Pineal Germinoma With a Prominent Epithelioid Cell Granuloma Component
—Case Report—

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Abstract

A 20-year-old man presented with a rare case of germinoma with a large component of epithelioid cell granuloma manifesting as oscillopsia. Magnetic resonance imaging demonstrated a mass in the pineal region with homogeneous enhancement with gadolinium. Craniotomy was performed, ending in biopsy. The initial histological diagnosis was epithelioid cell granuloma, but systemic investigation detected no evidence of granulomatous disorder. A revised diagnosis of germinoma was based on positive immunohistochemical staining for placental alkaline phosphatase (PLAP) and c-kit. Histological diagnosis is sometimes incorrect if granulomatous reaction is dominant. Immunohistochemical staining for PLAP and c-kit should be performed if germinoma is clinically suspected.

Key words: germinoma, granulomatous reaction, placental alkaline phosphatase, c-kit

Introduction

Germinomas usually exhibit a two-cell pattern consisting of large neoplastic cells and small lymphocytes. Granulomatous reaction is common (50–60%) in seminoma and dysgerminoma, but rare in intracranial germinoma. Most infiltrating lymphocytes are T-cells and are cytotoxic to the autologous tumor cells. Chemical mediators such as tumor necrosis factor-alpha, granulocyte/macrophage-colony-stimulating factor, and interferon-gamma produced by the T-cells are important in granuloma formation in gonadal germinomas. The immune system in the brain differs substantially from that in the testis and ovary, because of the presence of the blood-brain barrier and absence of the lymphatic system, which may explain why granulomatous reactions are rare in intracranial germinomas. Consequently, the incorrect histological diagnosis may be established in cases of intracranial germinoma with granulomatous reaction if the granulomatous reaction is dominant and few neoplastic cells are present. Such misdiagnosis could potentially lead to disastrous outcomes.

Here we describe a case of germinoma with granulomatous reaction.

Case Report

A 20-year-old man was admitted to our hospital with a 2-month history of oscillopsia. His medical and family histories were unremarkable. Neurological examination identified only upward gaze palsy. Magnetic resonance (MR) imaging identified only upward gaze palsy. Magnetic resonance (MR) imaging showed a mass in the pineal region appearing as isointense on both T1- and T2-weighted imaging, with homogeneous enhancement with gadolinium (Fig. 1). Bilateral carotid angiography revealed no tumor staining. Laboratory examinations showed serum alpha-fetoprotein (AFP) level was 2 ng/ml, and serum beta-human chorionic gonadotropin (HCG-β) level was <0.1 ng/ml.

Craniotomy was performed and resection of the tumor was attempted via an infratentorial supracerebellar approach in October 2005. Intraoperatively, a pinkish, aspirable, and hypovascular tissue was detected around the calcified pineal gland. No dissecting plane was found between the abnormal tissue and brain, so the operation was limited to biopsy. Histological investigation revealed...
Fig. 1  $T_1$- and $T_2$-weighted magnetic resonance images demonstrating an isointense mass in the pineal region (A, B), with homogeneous enhancement with gadolinium (C: axial view, D: sagittal view).

Predominantly granulomatous changes consisting of Langerhans giant cells, epithelioid histiocytes confirmed by immunoreactivity for KP-1, and lymphocyte infiltration. Therefore, the initial diagnosis was epithelioid cell granuloma (Fig. 2A, B).

Granulomatous disorder such as sarcoidosis was suspected, but chest and abdominal computed tomography showed no abnormalities, and serum levels of angiotensin-converting enzyme and adenosine deaminase were 5.9 IU/l and 11.8 IU/1, respectively. Review of the histological findings identified a few large cytoplasm-rich cells underlying the lymphoid infiltration, so immunohistochemical staining for placental alkaline phosphatase (PLAP) and c-kit was performed. PLAP was positive on the membrane of these large cytoplasm-rich cells (Fig. 2C), and cytoplasmic and membranous immunoreactivity of c-kit was observed (Fig. 2D), whereas AFP and HCG-$\beta$ staining were negative. Therefore, a revised histological diagnosis of germinoma was made.

The patient underwent 3 courses of chemotherapy with cisplatin 20 mg/m²/day and etoposide 100 mg/m²/day for 5 days every 4 weeks, followed by radiotherapy 24 Gy. Follow-up MR imaging after the first course of chemotherapy showed complete disappearance of the tumor (Fig. 3).

Discussion

Only 18 similar cases of germinoma with granulomatous reaction have been reported. Age distribution was slightly older than that for common germinoma, but locations, symptoms, and neuro-
imaging findings were similar. Therefore, preoperative identification of germinoma with granuloma is difficult. Intraoperative findings of a grayish, elastic hard mass may help to recognize this type of germinoma, but the lesion was pinkish and soft in our case. Stereotactic biopsy has failed to establish the diagnosis in some cases, so further biopsies or direct surgery may be required.

Germinoma of the pineal region is deep-seated, so specimens obtained by surgery may be too small to obtain the correct histological diagnosis if granulomatous reaction is dominant and few neoplastic cells are present. Immunohistochemical staining such as c-kit (CD117) is quite important in such cases. PLAP is also useful but care should be taken, as negative results may be obtained even in germinoma identified with a two-cell pattern and/or c-kit. Expression of the proto-oncogene c-kit is reported in malignant melanoma, breast cancer, small and non-small cell lung cancer, and thyroid tumors. Recent studies have also confirmed that c-kit is expressed in germinoma cells and could be a more reliable tumor marker than PLAP.

Prognosis of germinoma with granulomatous reaction remains unclear, but favorable outcomes could be achieved as with common germinoma due to the sensitivity to chemo- and radiotherapy.

The present case indicates that if granulomatous inflammation is identified in a patient with the clinical features of germinoma, immunohistochemical staining for c-kit and PLAP should be performed, even if re-exploratory surgery for another specimen is needed.

References


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