrast-enhanced multidetector computed tomography revealed an 8-mm right inferior pulmonary lobe nodule with a right testicular mass (Figure 1B), as well as spinal cord compression by a lesion of the 1st lumbar vertebra with epidural extension (Figure 2A). Magnetic resonance imaging of the full spinal cord revealed lumbar compression (Figure 2B), a neoplastic medullar replacement at the C4-C5 level, and a leptomeningeal increment in front of thebrain stem. Cerebral MRI showed no other signs of leptomeningeal carcinomatosis.

To relieve the spinal cord compression, laminectomy was performed with vertebroplasty and fixation of the first lumbar vertebra. Right orchidectomy was also performed while the patient was under anaesthesia. The cervical lesion was considered stable and was not operated. A post-operative bone scan and 18-fluorodeoxyglucose positron emission tomography (^{18}FDG-PET) revealed no additional lesions.

Pathological analysis revealed a malignant NSGCT comprising a major component of yolk sac tumour cells and a smaller component of anaplastic seminoma cells. At the centre of the tumour, these cells formed a structure called a Schiller-Duval corpus, which is a tapestry of loose tissue centred around a blood vessel with thin walls (Figure 3). The tunica vaginalis and albuginea were infiltrated, and there was substantial vascular permeation, but the epididymis and spermatic duct showed no invasion. Immunohistochemistry revealed diffuse alpha-foetoprotein expression among the tumour cells, with particularly high intensity seen in the yolk sac tumour cells. This cell population also exhibited cell membrane expression of the cytokeratins AE1/E3 and CD_{117} (c-kit). The minority tumour cells (anaplastic seminoma) were highly positive for PLAP and CD_{117}. The tumour cells were negative for CD_{30}, and beta-HCG was not contributive.

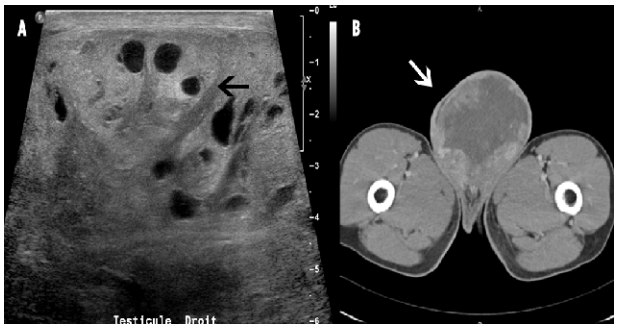

Figure 1: (**A**) Ultrasound image of the right testicular mass, showing a heterogeneous echo structure with multiple small cystic components. (**B**) Axial contrast-enhanced multidetector computed tomography image showing a large heterogeneous testicular mass.

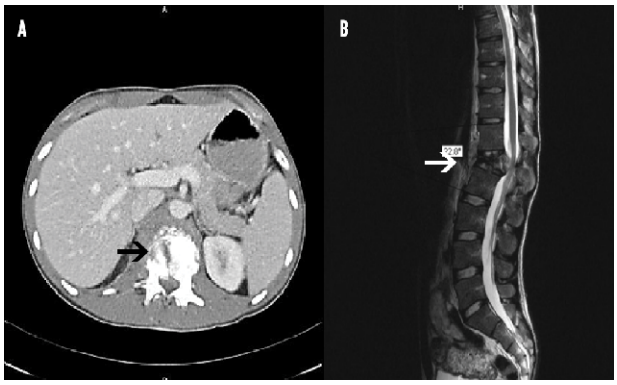

Figure 2: (**A**) Axial contrast-enhanced multidetector computed tomography image at the level of the first lumbar vertebral body, showing vertebral fracture with peripheral soft tissue bulging. (**B**) Sagittal T2-weighted MRI of the spine showing pathological fracture of first lumbar vertebra with spinal cord compression.

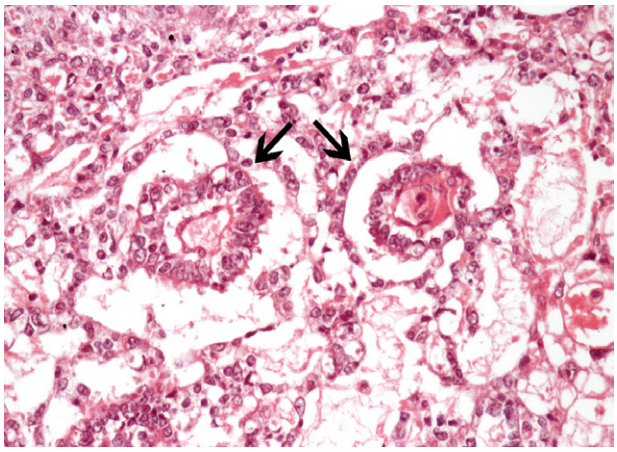

Figure 3: Malignant germ cell tumour comprising a major component of yolk sac tumour cells and a smaller component of anaplastic seminoma cells. At the centre of the tumour is a structure called a Schiller-Duval corpus (arrow), in whichthe tumour cells form a tapestry of loose tissue centred around a blood vessel with thin walls (H&E staining, magnification ×20).

The final staging of the cancer was Stage IV $pT_4\,cN_0\,pM_{1b}\,S_3$ yolk sac testicular neoplasia. After multidisciplinary meeting of oncology (MMO), the proposed treatment included 3 cycles (3 weeks each) of bleomycin, etoposide, and platinum (BEP) chemotherapy, followed by consolidation radiotherapy. Sperm cryopreservation was performed before starting BEP chemotherapy.

Twenty-four days after the patient's arrival in the emergency room, the first cycle of BEP chemotherapy was started. After 3 cycles, the decrease of alpha-foetoprotein to 16.4 ng/ml (normal range: <7 ng/ml) was so encouraging that we decided to continue treatment with cisplatin for three more cycles, but to stop treatment with bleomycin to spare the pulmonary function. After 4 cycles of EP chemotherapy (cisplatin and VP_{16}) the alpha-foetoprotein level decreased to 4.2 ng/ml, which is within the normal range of <7 ng/ml.

One month after the end of the sixth cycle, bone scan imaging

indicated disease expansion at the thoracic level, spreading to the 6th cost-vertebral articulation and articular epiphysis of L_2. Thus, the patient was administered locoregional radiotherapy centred on L_1, L_2, and D_6, with a total dose of 40 Gy over one month.

One year after the diagnosis, the primary neurologic symptoms recurred. This was found to be caused by an expulsion of the vertebroplasty cement into the spinal canal. We performed an L_1 corporectomy, followed by osteosynthesis from T_{11} to L_3. The removed fragments were sent for pathological analysis, which did not reveal any residual tumour cells. One year later, the patient started consolidation treatment with zoledronic acid (Zometa®) IV perfusion once every 4 weeks. The final administration of zoledronic acid was made 3.5 years after the surgery.

Following 3 cycles of BEP chemotherapy, 3 cycles of cisplatin + VP_{16} chemotherapy, local radiotherapy, and 2 surgeries, the patient was in remission. Chemotherapy was well tolerated, and the patient showed a good response. Alpha-foetoprotein levels were completely normalized after only 4 cycles of platinum. The patient's Karnofsky performance scale index was maintained, and the spinal cord carcinomatosis on the cervical vertebrae remained stable. As of the most recent follow-up in September of 2018, 12 years after the initial diagnosis, the patient remains well and in complete remission.

Discussion

Pure yolk sac tumours account for 70% of paediatric testicular germ cell tumours andare almost always found in infants and young children. On the other hand, pure yolk sac tumours are rare in adults [8], constituting only about 2.4% of testicular germ cell tumours and are identified as a component in 40% of mixed germ cell tumours [9]. The physiopathology of such tumours remains unclear. During the second half of the 20th century, an increasing incidence of testis tumours has been reported [10], but the reasons for this increase are unknown since the disease risk factors are poorly understood. Some research suggests that exposure to various factors in utero or during early childhood are likely important in determining an individual's risk level. Other findings indicate that testicular cancer development may be related to exposure to various factors in adolescence and adulthood, including occupational exposures in firefighting and aircraft maintenance, and environmental exposure to organochlorine pesticides [11]. Cryptorchidism is an established risk factor, associated with a relative risk of 2.23 if orchidopexy is performed before the age of 13 years and a relative risk of 5.54 if not [12]. However, in the vast majority of testicular cancer cases, the cause is unknown.

While prepubertal testicular teratomas rarely metastasize and have a good prognosis after orchidectomy alone, yolk sac tumours in adults are frequently malignant [13]. Thus, it seems that pure yolk sac tumours in adults behave differently from their juvenile counterparts and are comparable to other non-seminomatous germ cell tumours in the adult testis. Adult yolk sac tumours are also more likely to exhibit lymphatic spread, while juvenile tumours more commonly exhibit hematogenous spread, indicating that retroperitoneal lymph node dissection may be a reasonable treatment option in adult patients [14]. Our presently described patient did not present retroperitoneal lymphatic metastasis at the time of diagnosis. Therefore, the neurological metastasis was probably of hematogenic origin.

Historically, alpha-foetoprotein is the marker most widely used to diagnose yolk sac tumours. However, although alpha-foetoprotein immunoreactivity is found in the majority of tumours, it is often variable and weak in intensity, and negative immunostaining for alpha-foetoprotein does not exclude the diagnosis [15]. A more recently described immunohistochemical marker is SALLA4, which is strongly positive in yolk sac tumours, including metastases, and appears to be a more sensitive marker than glypican-3 and alpha-foetoprotein [16].

The protocols for adjuvant therapy in paediatric cases of yolk sac tumours have changed haver time to avoid overtreatment and to minimize drug toxicity to the patients [17]. Multidrug chemotherapy protocols using platinum-based regimens have improved survival to near 100% among prepubertal patients with yolk sac tumours [18,19]. Our present case is atypical due to the patient's age at onset. Yolk sac tumours usually affect paediatric patients [5,6]. Although our present patient was older than the paediatric patients treated in the literature [5], we decided to apply the standard yolk sac tumour treatment in our patient. The utilized chemotherapy regimen has also been used to treat other yolk sac tumours in the vertebral column, but those cases did not involve a primary testicular tumour [9,10]. Cisplatin-based treatment is reportedly an excellent adjuvant chemotherapy, that shows substantial benefits when treating stage II_b (or higher) NSGCTs [3]. Our patient also received local radiotherapy. In the literature, it is recommended that treatment include a total dose of 30 Gy, administered in 10 fractions of 3 Gy each, because it has not been proven that 40 Gy produces better results in these kinds of metastases [18]. However, since the disease was discovered late in our present case, the radiotherapists deemed it appropriate to administer 40 Gy in total.

Another atypical aspect of our present case is that we identified a bone metastasis without finding any lymphatic node involvement upon ^{18}FDG-PET. Thus, this case involved a high-grade cancer with no affected lymphatic nodes. Our patient was considered to have a poor prognosis based on the high alpha-foetoprotein level, and the presence of extrapulmonary metastases. Stage III NSGCTs reportedly have 5-year overall and disease-free survival rates of 44% and 29%, respectively [20]. However, our patient had stage IV cancer with a poor prognosis, and is still alive twelve years later. Moreover, our patient has a perfect normal life, with a Karnofsky performance scale index of 0. He has had no late side effects from the treatment and shows no signs of relapse.

Conclusion

Spinal cord compression syndrome caused by yolk sac tumour metastasis is extremely rare in adulthood, and usually has a bad prognosis when diagnosed late. The patient in the present case was managed using spinal cord decompression, vertebral stabilization, orchiectomy, and early adjuvant radio chemotherapy, which produced good results in less than a year and a half, and over 12 years of disease-free survival. Alpha-foetoprotein showed great value in the monitoring of this patient and could be useful for detecting long-term relapse.

Ethics Approval and Consent to Participate

Not applicable.

Authors' Contributions

Marcelo Di Gregorio: Conceived, coordinated and designed of study. Took care of the patient in the emergency service and performed the surgery.

Francis Lorge: Helped to draft the manuscript and took care of the patient in the emergency service and performed the surgery.

Corentin Pochet: Helped to write the manuscript

Michaël Dupont: Radiologist (CHU UCL Namur site Godinne), performed the radiology examinations to discover the lesion.

Marie Cécile Nollevaux: Anatomopathologist (CHU UCL Namur site Godinne) performed pathological analysis revealed the malignant NSGCT.

Lionel D'Hondt: Oncologist (CHU UCL Namur site Godinne), has followed the patient to the oncology level and for his chemotherapy treatments. All authors read and approved the final manuscript

Acknowledgements

The authors acknowledge Axel Baily for picture edition and Edith Botek for reading support.

Consent for Publication

Written informed, consent was obtained from the patient for publications of this case reports and any accompanying images.

Availability of Data and Material

Data are available at the CHU UCL Namur.

Competing Interests

The authors declare that they have no competing interests.

Funding

No funding was obtained for this study.

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