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Case Report

De Novo Pineal Region Germinoma in the Seventh Decade of Life: A Case Report

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Germ cell tumors typically occur in children and adolescents. We here report a rare case of *de novo* pineal region germinoma in the seventh decade of life. A 62-year-old man presented with double vision. Computerized tomography and magnetic resonance imaging (MRI) identified a heterogeneously enhanced tumor with calcification in the pineal region with ventricular dilatation due to aqueduct stenosis. The tumor had not been observed at all on MRI obtained 2 years previously. The patient underwent endoscopic biopsy and third ventriculostomy for the obstructive hydrocephalus. The tumor was histopathologically diagnosed as a pure germinoma. The patient underwent radiomonotherapy, resulting in his complete remission, which was confirmed by a series of follow-up MRI studies and hematological examinations. Intracranial germinoma should be considered in the differential diagnosis of pineal region tumors regardless of age, even though the tumor was undetectable on the previous neuroimaging.

Keywords: pineal region tumor, *de novo,* elderly adult, germinoma, neuroendoscopic biopsy

Introduction

Germ cell tumors (GCTs) typically affect children and adolescents.[1–4] Pineal region GCTs mainly affect males, while neurohypophyseal GCTs have no sex predominance. However, the natural history of pineal region GCTs is not well known. Intracranial *de novo* germinoma, which is defined as a tumor undetectable on the previous neuroimaging, is very rare.[5] Moreover, intracranial germinomas are also rare in the elderly, though a few cases in patients beyond their sixth decade of life have been reported.[2,6–9] We present a case of *de novo* pineal region germinoma in a 62-year-old man treated successfully with neuroendoscopic biopsy and subsequent radiotherapy.

Case Report

A 62-year-old man presented with a 1-month history of diplopia. At the age of 60, he had tension headache and had undergone magnetic resonance imaging (MRI) that revealed no abnormal findings (Fig. 1). Two years after the MRI, he was examined with computerized tomography (CT) and MRI for diplopia. CT revealed a heterogeneously enhanced tumor, 3 cm in diameter, with calcification in the pineal region (Fig. 2A). The tumor showed isointensity on T_1-weighted MRI (T_1WI, Fig. 2B); slight hypointensity on T_2WI (Fig. 2C) and fluid-attenuated inversion recovery image (Fig. 2D); and obvious hypointensity on T_2^*WI (Fig. 2E), and diffusion WI (Fig. 2F), which was heterogeneously enhanced by gadolinium on T_1WI (Fig. 2G). No tumor existed in the neurohypophyseal region on gadolinium enhanced sagittal T_1WI (Fig. 2H). Hydrocephalus was due to aqueduct stenosis caused by the tumor. The patient was referred to our hospital. On admission, his diplopia was improved, and his ocular movement was full and smooth. His mental functions were slightly deteriorated according to Mini-Mental State Examination and Wechsler Adult Intelligence Scale. His serum levels of the following tumor markers were within normal ranges: alpha-fetoprotein, beta human chorionic gonadotropin (β-HCG), carcinoembryonic antigen, beta 2-microglobulin, luteinizing hormone 5.2 mIU/mL (reference value: 1.7–11.2), follicle-stimulating hormone 9.2 mIU/mL (reference value: 2.1–18.6), and testosterone 482.0 ng/dL (reference value: 220.9–715.8). Cerebral angiography revealed a faint tumor stain without any arteriovenous shunt. No tumor with the potential to metastasize to the brain was systematically detected by CT. Accordingly, various tumors were considered during the differential diagnosis, such as pineal parenchymal tumor, glioma, unknown-origin metastatic tumor, and cavernous angioma. Subsequently the patient underwent endoscopic biopsy and third ventriculostomy via a right frontal pre-coronal burr hole and with a steerable videoscope. The tumor was easily detected as a grayish mass in the pineal region containing old hemorrhages and calcification (Fig. 3A), suspected to disseminate to the infundibulum (Fig. 3B). Biopsy specimens were obtained from several different sites. Minor bleeding from the tumor occurred during biopsy and was easily stopped by irrigation. Postoperatively, no complication occurred. β-HCG in the craniospinal fluid (CSF) obtained intraoperatively was 0.12 mIU/mL, slightly elevated. No tumor cells were detected in the CSF. Histopathologically, the tumor displayed a 2-cell pattern, with large epithelioid cells and small lymphocytes (Figs. 4A and 4B). The former cells stained positive for placental alkaline phosphatase (Fig. 4C) and c-kit (Fig. 4D). No other GCT components were observed. Thus, the histopathological diagnosis of this tumor confirmed pure germinoma.

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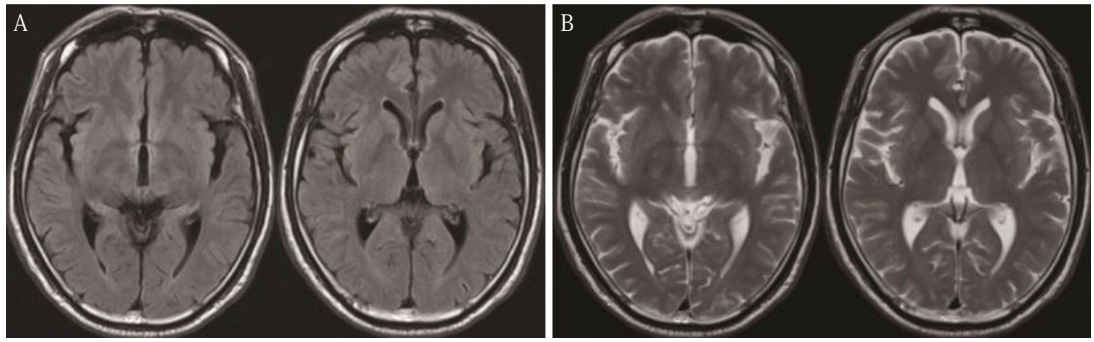

Fig. 1 Magnetic resonance images (1.5 Tesla) performed 2 years before admission. Note that no tumor can be seen in the pineal region on the fluid-attenuated inversion recovery image (A) or the T_2-weighted image (B).

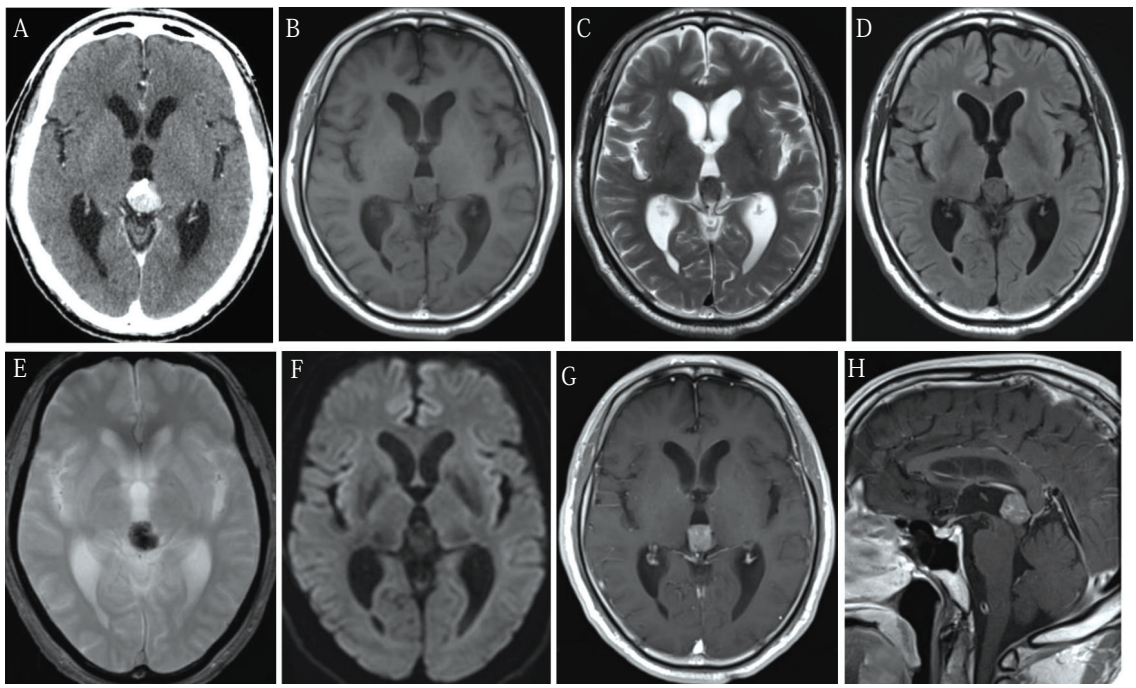

Fig. 2 Computerized tomography (CT) and magnetic resonance images (1.5 Tesla) performed immediately before admission. Note that the pineal region tumor shows mixed density with calcification on CT (A); isointensity on T_1-weighted image (T_1WI) (B); slight hypointensity on T_2WI (C) and fluid-attenuated inversion recovery image (D); obvious hypointensity on T_2*WI (E), diffusion WI (F); and heterogeneous enhancement with gadolinium administration (G). No tumor existed in the neurohypophyseal region on gadolinium enhanced sagittal T_1WI (H).

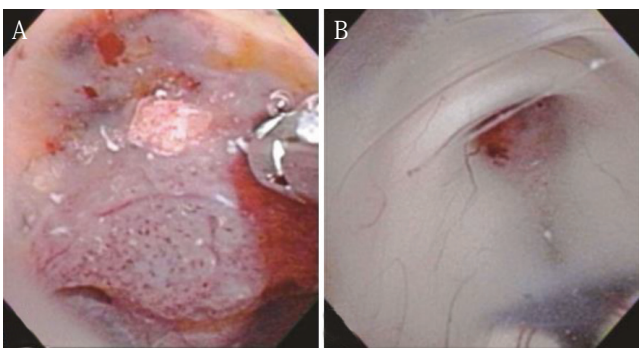

Fig. 3 Intraoperative photographs of the tumor viewed with a steerable videoscope. Note the pineal region tumor observed as a grayish mass containing old hemorrhages and calcification (A), suspected to disseminate to the infundibulum (B).

The patient received radiation monotherapy: low-dose prophylactic irradiation (25.2 Gy) to the craniospinal axis and radiation boost (25.2 Gy) to the primary tumor site because of his ventricular dissemination, although no signs of spinal dissemination were observed using MRI.[10] After the radiotherapy, the tumor disappeared completely and without any neurological deficits. Levels of β-HCG in his CSF normalized. Recurrence of the tumor was not found after serial follow-up MRI studies and β-HCG tests after 4 years radiomonotherapy.

Discussion

In this case, MRI 2 years before disease onset had not revealed a pineal region mass; i.e., a *de novo* germinoma developed later. This is the first case of *de novo* pineal

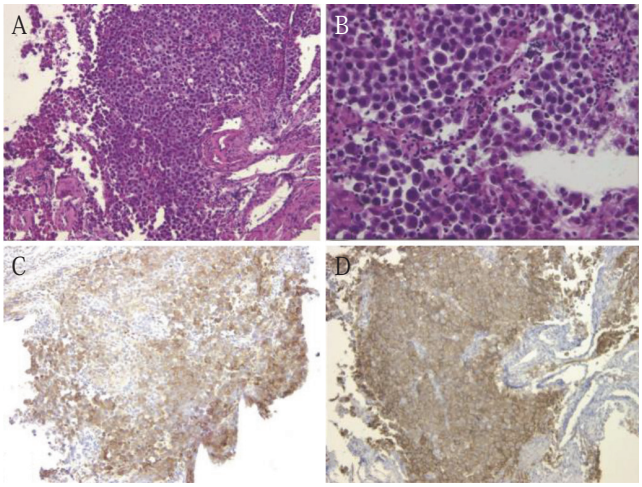

Fig. 4 Microphotographs of surgical specimen. Note 2-cell pattern, with large epithelioid cells and small lymphocytes [A: hematoxylin and eosin stain (H&E), original magnification, 100×; B: HE, original magnification, 200×]. Large epithelioid cells stained positive for placental alkaline phosphatase (C: original magnification, 100×) and c-kit (D: original magnification, 100×).

germinoma, although in the literature 1 case of *de novo* germinoma in the temporal lobe and hypothalamus, albeit a case with Klinefelter's syndrome, was reported.[5)]

The mechanism of onset of germinomas in the elderly is unclear. Germinoma is believed to arise from pre-existing primordial germ cells,[11,12)] which are distributed to various organs at an early stage of embryonic development. However, it is unclear how the primordial germ cells could be delivered to and maintained in the diencephalopineal region and how the tumorigenic transformation could occur.[13)] In patients with Klinefelter's syndrome, increased secretion of gonadotropin is assumed to be responsible for the occurrence of GCTs from the primordial germ cells.[7,13,14)] It is also speculated that GCTs associated with cases of cryptorchidism, testicular feminization, and gonadal dysgenesis might be ascribed to increased gonadotropin secretion.[7,14)] That is also presumed to be why the incidence of GCTs is relatively greater during infancy and adolescence, i.e., periods of changing gonadotropin secretion, compared with senescence.[7)] However, our patient was a 62-year-old man whose testosterone and gonadotropin levels were within normal ranges. Hence, some factors other than increased gonadotropin secretion, such as chromosomal abnormalities, are probably related to the tumorigenesis of germinomas in the elderly. Recent exhaustive genomic studies showed that mutations of the genes involved in the MAPK and/or PI3K pathways are common in intracranial germ cell tumors.[15)]

Pineal region tumors comprise various types of tumors, including germinomas (46.6%), pineal parenchymal tumors (13.2%), GCTs excluding germinoma (9.8%), epidermoid tumors (1.2%), dermoid tumors (0.4%), gliomas (0.4%), craniopharyngiomas (0.2%), and others (28.2%).[16)] GCTs are also characterized by various histopathologies, for which surgical strategies vary widely. While germinomas require only biopsy because of their high curability by radiochemotherapy, non-germinomatous GCTs, such as yolk sac tumor, choriocarcinoma, and immature teratoma, require radical surgical resection combined with radiochemotherapy.[14,17)] Hence, to provide appropriate therapeutic strategies to patients with pineal region tumors, endoscopic multisite biopsy—and concomitant third ventriculostomy if the tumor is associated with hydrocephalus—is necessary and useful.[18–20)]

At our institution, radiation monotherapy—prophylactic craniospinal or whole—brain irradiation paired with a radiation boost to the primary tumor—is the standard treatment for intracranial germinomas. Because we retrospectively analyzed data obtained in 46 patients who had been treated for intracranial germinomas. None of the 38 patients who received radiation monotherapy developed a recurrent lesion.[10)]

In the English-language literature, germinomas in the elderly are rarely reported: only five reports describe patients over 60 years of age having intracranial germinoma. In these reports, four patients are described in the context of a series of patients and details such as sex, location, management, and outcome are unavailable.[1,4,5,12)] In well-documented reports the oldest patient was a 61-year-old with pineal region germinoma.[9)] Hence, intracranial germinoma, albeit rare,[2,6–9)] must be considered in the differential diagnosis of pineal region tumors, even in elderly patients.

We described the patient with *de novo* pineal region germinoma in the seventh decade of life; he was successfully treated with radiomonotherapy following diagnostic confirmation by endoscopic multisite biopsy. This case, we believe, is significantly important from clinical and scientific viewpoints. First of all, the endoscopic biopsy seems necessary and useful to make appropriate decisions about treatment of patients with pineal region tumors. Second, germinoma should be considered in the differential diagnosis of pineal region tumors regardless of age, even in the elderly, and no tumors on previous neuroimaging.

Conflicts of Interest Disclosure

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

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