


Case Report

Brain and spinal cord metastases with seminoma: A case report

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Abbreviations & Acronyms

BEP = bleomycin, etoposide, and cisplatin
 HCG = human chorionic gonadotropin
 LDH = lactate dehydrogenase
 MRI = magnetic resonance imaging
 PET-CT = positron emission tomography-computed tomography
 STCs = syncytiotrophoblastic cells
 TIP = paclitaxel, ifosfamide, and cisplatin

Introduction: Brain and spinal cord metastases from testicular cancer occur rarely, and metastases with seminoma are extremely rare.

Case presentation: A 42-year-old man who was diagnosed with seminoma and multiple metastases underwent first-line and salvage chemotherapy. Brain metastases were noted; consequently, surgery, third-line chemotherapy, and whole-brain irradiation were performed. Subsequently, paralysis developed, and spinal cord metastases were detected. He received fourth-line chemotherapy but died. Pathological autopsy revealed metastases only in the spinal cord. The cause of death was considered respiratory failure due to cervical spinal cord involvement from spinal metastases.

Conclusion: Brain and spinal cord metastases from seminoma are rare. Thus, similar future cases should be treated appropriately.

Key words: brain metastases, chemotherapy, pathological autopsy, seminoma, spinal cord metastases.

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Keynote message

A 42-year-old man who was diagnosed with seminoma and multiple metastases underwent first-line and salvage chemotherapy. Brain metastases were noted; consequently, surgery, third-line chemotherapy, and whole-brain irradiation were performed. Unfortunately, paralysis developed, and spinal cord metastases were detected, and received fourth-line chemotherapy but died. Similar future cases should be treated appropriately.

Introduction

Brain metastases from testicular cancer are rare, and spinal cord metastases are even rarer. Approximately 1%–2% of all patients with testicular cancer present with brain metastases.¹ Most cases with brain metastases are nonseminoma.² There are only a few case reports of spinal metastases.^{3,4} Herein, we report a rare case of seminoma with brain and spinal cord metastases.

Presentation of case

The patient was a 42-year-old man. On his first visit, the patient had a right testicular cancer, retroperitoneal and mediastinal lymph node, and multiple lung metastases (Fig. 1). He had an alpha-fetoprotein level of 1.8 ng/mL, LDH 5295 U/L, human chorionic gonadotropin (HCG) level of 952.9 mIU/mL, and HCG- β level of 4.7 ng/mL. He underwent right high orchiectomy, and pathological examination showed seminoma pT1. His diagnosis was seminoma pT1N3M1aS3.

The clinical course is shown in Figure 2. After surgery, the patient underwent four cycles of chemotherapy, bleomycin, etoposide, and cisplatin (BEP). His LDH, HCG, and HCG- β levels were normal, but lung metastases remained. Therefore, he received two cycles of paclitaxel, ifosfamide, and cisplatin (TIP) as salvage chemotherapy. After TIP, the tumor marker levels were normal, and lung metastases disappeared. He was placed under observation. Three months later, the HCG level was 8.0 mIU/mL, and lung metastases progression was observed.

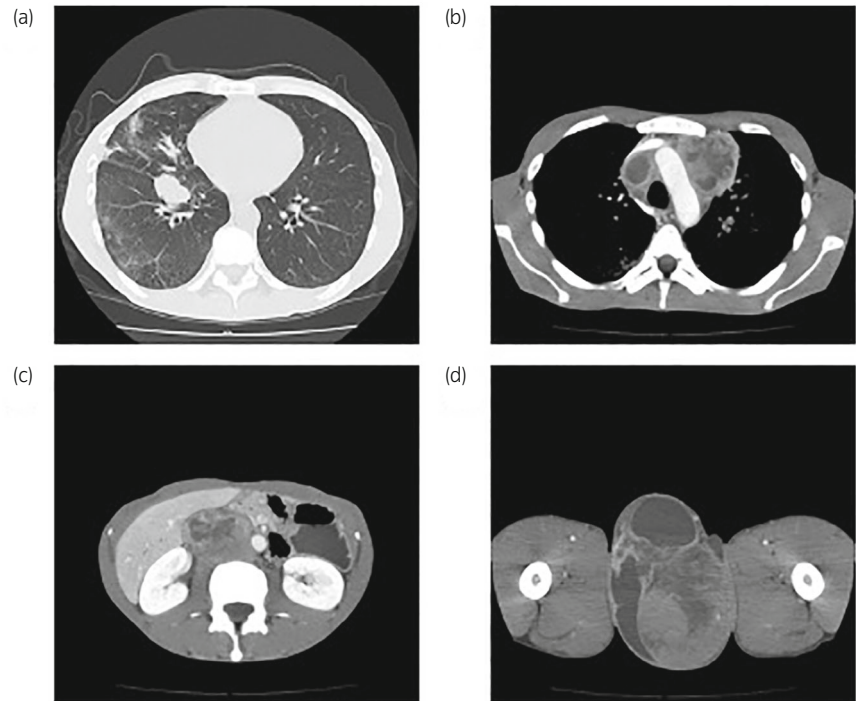


Fig. 1 (a) Multiple lung metastases. (b) Mediastinal lymph node metastasis. (c) Retroperitoneal lymph node metastasis. (d) Right testicular cancer.

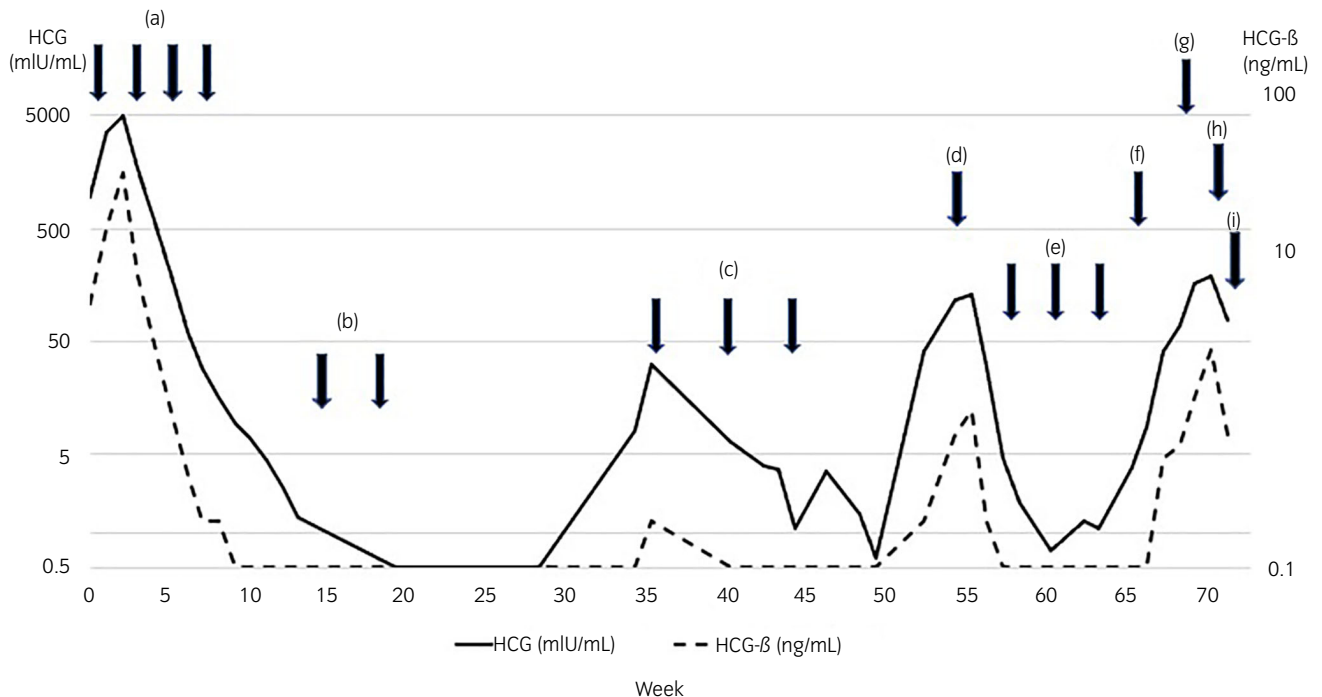


Fig. 2 (a) The patient underwent right high orchiectomy and received four cycles of bleomycin, etoposide, and cisplatin. (b) Only lung metastases remained, and two cycles of paclitaxel, ifosfamide, and cisplatin (TIP) were performed as salvage chemotherapy. (c) The patient's tumor marker levels (HCG and HCG- β) were elevated, lung metastasis progression was observed, and three cycles of TIP were performed. (d) His tumor marker levels (HCG and HCG- β) increased, cerebellum metastasis was detected, and the brain tumor was removed. (e) Three cycles of toposide, ifosfamide, and cisplatin were performed. (f) Whole-brain irradiation of 30 Gy was performed. (g) His tumor marker levels (HCG and HCG- β) elevated, and meningeal dissemination was detected. (h) One cycle of methotrexate, etoposide, and actinomycin D was given. (i) Death. (j) HCG, human chorionic gonadotropin.

After three cycles of TIP, tumor markers became negative, and lung metastases were scheduled for resection. However, during the waiting period, tumor marker levels increased

again. Cerebellar metastases appeared on magnetic resonance imaging (MRI) of the head (Fig. 3a). Brain tumor resection was performed. Pathological examination confirmed that the

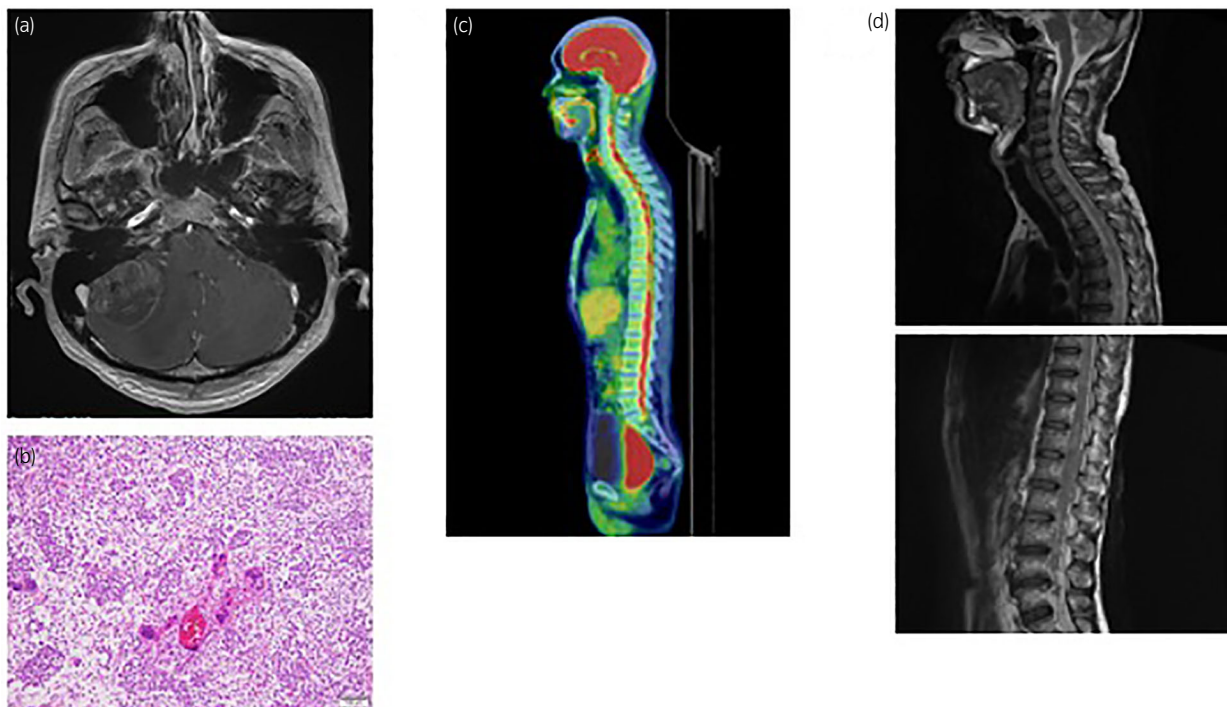


Fig. 3 (a) Brain magnetic resonance imaging: a 3.9-cm tumor in the right cerebellar hemisphere. (b) Brain tumor pathology: seminoma containing syncytiotrophoblastic cells. (c) Positron emission tomography-computed tomography: Heterogeneous hyperaccumulation in the spinal cord and diffuse hyperaccumulation in the spinal canal at the level of the lumbar spine (SUVmax = 11.8). (d) T2-weighted images show multiple nodules and soft tissue shadows with equal signal to the spinal cord.

lesion was a seminoma containing syncytiotrophoblastic cells (STCs). Thereafter, three cycles of etoposide, ifosfamide, and cisplatin and whole-brain irradiation of 30 Gy were performed.

After irradiation, the patient complained of paralysis in the upper and lower limbs. Positron emission tomography-computed tomography (PET-CT) and spinal MRI were performed, which showed hyperaccumulation in the entire spinal cord metastases, respectively (Fig. 3b). Spinal cord metastases were diagnosed seminoma with STCs similar to brain metastases without biopsy, and chemotherapy including methotrexate, etoposide, and actinomycin D, was initiated considering the possibility that spinal cord metastases had a choriocarcinoma.⁵ After one cycle, tumor marker levels decreased. However, the patient developed progressive paralysis due to spinal cord metastasis and respiratory failure, and he subsequently died.

Pathological autopsy showed metastases only in the spinal cord. Tumor cells were observed circumferentially throughout the lumbar and sacral spinal cord, mainly in the cervical spinal cord. The anterior horn cells showed chromatolysis and tumor cell infiltration within the anterior horn gray matter with a few normal neuronal cells. The pathology of the cervical cord is shown in Figure 4. The tumor was seminoma containing STCs, as was the tissue of brain metastases, only STCs were hCG positive, with no cytotrophoblastic cells and no choriocarcinoma. The tumor cells were mostly viable cells. The cause of death was considered respiratory failure due to cervical spinal cord metastases.

Discussion

Brain metastases from testicular cancer are relatively rare, and 1%–2% of testicular cancer present with brain metastasis. Brain metastasis occur almost exclusively in patients with nonseminoma, and the rate of brain metastases with seminoma is approximately 5%.^{1,2,6} The 5-year survival rate for cases with brain metastases at initial diagnosis is 45%, and with brain metastasis during primary treatment or in recurrence is 12%.⁷ In a report comparing cases with brain metastases at initial diagnosis with those with recurrence due to brain metastases, overall survival was significantly worse in those with recurrence ($P < 0.001$).^{2,8}

There is no evidence on the treatment of brain metastases, and decisions are made by individual institutions. The National Comprehensive Cancer Network guidelines recommend cisplatin-based chemotherapy as the initial treatment for brain metastases, and the addition of radiotherapy should be considered. Surgical resection should be performed if clinically indicated and possible. In cases with high HCG- β levels and extensive lung metastases, a search for brain metastases is necessary.⁹ The European Association of Urology guidelines state that chemotherapy should be the initial treatment for brain metastases, radiotherapy should be administered after chemotherapy, and surgical treatment should be considered depending on the general condition, histological type of the primary tumor, and metastasis site.¹⁰ The Japanese Urology Association guidelines state that chemotherapy should be started as soon as possible unless there are serious neurological symptoms to control.

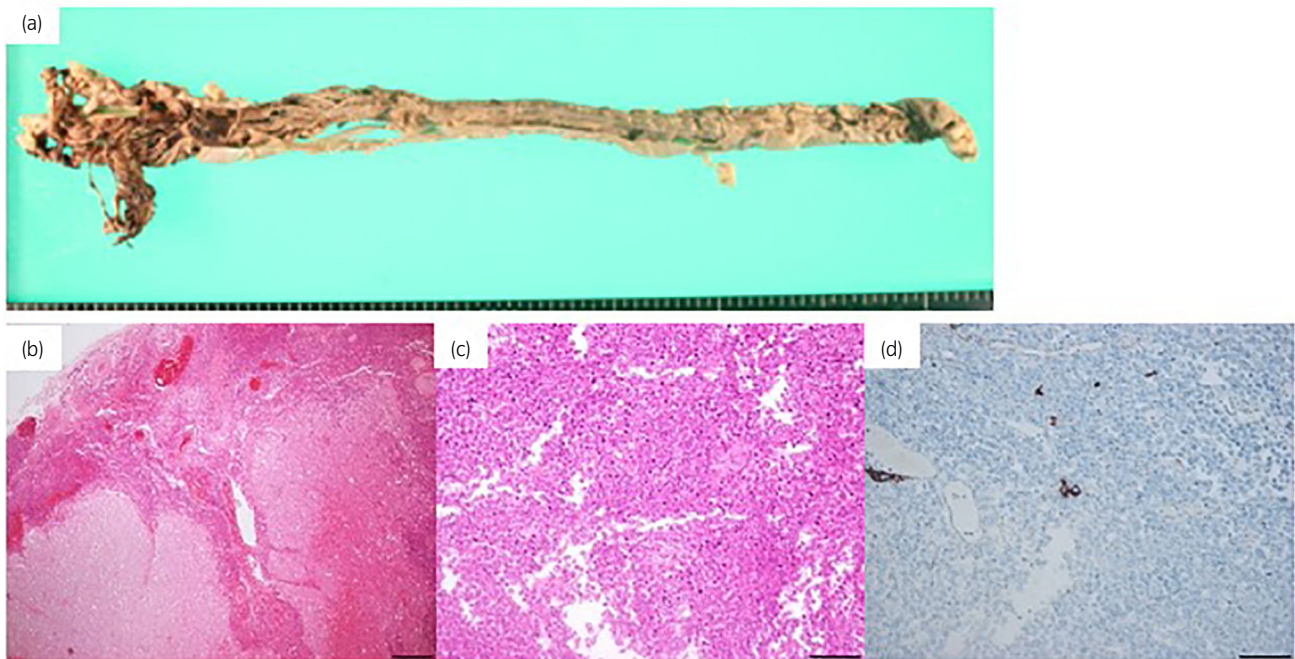


Fig. 4 (a) Spinal cord. (b, c) Cervical cord (HE). (d) Human chorionic gonadotropin immunohistochemistry: syncytiotrophoblastic cell was positive.

Few papers have reported on spinal cord metastases.^{3–6} Lee et al. performed emergency surgical resection for tissue diagnosis and spinal decompression for spinal cord metastases of the yolk sac tumor.³ Mukendi et al. reported an emergency radiotherapy with 8 Gy, corticosteroid therapy, and one cycle of BEP therapy; however, the patient died a few days later because of disease progression.⁴ Kaylyn et al. have reported craniospinal proton-beam radiation for spinal cord metastases of seminoma with no subsequent imaging evidence of disease progression.⁵ John et al. reported a relapsed seminoma involving only the central nervous system and successful salvage therapy with craniospinal axis irradiation.⁶ Generally, the treatment for spinal cord metastases includes radiotherapy, chemotherapy, and intrathecal chemotherapy. Regarding intrathecal chemotherapy, methotrexate is often used.¹¹ To the best of our knowledge, no studies have reported intrathecal chemotherapy for testicular cancer. A review on spinal metastases revealed that spinal stereotactic ablative radiotherapy is a possible effective treatment option for patients with well-selected spinal metastases, achieves high local tumor control rates, and has moderate side effects.¹² There is no clear evidence for the treatment of spinal cord metastases, and treatment options should be considered on a case-by-case basis.

In the present case, the patient had a high HCG level, extensive lung metastases at initial presentation, and high likelihood of brain metastases. Brain metastases appeared iatrogenic, suggesting a poor prognosis. We performed chemotherapy along the lines of choriocarcinoma due to STCs. However, this did not have a dramatic effect, as the patient died subsequently. As regards the cause of death, pathological autopsy revealed no metastases other than the spinal cord, which ultimately resulted in respiratory failure from spinal metastasis.

In conclusion, the findings of the present case suggest that although brain and spinal cord metastases of a seminoma

rarely occur, it is necessary to establish treatment for cases of brain and spinal cord metastases of testicular cancer.

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None.

Author contributions

Tetsuya Yumioka: Conceptualization; writing – original draft. Shuichi Morizane: Writing – review and editing. Karen Makishima: Visualization. Tadashi Adachi: Investigation; visualization. Emika Moriyasu: Data curation. Hideto Iwamoto: Data curation. Katsuya Hikita: Data curation. Masashi Honda: Writing – review and editing. Yoshihisa Umekita: Investigation. Astushi Takenaka: Supervision.

Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an institutional reviewer board

22J001.

Informed consent

Not applicable.

Registry and the Registration No. of the study/trial

Not applicable.

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