

Granulomatous Response in Intracranial Germinomas: Diagnostic Problems

Abstract

Intracranial germinomas are rare and account for <0.5% of primary intracranial tumors. In contrast to the gonadal germinomas, these do not show granulomatous response within the tumor. In rare cases, the granulomatous component may obscure the tumor proper and lead to diagnostic difficulties/dilemmas. We report a case of suprasellar germinoma in a 17-year-old boy which showed granulomatous response. We discuss the differentials to be considered in such a scenario and discuss the utility of squash cytology and immunohistochemistry in these lesions.

Keywords: *Granulomatous response, intracranial germinomas, squash cytology and Immunohistochemistry*

Introduction

Germinomas, gonadal, and extragonadal are known to exhibit granulomatous response.^[1] The presence of this granulomatous response is seen rarely in intracranial germinomas. However, the presence of extensive granulomatous response in intracranial germinomas often leads to misdiagnosis and many times delays diagnosis. As germinomas show good response to chemotherapy and radiotherapy, prompt diagnosis is very essential in patient management. We report a case of germinoma with extensive granulomatous response and discuss the diagnostic difficulties associated with it.

Case Report

A 17-year-old boy presented with a history of headache for 8 months, progressive painless diminution of vision (right > left) and polyuria for 6 months. The patient had remained short in stature and had failed to develop secondary sexual characters. His general examination was unremarkable. Perimetry revealed a bitemporal hemianopia. Fundus examination showed bilateral disc pallor and primary optic atrophy. Tanner's sexual maturity rating would be 2/3. Hormone profile showed low basal cortisol and testosterone levels. FSH and LH were undetectable with mildly elevated prolactin. Magnetic resonance imaging brain showed

large lesion in the suprasellar area with solid and cystic components and no calcifications, filling the interpeduncular fossa. There was no hydrocephalus.

An open biopsy was done and tissue was sent for histopathological examination. The lesion showed predominant granulomatous response with collections of Langhans type of giant cells, epithelioid cells with a peripheral cuff of lymphocytes [Figure 1a and b]. Adjacent to this, there was a minor component of undifferentiated round cells with moderate to abundant clear cytoplasm, round nucleus with inconspicuous nucleoli [Figure 1c]. The squash smears which were processed in a separate section of our department were looked out for better cytomorphology. The squash smears showed large polygonal cells with moderate vacuolated fragile cytoplasm, round nucleus with conspicuous nucleoli in some cells. The background was tigroid and showed scattered mature lymphocytes [Figure 2]. The cytomorphological features were of germinoma. In the light of the squash smears, the histopathology slides were reviewed, and immunohistochemistry (IHC) with placental alkaline phosphatase (PLAP) and CD117 (c-kit) was done to confirm the tumor. PLAP and CD 117 showed diffuse membranous positivity in the tumor [Figure 1d and e], thus confirming the diagnosis of germinoma. A final diagnosis of suprasellar germinoma with extensive granulomatous response was made.

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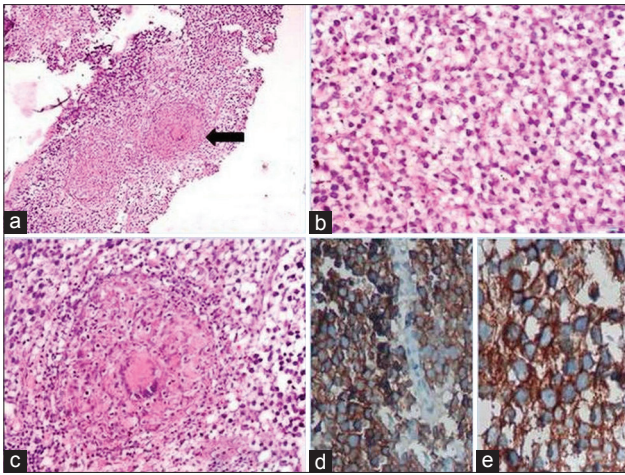


Figure 1: (a) Stereotactic biopsy showing tumor along with a granuloma (arrow) (H and E, $\times 20$); (b) polygonal tumor cells, round vesicular nucleus, abundant cytoplasm; (c) granuloma showing Langhans giant cell, epithelioid cells, and lymphocytes (H and E, $\times 40$); (d) placental alkaline phosphatase positivity (DAB, $\times 10$); (e) CD117 positivity (DAB, $\times 40$)

Postoperative period was uneventful. Postoperative contrast-enhanced computed tomography showed residual tumor in the suprasellar area adherent to the floor of the III ventricle. The patient received six cycles of radiotherapy. No residual tumor was seen at the last follow-up.

Discussion

Germ cell tumors (GCTs) of central nervous system (CNS) most commonly occur in the pineal gland and suprasellar regions.^[1] Approximately 80%–90% of CNS GCTs are seen in younger than 25 years of age, with a peak between 10 and 14 years and a male predominance. Germinomas are the most common GCTs in the adolescent age group. Neurohypophyseal/suprasellar germ cell tumors present with visual field defects, diabetes insipidus (DI), and manifestations of pituitary failure which include retarded growth and sexual immaturity, as in our case.

Granulomatous response is known in gonadal and extragonadal germinomas and is due to the cytokines secreted by tumor infiltrating T-cells. However, this response is seen rarely in intracranial germinomas because of the presence of blood brain barrier and the absence of lymphatic system in the brain.^[2] Granulomatous response is seen in 4.7% of germinomas.^[3] However, whenever this is extensive, it poses many diagnostic problems, unless adequate tissue is available.

There are quite a few lesions in the sellar and suprasellar regions which show granulomatous response. Neurosarcoidosis, tuberculosis, and fungal infection show granulomatous response, and a detailed clinical workup is necessary to look for systemic involvement. Granulomatous/lymphocytic hypophysitis, ruptured Rathke's cleft cyst, and cystic craniopharyngiomas are some other causes of granulomatous response in the sellar

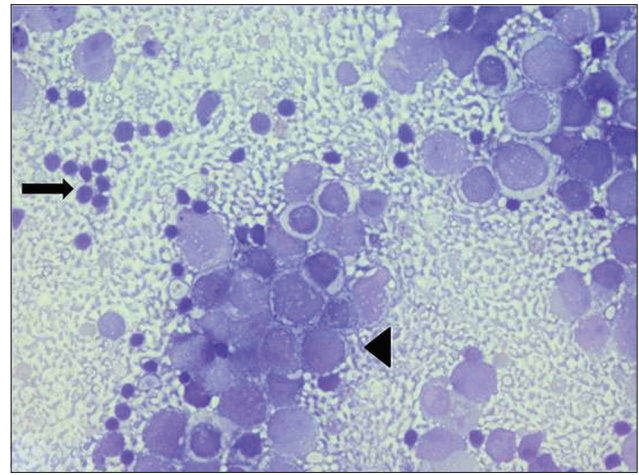


Figure 2: Squash smear showing tigroid background and dual population of cells; large polygonal tumor cells with vesicular chromatin, moderate amount of fragile vacuolated cytoplasm (arrow head) and mature lymphocytes in the background (arrow) (May Grunwald Giemsa X400)

and suprasellar regions. Hence, in any granulomatous lesion not responding to appropriate treatment, a possibility of germinoma should be considered and ruled out.

Intracranial GCTs occur at sites that are surgically difficult to access and the surgical biopsy material is often limited. Many times, if the material is obtained from the periphery of the tissue which shows granulomatous response or if the underlying tumor is masked by granulomatous response, there is a diagnostic error. Endo *et al.* reported a case of germinoma which was initially diagnosed as granulomatous hypophysitis due to the predominant granulomatous component.^[4] Mikami-terao *et al.* in their report conclude that germinoma should be suspected in all patients with DI and pituitary stalk thickening and propose that lymphocytic hypophysitis in children may represent the first sign of a host reaction to an occult germinoma.^[5]

Mueller *et al.* in their report discusses the diagnostic problems encountered in germinomas with a peripheral granulomatous response on stereotactic and endoscopic biopsies. They conclude that in a midline lesion with clinical suspicion of germinoma, stereotactic and endoscopic surgery should sample several different target points within the lesion.^[6] Because of tumor heterogeneity of germinoma, the open biopsy approach is advantageous compared to endoscopic or stereotactic techniques for germinoma and should be considered if a germinoma is in the differential diagnosis and if allowed by the clinical situation.

Radiographic characteristics of CNS-GCTs alone are unable to reliably differentiate germinoma from nongerminomatous GCTs. Hence, histopathology is the main diagnostic modality except in cases where characteristic serum/cerebrospinal fluid tumor marker elevation exists, thus helping in choosing treatment regimen. Mori *et al.* emphasizes the use of IHC

with CD117 (c-kit) and PLAP to highlight the tumor cells.^[2] Although CD117 positivity can be seen in many tumors, it has been used as a reliable marker in germinomas.

Squash cytology is helpful for the intraoperative diagnosis of intracranial germinomas because scant germ cells are easily recognized and distinguished from intermingled inflammatory cells.^[7] Hence, squash cytology should be done wherever possible as it acts as an invaluable adjuvant to histomorphology and gives explicit morphology in identifying the bimodal population of large polygonal cells and mature lymphocytes.

As germinomas are associated with a very good prognosis with radiotherapy, with regression to total disappearance of the tumor, a meticulous histopathological examination will avoid delay in diagnosis and multiple biopsies.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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