



Case Report

## Multiple Midlines Intracranial Germinomas: A Case Report and Review of Literature

Deb Kumar Boruah, Vinay Kumar Doddaballapur Prasanna Kumar, Arjun Prakash, Skandesh B M

Assam Medical College, Assam, India.

Corresponding Author: Vinay Kumar Doddaballapur Prasanna Kumar

Received: 11/12/2014

Revised: 14/01/2015

Accepted: 21/01/2015

### ABSTRACT

Germinomas are the most common intracranial germ cell tumors commonly found in children and adolescents with a mean age of 8-10 years. Intracranial germinomas occur with a strong male predominance and approximately 95% are found in the midline in the pineal (65%) and suprasellar (about 25%) regions. We report a case of multiple midline intracranial germinomas in the pineal, suprasellar and optico-chiasmatic regions presenting in a patient aged 20 years. Synchronous lesions in suprasellar and pineal regions are very rare and are almost exclusively germinomas accounting for 2-13% of all intracranial germ cell tumors and can be concluded that no further evaluation is necessary before initiating therapy in a case of synchronous pineal and sellar lesions with typical neuroimaging features and normal serum oncoproteins

**Keywords-** germinoma, multiple midline tumors, oncoproteins, CSF (cerebral spinal fluid), MRI (Magnetic Resonance Imaging).

### INTRODUCTION

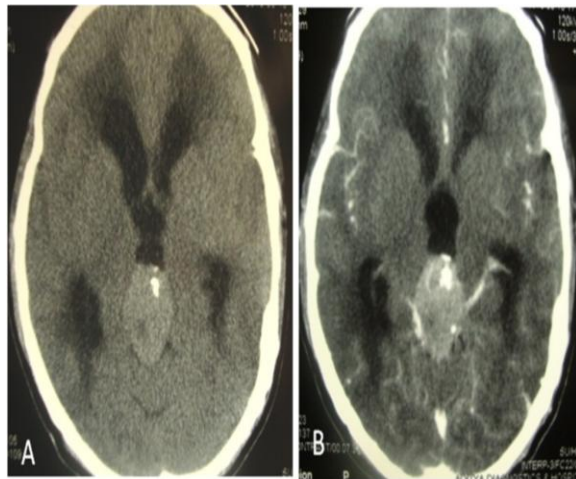
Germ cell tumors most frequently arise in the pineal and suprasellar region and, in general, pineal region germ cell tumors outnumber suprasellar tumors by a ratio of 2:1. Germ cell tumors peak in incidence near the time of puberty. [1] Germinomas characteristically infiltrate locally, and spread by dissemination through the craniospinal and subarachnoid spaces. MRI scan of the entire neuraxis is necessary to search for CSF dissemination. Germinomas are exquisitely sensitive to radiotherapy. The role of surgery, beyond biopsy for tissue diagnosis, remains controversial. Surgical resection exposes the

patient to the operative risks and the possibility of regional tumour dissemination. The presence of a relatively homogeneous, well-circumscribed, extra-axial, enhancing pineal region mass in a young male is so characteristic of a germinoma that diagnostic radiotherapy can be justified. Herein we are presenting a case of young male presenting with synchronous pineal and suprasellar germinomas with typical radiologic features. [2]

### CASE REPORT

A 20 year male was referred to our hospital for evaluation of persistent headache and physical examination as well

as visual acuity was normal. Initially the CT scan was performed which showed a well defined hyperdense mass engulfing the pineal gland calcification in pineal region just posterior to third ventricle leading to obstructive hydrocephalus at 3<sup>rd</sup> ventricular level ( Fig.1 a and Fig 1 b)

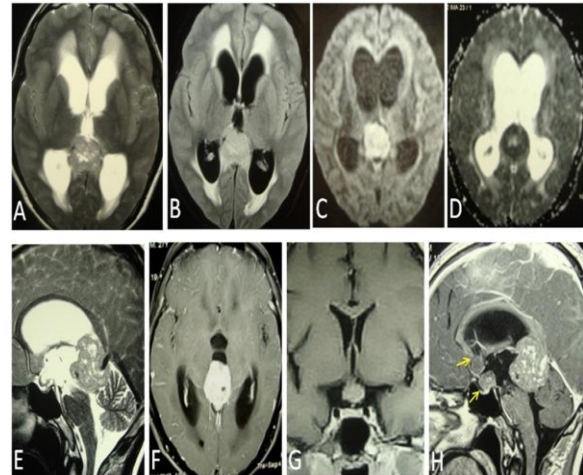


**Figure 1:** Plain (A) and contrast enhanced (B) CT images of brain showed a well defined hyperdense mass in pineal region engulfing the pineal gland calcification and causing posterior third ventricular obstruction and consequent decompensated obstructive hydrocephalus. The lesion showed homogenous post contrast enhancement.

For better characterization MRI scan was done in 1.5 Tesla Siemens Machine in all three orthogonal planes with post gadolinium study.

### **Imaging Findings**

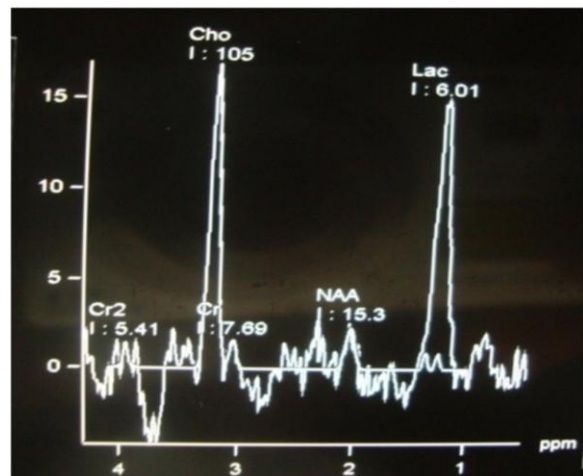
MRI shows a large lobulated T1 iso and T2 hypo to heterogeneously mixed signal intensity homogeneously enhancing mass lesion of size 3.3cm x 2.72cm x 2.6 cm(cc) in pineal region and engulfing the GRE ( gradient recalled imaging ) bloomed pineal calcification(Fig 2a-g). But MRI also revealed synchronous enhancing lesions in suprasellar region and opticochiasmatic regions (Fig 2h). MRI scan of the spinal cord did not reveal any evidence of seeding, and ultrasound of the scrotum and abdomen were insignificant.



**Figure 2:** A well defined lobulated T2 mixed signal intensity and FLAIR hyperintense mass lesion in pineal region showing diffusion restriction with low ADC value causing posterior 3<sup>rd</sup> ventricular obstruction and subsequent obstructive hydrocephalus. Post gadolinium post contrast scan in different planes showed moderate homogenous enhancement on Pineal region mass. Similar smaller enhancing masses are noted in suprasellar cistern and optico-chiasmatic region (yellow arrows in H).

### **Biochemical Findings**

The CSF revealed no abnormalities, neither  $\alpha$  -fetoprotein nor HCG were present. Serum angiotensin-converting enzyme (ACE) was normal, and autoantibody screen was negative.



**Figure 3:** Single voxel MR spectroscopy in low TE (TE 30), shows raised choline and lipid/lactate peaks with reduced NAA peak in the Pineal lesion.

### **Diagnosis**

The imaging findings of multiple midline tumors with negative oncoproteins

were considered compatible with multiple midline germinomas. The patient was referred for radiation therapy following which the tumor regressed demonstrating the excellent response of these tumors to radiation.

**Table-1**

<b>Differential Diagnosis of Germ cell tumours in relation to Tumour Markers</b>		
Tumours	HCG (Human Chorionic Gonadotropin)	AFP (alfa fetoprotein)
Germinoma	+/-	-
Embryonal Cell Carcinoma	+	+
Yolk Sac tumour	-	+
Choriocarcinoma	+	-
Teratoma	-	+
Mixed	+	-

**Table -2 – Summary Table**

Etiology	Not Clear as to actual spread of tumor or simultaneous development
Incidence	2-13% of all germ cell tumors
Gender ratio	2:1 in pineal region tumors, no such predilection for suprasellar region
Age Prediliction	< 20 years
Treatment	Radiotherapy is preferred
Prognosis	Good prognosis with over 90% treated with radiation
Findings on Imaging	Synchronous T1 and T2 Isointense pineal and suprasellar masses which show relatively uniform post contrast enhancement

**Table-3 Differential Table for synchronous pineal and suprasellar lesions**

Pathology	Clinical picture and Imaging findings
Lymphoma	Lymphoma can occur in extraaxial location in adults and children making synchronous lymphomas in pineal and suprasellar region a possibility, however rare.
Germ cell tumors	These are one of the more common intracranial tumors in children and young adults and are located in either pineal or suprasellar region in 95% of cases . Synchronous germinomas are seen in about 5% of cases which is a rare phenomenon in other tumors making this the first choice diagnosis.
Metastases	Intracranial metastases are uncommon in this age group. Moreover metastases tend to be intraaxial rather than extraaxial making this diagnosis unlikely.

## DISCUSSION

Central nervous system germinomas are relatively rare neoplasms, accounting for not more than 5% of paediatric brain tumors. The most common subtype, germinoma usually arises in midline diencephalic structures, particularly the pineal and

suprasellar regions. [3] Similar to their histological counterparts, testicular seminoma and ovarian dysgerminoma, germinomas are extremely radiosensitive and have an excellent overall survival rate of 91-97%. [4]

A review of the literature shows that simultaneous pineal and suprasellar germinomas may be found only in 2-13% of all germ cell tumors. This bifocal disease occurs primarily in patients with germinomas, and it is unclear whether it represents actual spread of the tumor or the simultaneous development of tumors in two sites. Males are approximately two times more likely than females to develop germ cell tumors. The male predominance of germinomas is primarily limited to the pineal region, as suprasellar germinomas are more frequent in females. [5]

The presence, or absence, of specific protein markers, produced and/or secreted by tumor cells, has been an extremely important adjunct in the diagnosis of germ cell tumors. At high levels, these protein markers can be measured in the serum, although cerebrospinal fluid levels are a more sensitive and reliable measure of tumor presence. [6] The usual pattern of tumor marker secretion in germ cell tumors is outlined in Table 1.

Germinomas of the pineal region account for 50%-65% of intracranial germinomas, with male preponderance with an estimated ratio of 2:1. Most patients are less than 20 years old. [7,8] Approximately 95% of the primary brain germ cell neoplasms are found in the midline, in the pineal or suprasellar regions. According to the literature, at the time of diagnosis about 5-10% of all germ cell tumors are found simultaneously in both regions, predominantly in patients with germinomas. [9] The clinical expression of these tumors is usually related to their location, size and speed of growth. [10]

In our case, the diagnosis was made on the basis of the clinical picture and the demonstration of multiple tumours in the midline region with CT and MRI. Although our case was not confirmed by histology, previous studies however suggest that a diagnosis of multiple midline germinomas be made on the basis of a typical clinical presentation and typical radiological findings and assessment of tumor markers itself without histological verification.

A pure germinoma may contain HCG, but this is usually not the case;  $\alpha$  -fetoprotein is not found in pure germinomas. So, in case of intracranial multiple midline tumours with normal values of the tumour markers HCG and  $\alpha$  -fetoprotein in serum and CSF the only possible diagnosis are a germinoma. We feel that under such circumstances no histology is required to confirm this diagnosis as surgical resection exposes the patient to the operative risks and the possibility of regional tumour dissemination. [11] This suggestion is in line with published reports of multiple midline tumours in which biopsy revealed the histological picture of germinoma in all cases with normal tumour markers.

On the other hand if both HCG and  $\alpha$  -fetoprotein are elevated in serum or CSF the only diagnosis is embryonal cell carcinoma. In such a situation a biopsy is not needed either. In case of elevation of either HCG or  $\alpha$  -fetoprotein, there is a differential diagnosis as summarised in table 1 , necessitating biopsy for histological conformation.

### ***Imaging and Differential Diagnosis***

The most common tumours in the pineal region are Germ cell tumours like germinoma and teratoma and pineal parenchymal tumours such as pineocytoma and pineoblastoma. The pineal parenchymal tumours are less frequently seen (approximately 28% of the total) and are believed to be differentiated from other cell

types by their characteristic dispersion rather than engulfment of the pineal calcifications, as seen in germinomas.

Most of the pineal germinomas showed hypointensity on T1WI and isointensity on T2WI, whereas isointensity on both T1WI and T2WI was reported in few cases .The age group of the patients is also a key factor in the diagnosis of pineal region tumors as pineal germinomas tend to occur in young adults , whereas the pineal parenchymal tumors like pineocytomas, PPTR and PPTIDs tend to occur in middle and old age patients.

Differential diagnosis of suprasellar tumours comprises craniopharyngioma, sarcoidosis, germ cell tumour and histiocytosis X. [12]

On the basis of these differential diagnoses of tumours in the suprasellar and pineal regions, the only possible diagnosis in case of synchronous midline tumours is a germ cell tumour. Further tumor marker workup will help in differentiating between the various germ cell tumors. Other abnormalities that can occur in the suprasellar region do not occur in the pineal region and vice versa.

### ***Treatment and Prognosis***

The management of intracranial germ cell tumors in both children and adults remains unsettled. Germinomas have a good prognosis, as over 90% of patients can be effectively treated with radiation therapy. Because of their excellent prognosis after radiotherapy, some feel that radiotherapy can be started without tissue diagnosis in case of multiple tumours located in the midline of the brain, in the pineal and suprasellar regions with normal oncoproteins . Factors affecting the response of intracranial germinomas to radiation therapy have not been reported. The cystic change of the tumor before irradiation was the most notable factor determining radio-responsiveness of intracranial germinomas.

Large tumors with-out cystic components usually decreased in size after 20-56 Gy of irradiation and tended not to have residual lesions. In general, solid tumors tend to be more radioresponsive than cystic tumors because solid tumors have more viable tumor cells, better vascular supply, and higher oxygen tension than cystic tumors.

[13,14] Residual lesions were more frequently detected in patients with large tumors or with CSF seeding than in patients with small tumors or without CSF seeding.

### **Teaching Point**

Typical imaging findings on MRI in a case of synchronous midline tumors with normal CSF and serum tumor markers obviate tissue diagnosis and the patient can be taken for chemoradiation. In the present case report, we have presented the imaging findings of multiple midline germinomas involving pineal, suprasellar and opticochiasmatic regions which could be helpful for radiologists to guide physicians in planning a proper course of management in such patients. Hereby we conclude that no further evaluation is necessary before initiating therapy in a case of synchronous pineal and sellar germinomas with typical neuroimaging features followed by tumor marker work up.

### **Abbreviations**

CT- Computed Tomography

MRI – Magnetic Resonance Imaging

PPTR- Papillary tumor of the pineal region

PPTID- Pineal parenchymal tumors of intermediate differentiation

**Authors' Contribution:** Authors have participated in the present study equally.

**Financial Disclosure:** No financial interest relevant to this article has been reported.

**Funding/Support:** The authors have no funding or support regarding this study.

### **REFERENCES**

1. Jennings MT, Gelman R, Hochberg F. Intracranial germ-cell tumors: natural history and pathogenesis. *J Neurosurg* 1985;63:155-167
2. Jakacki R. Central nervous system germ-cell tumours. *Curr Treat Options Neurol* 2002; 4: 139–145.
3. Alyssa T. Reddy, John C. Wellons, III, Jeffrey C. Allen. Refining the staging evaluation of pineal region germinoma using neuroendoscopy and the presence of preoperative diabetes insipidus. *Neuro-oncol.* 2004 April; 6(2): 127–133
4. Van Battum P, Huijberts MS, Heijckmann AC, Wilmink JT, Nieuwenhuijzen Kruseman ac. Intracranial multiple midline germinomas: is histological verification crucial for therapy? *Neth J Med.* 2007; 65(10):386-9.
5. Packer RJ, Cohen BH, Cooney K: 2000, Intracranial germ cell tumors. *Oncologist* 5:312–320.
6. Allen JC, Nisselbaum J, Epstein F et al. Alphafetoprotein and human chorionic gonadotropin determination in cerebrospinal fluid: an aid to the diagnosis and management of intracranial germ-cell tumors. *J Neurosurg* 1979;51:368-374
7. Lafay-Cousin L, Millar BA, Mabbott D, et al. Limited-field radiation for multiple germinoma. *Int J Radiat Oncol Biol Phys* 2006;65: 486-92.
8. N. Dumrongpisutikul, J. Intrapromkul, D.M. Yousem. Distinguishing between Germinomas and Pineal Cell Tumors on MR Imaging. *AJNR Am J Neuroradiol* 33:550 –55 Mar 2012
9. Ara Kaprelyan, Nadezhda Deleva, Alexandra Tzoukeva et al. CNS germinoma with synchronous lesions in the suprasellar and pineal regions: clinical, ct and immunological follow-up. *Journal of IMAB - Annual Proceeding (Scientific Papers)* 2006, vol. 12, issue 1
10. Moon, W. K., Chang, K. H., Han, M. H., & Kim, I. O. (1999). Intracranial

germinomas: correlation of imaging findings with tumor response to radiation therapy. AJR. American journal of roentgenology, 172(3), 713-716.

11. Reis F, Faria AV, Zanardi VA, et al. Neuroimaging in pineal tumors. J Neuroimaging 2006;16:52–58
12. Hadjikitis S, Hughes T Germinoma with synchronous involvement of the

pineal gland and the suprasellar region: a treatment cause of visual failure in a young adult. Eye 2004. 18:525–526.

13. Huh SJ, Shin KH, Kim IH, Ahn YC, Ha SW, Park. CI. Radiotherapy of intracranial germinomas. Radiother Oncology 1996;20(7):19-23.
14. Moss WT. Brand WN. Battifora H. Radiation on-colog. 5th ed. St. Louis: Mosby. 1979: 1-36.

How to cite this article: Boruah DK, Vinay Kumar DPK, Prakash A et. al. Multiple midline intracranial germinomas: a case report and review of literature. Int J Health Sci Res. 2015; 5(2):418-423.

\*\*\*\*\*

#### **International Journal of Health Sciences & Research (IJHSR)**

#### **Publish your work in this journal**

The International Journal of Health Sciences & Research is a multidisciplinary indexed open access double-blind peer-reviewed international journal that publishes original research articles from all areas of health sciences and allied branches. This monthly journal is characterised by rapid publication of reviews, original research and case reports across all the fields of health sciences. The details of journal are available on its official website ([www.ijhsr.org](http://www.ijhsr.org)).

Submit your manuscript by email: [editor.ijhsr@gmail.com](mailto:editor.ijhsr@gmail.com) OR [editor.ijhsr@yahoo.com](mailto:editor.ijhsr@yahoo.com)