Sertoli cell tumor of the testis causing intracranial metastasis two years after orchiectomy. Report of a rare case and review of the literature

Antonio Colamaria
Matteo Sacco
Giovanni Parbonetti
Nicola Pio Fochi
Francesco Carbone (francesco.carbone615@gmail.com)
University of Foggia: Universita degli Studi di Foggia https://orcid.org/0000-0002-6351-9999
Matteo de Notaris

Research Article

Keywords: Sertoli cell tumor, brain metastasis, intracranial tumor, testicular tumor

Posted Date: December 3rd, 2021

DOI: https://doi.org/10.21203/rs.3.rs-1121557/v1

Abstract

Sertoli cell tumor of the testis (SCTT) accounts for less than 1% of all testicular tumors with only 10% of cases exhibiting malignant behavior. In the present report, a case of malignant SCTT causing multiple metastases in a 32-year-old man is described. After being diagnosed and treated for bone and lymph nodes metastases, the patient presented with a brief history of worsening headaches and visual impairment. A head MRI demonstrated an extra-axial tumor located in the right fronto-parietal junction exhibiting avid contrast enhancement and leptomeningeal involvement. To the best of the authors' knowledge, this represents the second case of intracranial metastasis from SCTT described to date.

Introduction

Sertoli cell tumor of the testis (SCTT) is a rare, non-germinal testicular malignancy that can occur at any age, representing less than 1% of all testicular tumors.[10] Although generally benign, approximately one in ten patients presents with signs of a malignant SCTT, including increased mitotic activity and distant metastases.[3] In their metanalysis, Grogg et al.[4] considered a cohort of 50 patients with metastatic SCTT where the most frequent locations included retroperitoneal lymph nodes, lung, bone, inguinal lymph nodes, liver, kidney, with only one case of brain metastasis.

In this report, a case of multimetastatic, highly malignant SCTT causing an extra-axial, intracranial metastasis presenting two years after the initial orchiectomy is described. Clinical manifestations included worsening headaches and visual impairment and a head MRI demonstrated an intracranial ovular mass located in the right frontal lobe.

Case Description

A 32-year-old male presented with intense, worsening headaches associated with conjugated gaze palsy to the left and ipsilateral photophobia. Two years prior to presentation he was diagnosed with SCTT that was treated with right orchiectomy followed by retroperitoneal lymph node dissection (RPLND) that revealed cancer-free lymph nodes. Additionally, systemic chemotherapy and pelvic irradiation were performed due to malignant secondary infiltration of the pelvic lymph nodes. One year after the initial diagnosis, the finding of a metastatic infiltration of the right homerus led to seven cycles of radiation therapy followed by surgical resection of the tumor and metal plates osteosynthesis. This surgery, although necessary, resulted in severe movement impairment with preservation of flexion and extension movements of the forearm alone.

At admission, neurological examination disclosed left sixth nerve palsy without any other significant focal deficit, whereas blood tests showed normal levels of the free ß-subunit of the human chorionic gonadotropin (ß-hCG), lactate dehydrogenase (LDH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and testosterone, with significant elevation of serum α-fetoprotein levels. A total body computed tomography (CT) revealed the presence of two nodules located in the superior lobe of the right

lung with associated confluent lymph node enlargement, and multiple round lesions of the hepatic segment VII. A magnetic resonance (MRI) of the head showed an extra-axial, ovular mass located in the right frontal lobe extending to the parietal hemisphere, exhibiting avid contrast enhancement and leptomeningeal involvement (Figure 1). In the suspect of an intracranial metastasis from SCTT, the patient was treated with a right fronto-parietal craniotomy, followed by complete resection of the extra-axial tumor. Intraoperatively, diffuse infiltration of the epicranial soft tissues, diploe, and dura mater was noticed and the tumor appeared greyish to light brown in color with a jelly-like surface and consistency.

Histological examination of the lesion demonstrated the presence of moderately large, pleomorphic cells, with pale cytoplasm, exhibiting a trabecular architecture and nested growth pattern (Figure 2). Peculiar features included a high mitotic index and multiple necrotic areas. The tumor cells were moderately immunoreactive to inhibin, vimentin, and CEA but negative for EMA. Pathological diagnosis confirmed the metastatic origin of the intracranial lesion.

Postoperatively, the headaches disappeared, and the visual impairment significantly improved, and the patient was referred to the oncology department for the optimal management of the pulmonary nodules. One month after surgery, he underwent six courses of chemotherapy with cisplatin, etoposide, and bleomycin obtaining complete regression of the lesions. Unfortunately, he died 16 months later of pulmonary insufficiency caused by a local recurrence.

Discussion

Malignant SCTT and histological subtypes

Due to the paucity of case descriptions of malignant SCTT, too many questions regarding treatment options, prognosis, and minimum follow-up times remain unanswered. The 2016 WHO classification identifies tumor size > 5 cm, evidence of intratumoral hemorrhage, necrosis, lymph vascular invasion, and cellular pleomorphism as risk factors for malignant disease.[4] It is still unclear whether age acts as an independent risk factor and, despite several authors having included it among the proposed prognosticators, Adayener et al.[1] reported the case of a 12 years old who developed interaortocaval lymph node metastases 8 years after initial orchiectomy. Additionally, other variables that seem to be associated with metastatic disease, either at initial presentation or at follow-up, are tumor diameter > 24mm and high mitotic index. No considerable statistical difference in the frequency of metastatic disease was found between histological subtypes.[4]

From a histological point of view, SCTTs are divided into two specific subtypes: large cell calcifying and sclerosing; nonetheless, further described variants have not been classified into specific subtypes and are considered as part of the not otherwise specified (NOS) SCTTs.[2] However, the 2016 WHO classification of sex-cord stromal tumors considers the sclerosing type as a morphological variant of NOS SCTTs, while the large cell calcifying remains a distinct entity. Another histological variant, often associated with Peutz-Jeghers syndrome, is defined as intratubular large cell hyalinizing Sertoli cell neoplasia.[7]

Diagnosis and Prognosis

Immune cell profiling has become an essential tool in differential diagnosis and the prediction of malignancy potential.[3] In the present case, the tumor exhibited positivity for inhibin in ¼ of neoplastic cells and focal positivity for vimentin. Similar results were reported by Grogg. et al.[4], with 31% and 16% of examined patients showing positivity for inhibin and vimentin, respectively. On the other hand, seminomas and other germ cell tumors are usually negative for α-inhibin.[6, 8]

Serum ß-hCG levels are reported to be elevated in 0.7% of patients diagnosed with SCTT and in 10-25% of patients presenting with seminoma, which is also an unusual finding after the age of 55.[2, 5] In their metanalysis, Grogg et al.[4] examined data of 435 patients diagnosed with SCTT, 50 of whom presented with metastatic disease with a median recurrence time of 12 months, and an overall median life expectancy of 20 months. The most frequent metastatic sites were retroperitoneal lymph nodes (16), lung (8), bone (4), inguinal lymph nodes (3), liver (1), brain (1), and kidney (1). The only brain metastasis case of the group was found at initial staging, whereas in the present case brain metastasis developed 2 years after initial diagnosis.

To the best of the authors' knowledge, the present case represents the first documented brain metastasis from SCTT manifesting two years following initial diagnosis. Headaches, eventually followed by visual impairment, were the only symptoms associated with the intracranial lesion. Due to the rarity of brain metastasis from SCTT, neuroradiological assessments were only made after the patient developed significant visual impairment, suggesting a decompensated intracranial hypertension, which resulted in the need for a decompressing craniotomy. A careful clinical and radiological monitoring and a periodic follow-up could have prompted an early diagnosis of the brain and pulmonary metastases. As suggested by Adayener et al.[1], at least a 10-year follow-up is necessary.

Future perspectives

The absence of practical management guidelines for the treatment of metastasis from SCTT has led to the adoption of multiple approaches over time, including radiotherapy, chemotherapy, and surgical resection. The latter represents the gold standard since radiotherapy and chemotherapy alone were found unable to avoid disease progression.[4] Retroperitoneal lymph node dissection is a widely accepted procedure that proved to be effective in prolonging overall survival and progression-free survival, however recent evidence raised concerns over its ability to reduce the risk of local recurrence.[9] Despite the various therapeutic options, the poor life expectancy of these patients suggests that experimental targeted approaches should be taken into consideration.[4]

Conclusion

Patients diagnosed with SCTT should undergo careful and continuous clinical monitoring after orchiectomy, in order to investigate the presence of secondary lesions. The rarity of brain metastasis in

this group of tumors represents a determining factor for the late diagnosis and misjudgment of the clinical manifestations.

Declarations

Funding The authors did not receive support from any organization for the submitted work.

Conflict of interest The authors declare that they have no conflict of interest.

Availability of data and material Data and material exposed in the present work are available on reasonable request.

Code availability Not applicable.

Ethical standards The manuscript does not contain clinical studies or patient data.

Consent to participate Written informed consent was obtained from the parent.

Consent to publish The participant has consented to the submission of the case report to the journal.

References

1. Adayener C, Akyol I, Sen B et al (2008) Sertoli cell tumor of the testis: a case with late metastasis. Int Urol Nephrol 40:1005–1008
2. Anderson GA (1995) Sclerosing Sertoli cell tumor of the testis: a distinct histological subtype. J Urol 154:1756–1758
3. Demir A, Onol FF, Türkeri L (2003) Case report: malignant Sertoli cell tumor of the testis in an adult. Int Urol Nephrol 35:515–516
4. Grogg J, Schneider K, Bode PK et al (2020) Sertoli Cell Tumors of the Testes: Systematic Literature Review and Meta-Analysis of Outcomes in 435 Patients. Oncologist 25:585–590
5. Henley JD, Young RH, Ulbright TM (2002) Malignant Sertoli cell tumors of the testis: a study of 13 examples of a neoplasm frequently misinterpreted as seminoma. Am J Surg Pathol 26:541–550
6. Iczkowski KA, Bostwick DG, Roche PC, Cheville JC (1998) Inhibin A is a sensitive and specific marker for testicular sex cord-stromal tumors. Mod Pathol 11:774–779
7. Idrees MT, Ulbright TM, Oliva E et al (2017) The World Health Organization 2016 classification of testicular non-germ cell tumours: a review and update from the International Society of Urological Pathology Testis Consultation Panel. Histopathology 70:513–521
8. Kommoss F, Oliva E, Bittinger F et al (2000) Inhibin-alpha CD99, HEA125, PLAP, and chromogranin immunoreactivity in testicular neoplasms and the androgen insensitivity syndrome. Hum Pathol 31:1055–1061

9. Mosharafa AA, Foster RS, Bihrle R et al (2003) Does retroperitoneal lymph node dissection have a curative role for patients with sex cord-stromal testicular. tumors? Cancer 98:753–757
10. Richie JP, Steel GS (2002) Neoplasms of the testis. In: Campbell's Urology, 8th edn. W.B. Saunders Co., Chapt. 81: 2906

Figures

Figure 1

a) Axial, b) coronal, and (c) sagittal scans of brain MRI demonstrating an extra-axial, contrast-enhancing metastasis located in the right frontal lobe exhibiting leptomeningeal enhancement

Figure 2

Microphotography showing the presence of moderately large, pleomorphic cells with a pale cytoplasm exhibiting a nested growth pattern. These features, along with results of immunohistochemical analysis, were compatible with the diagnosis of SCTT metastasis