

# Intramedullary recurrence of germinoma in the spinal cord 15 years after complete remission of a pineal lesion

## Case report

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The authors present a case of germinoma that was initially found in the pineal region and recurred 15 years later in the intramedullary cervical spinal cord after intensive chemo- and radiotherapy and diagnosis of complete remission.

This 28-year-old man initially presented with seizures. Hydrocephalus and a pineal tumor were found on radiological examination, and partial resection of the tumor was performed. Histological diagnosis showed a pure germinoma. Following surgery, the patient received a combination of chemo- and radiotherapy, and a complete remission was shown. However, after 15 years of follow-up, he presented with gait disturbances. Spinal MRI showed an intramedullary mass lesion in the cervical spinal cord. The cervical lesion was biopsied, and histological examination again revealed a pure germinoma.

With germinomas, the possibility of a drop metastasis from an intracranial lesion to the spinal cord must be considered during follow-up. However, in the present case, analysis of a CSF sample showed no abnormalities as in previously published cases. In recent years, multidisciplinary treatments have demonstrated good event-free survival rates in cases of pure germinomas, but long-term outcomes over the decades are not fully known. Continual follow-up of such cases is recommended even after complete remission has been achieved.

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**KEY WORDS** • complete remission • germinoma • oncology • intramedullary recurrence

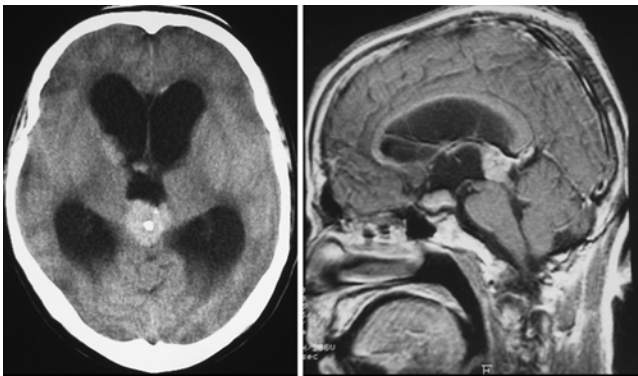
**I**NTRACRANIAL germ cell tumors are predominantly found in the younger population and primarily occur as suprasellar and pineal lesions.<sup>1,2,4,6,11,14,19</sup> Treatment protocols include radical surgery, chemotherapy, and radiotherapy, and they largely depend on the pathology of the tumor.<sup>5,8,16,18</sup> Because germinomas respond well to both chemo- and radiotherapy and hardly ever recur in the spinal cord after such intensive treatment, routine prophylactic spinal irradiation is generally not performed.<sup>12,17,18,20,21</sup> While modern treatment protocols are successful in the majority of patients with germinomas, it is important to note that most reported treatment outcomes have been based on relatively short follow-up periods.<sup>1,2,4–6,8,11,14,16,19</sup> Outcomes more than 10 years after initial treatment remain unknown.

### Case Report

*History.* This 28-year-old man was referred to our hospital after presenting with an attack of generalized seizures. Head MRI and CT revealed a heterogeneously enhanced mass lesion in the pineal region with hydrocephalus (Fig. 1). Levels of tumor markers in the serum and the CSF, including those of  $\alpha$ -fetoprotein, carcinoembryonic

antigen, human chorionic gonadotropin, and the  $\beta$ -subunit of human chorionic gonadotropin, were all within normal limits. The lesion was partially removed via the occipital interhemispheric approach, and histopathological examination of the surgical specimen revealed a typical 2-cell pattern of a germinoma (Fig. 2 left). The tumor was diagnosed as pure germinoma, and the patient underwent chemotherapy (carboplatin 450 mg/m<sup>2</sup> for 1 day and etoposide 90 mg/m<sup>2</sup> for 3 consecutive days, repeated every 4 weeks for 3 courses) combined with fractionated radiotherapy for the residual tumor (whole brain 50 Gy). Because cytological examination of the CSF showed normal values, spinal cord radiotherapy was not performed. Following these treatments, the tumor was not visible on MRI and the patient was followed on an outpatient basis with annual MRI, and there were no neurological events.

*Examination.* However, during the 15th year of follow-up, the patient presented with gradual progressive gait disturbances and was admitted to our hospital. On neurological examination, we observed slight tetraparesis, with a marked spasticity in the lower extremities, and dysuria. Head MRI did not reveal tumor recurrence, but cervical MRI demonstrated a mass lesion that markedly enhanced after injection of Gd and extended from the

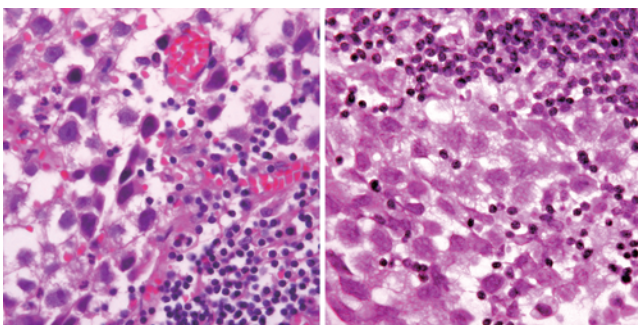


**FIG. 1.** **Left:** Initial enhanced CT scan showing an enhanced round mass in the pineal region and severe hydrocephalus. **Right:** Sagittal T1-weighted Gd-enhanced MR image on initial admission revealing a well-enhanced pineal mass.

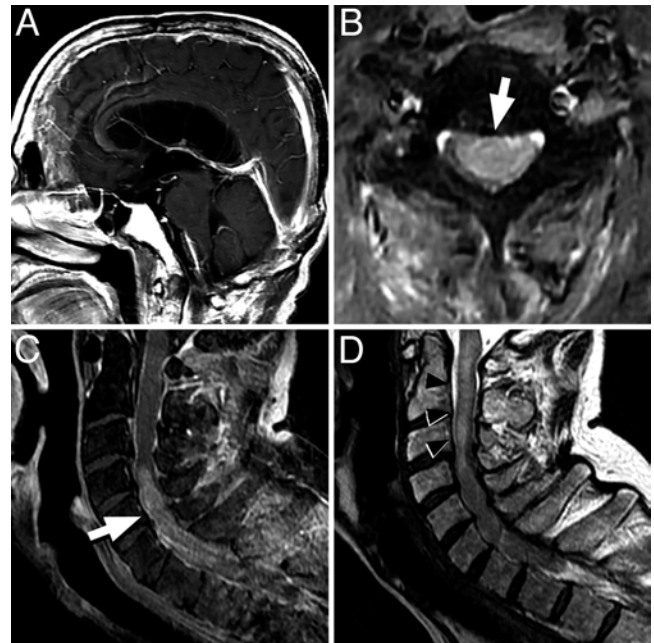
cervical to the upper thoracic level; marked swelling of the spinal cord was also apparent (Fig. 3). Analysis of the serum and the CSF, including tumor marker, and cytological examination showed no abnormal findings.

**Operation.** The patient underwent biopsy of the cervical lesion as well as C3–7 laminectomies. After opening the dorsal dura matter, a midline myelotomy of the posterior median sulcus was performed and a soft gray tumor was exposed. It was very difficult to distinguish the tumor margin even under a surgical microscope, and a small amount of the tumor tissue was obtained. Histopathological examination of the surgical specimen showed a typical 2-cell pattern of pure germinoma, identical to the histology of the pineal lesion treated 15 years before (Fig. 2 right).

**Postoperative Course.** Following surgery, the cervical lesion received 31 Gy of fractionated radiation, and cervical MRI studies obtained 1 month later revealed the disappearance of both the enhanced lesion and spinal cord edema. After a battery of treatments, the patient's motor symptoms rapidly improved. However, his respiratory function deteriorated and he had repeated aspiration pneumonia. After being transferred to a local hospital to continue his rehabilitation, he recovered from the



**FIG. 2.** Photomicrographs of surgical specimens of the primary pineal lesion (**left**) and the recurrent intramedullary lesion 15 years later (**right**) showing large clear cells with small infiltrating lymphocytes without a syncytiotrophoblastic cell component—a typical 2-cell pattern of germinoma. H & E, original magnification  $\times 200$ .



**FIG. 3.** **A:** Sagittal T1-weighted Gd-enhanced MR image revealing no sign of recurrence of the pineal lesion. **B and C:** However, spinal MR images on readmission showed an enhanced intramedullary lesion with a markedly edematous spinal cord from C-4 to T-1 (*arrows*). **D:** Sagittal T2-weighted MR image demonstrating extensive high-intensity lesions (*arrowheads*).

pneumonia and did not exhibit any respiratory problems. However, he had a relapse of severe pneumonia there and finally died of sepsis 3 months later. At the last follow-up examination, there was no evidence of tumor recurrence or increased edema on cervical MRI. Thus, the relationship between his deteriorated respiratory function and surgery or adjuvant radiation therapy was not clear.

### Discussion

Although there is the possibility, extremely rare, that both the intracranial and spinal lesions existed at the initial diagnosis, Matsutani et al.<sup>8</sup> reported no such cases at initial diagnosis in their large series of 153 cases of germ cell tumors. Thus, the spinal lesion in our case was regarded as a metastasis from the initial intracranial lesion.

Even after intensive chemo- and radiotherapy, intracranial germinomas sometimes cause metastases or dissemination of the tumor cells in the spinal cord through the CSF.<sup>3,7,9,10,15,22</sup> They are, however, usually found within a few years of the initial treatment for the intracranial lesion.<sup>3,7,9,10,15,22</sup> To the best of our knowledge, a few cases have been reported in the literature.<sup>7,9,15</sup> According to previous reports of intramedullary recurrence from an intracranial lesion, gonadotropin levels in the CSF were commonly elevated.<sup>7,15</sup> Similar to other cases with spinal cord recurrence, metastatic spread of the tumor cells into the CSF through the central canal was highly suspected. However, compared with those cases, there was no sign of recurrence of the primary intracranial lesion, and recurrence was found after such a long period and so distant

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from the original site, without change in CSF, that it is very difficult to simply explain the present case as a CSF metastasis or as a simultaneous lesion.

The mechanism of the pathogenesis of germ cell tumors is still controversial. In the present case, we hypothesized that, at the primary stage of embryogenesis, germ cells migrated with lateral mesoderm cells and were spread along the neural axis from the caudal area to the cranial area and that the cells showed neoplastic transformation at a later stage.<sup>13</sup> If multiple germ cells are spread along different neural axes (for example, with hypothalamic and pineal lesions), and if the neoplastic transformation occurs after a long period (as a time-lag attack), then such tumors could recur even after more than 15 years and also in regions distant from the primary tumor.

### Conclusions

Although intracranial germinomas are predominantly found in the younger population, there have been few reports on treatment outcomes based on over several decades of follow-up.<sup>5,6,8,10,17,18</sup> Because long-term outcomes remain unclear, continual follow-up for elucidation of decisive therapeutic results is recommended, even after complete remission has been achieved. The present case report suggests that, from the standpoint of sufficient long-term outcomes concerning intracranial germinomas, a long journey remains ahead.

### Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Hanakita, Watanabe, Shin. Acquisition of data: Hanakita, Takenobu, Kambe, Shin. Analysis and interpretation of data: Hanakita, Takenobu. Drafting the article: Hanakita. Critically revising the article: Watanabe, Shin. Reviewed submitted version of manuscript: Watanabe, Teraoka. Approved the final version of the manuscript on behalf of all authors: Hanakita. Administrative/technical/material support: Teraoka. Study supervision: Watanabe, Shin, Teraoka.

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