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Case Report

Pathology Section

Mixed Germ Cell Tumour of the Suprasellar Region: A Case Report

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ABSTRACT

Intracranial Germ Cell Tumours (GCTs) represent a rare and heterogeneous group of CNS malignancies that commonly arise in the second decade of life. They account for 0.5-11% of all intracranial neoplasms, with a male:female ratio of 2-2.5:1. Authors report a rare case of a 12-year-old female in paediatric outpatient department who presented with symptoms of raised intracranial pressure, vomiting (3-4 episodes/day), seizure and severe headache for three days associated with altered sensorium. Non-contrast MRI brain was suggestive of a suprasellar lesion causing obstructive hydrocephalus with differential diagnosis of craniopharyngioma and germinoma. Craniotomy was performed, and tissue was sent for Histopathological Examination (HPE). On gross examination, multiple greyish-white soft-tissue bits were received, measuring 3.0×2.5×2.0 cm. The HPE revealed a mixture of mature benign tissues of ectodermal, mesodermal, and endodermal origin, with discretely arranged pleomorphic cells, foci of lymphocytic infiltrate, and a few syncytiotrophic giant cells, favouring mixed GCT. Immunohistochemistry (IHC) showed positivity for OCT3/4, CD117, and ß-HCG in the germinoma component, as well as positivity for Glypican 3 and AFP in the yolk sac tumour component, and positivity for Cytokeratin (CK) in the mature teratoma component. CD30 and GFAP were negative. The diagnosis was confirmed through histopathological evaluation and a comprehensive IHC panel, which identified a mixed GCTs complex composition of mature teratoma (75%), germinoma (20%), and yolk sac tumour (5%). This case emphasises the necessity of meticulous subtyping, as the presence of even minor non-germinomatous components significantly alters the prognosis and necessitates a multimodal therapeutic approach. Precise histopathological diagnosis of GCTs is crucial, as it determines prognosis and guides treatment planning. These tumours generally have a favourable prognosis, with 5-year survival rates ranging from 65% to 95%. Mixed GCTs in the suprasellar region represent a rare form of malignancy. In the diagnostic setting, accurate histopathological evaluation supplemented with IHC is essential for subtyping GCTs and planning appropriate management, including surgical resection, chemotherapy, and conventional radiotherapy.

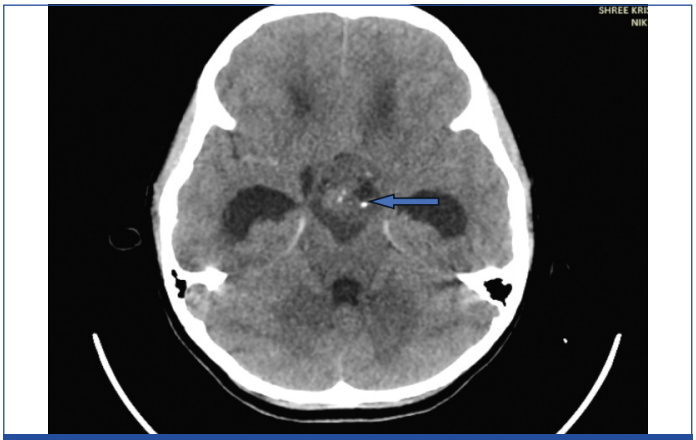
Keywords: Immunohistochemistry, Non-germinomatous tumour, Paediatric intracranial tumour, Suprasellar mass

CASE REPORT

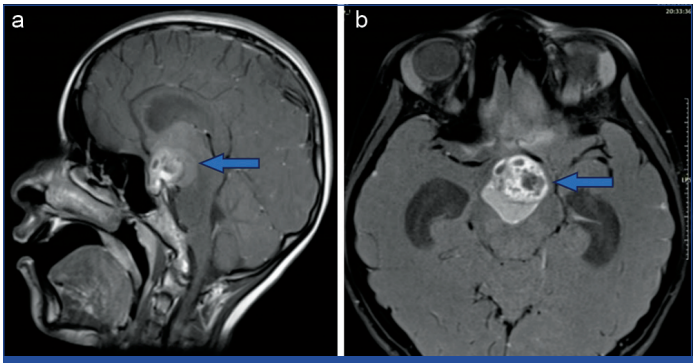
A 12-year-old female presented to the paediatric outpatient department with a three-day history of severe headache, persistent vomiting (3-4 episodes/day), and seizures, accompanied by altered sensorium. These clinical features were indicative of raised intracranial pressure secondary to obstructive hydrocephalus. Initial laboratory investigations revealed that serum tumour markers, including Alpha-Fetoprotein (AFP) and Human Chorionic Gonadotropin (β-HCG), were within normal limits. Furthermore, all biochemical, haematological, and microbiological parameters- including thyroid profile, prolactin levels, and Cerebrospinal Fluid (CSF) examination- showed no abnormalities.

Neuroimaging was performed to characterise the lesion and guide surgical planning. A non-contrast CT scan of the brain [Table/Fig-1] identified a well-defined, mixed solid-cystic lesion in the suprasellar region containing internal specks of calcification and associated with mild hydrocephalus. Subsequent non-contrast MRI [Table/Fig-2a,b] revealed a 3.5 × 2.7 × 2.7 cm (AP×TX×SI) mass extending inferiorly into the sella and encasing the pituitary infundibulum. The lesion laterally, abutted the bilateral cavernous segments of the internal carotid arteries and caused mild compression of the optic chiasma. Based on these radiological findings, the primary differential diagnoses were craniopharyngioma and germinoma.

The patient underwent a craniotomy for maximal safe resection and tissue from space occupying lesion of suprasellar region was sent for HPE. Gross examination of the excised tissue revealed multiple greyish-white soft tissue fragments measuring 3.0 × 2.5 × 2.0 cm. Microscopic evaluation using Haematoxylin and Eosin (H&E) staining revealed a distinct triphasic pattern. The germinoma

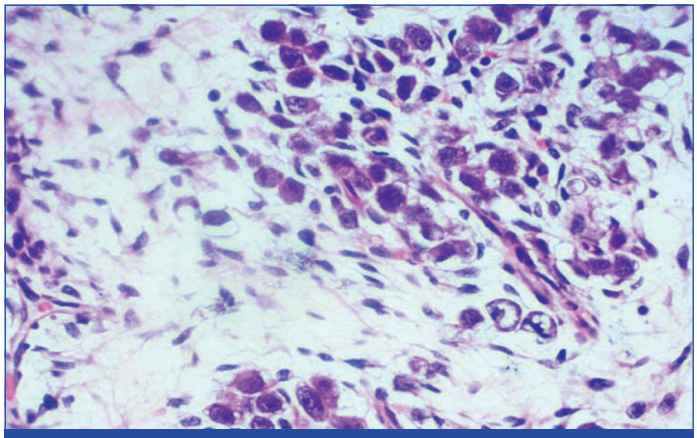


[Table/Fig-1]: Non-contrast CT scan of the brain identified a well-defined, mixed solid-cystic lesion in the suprasellar region with internal calcification.

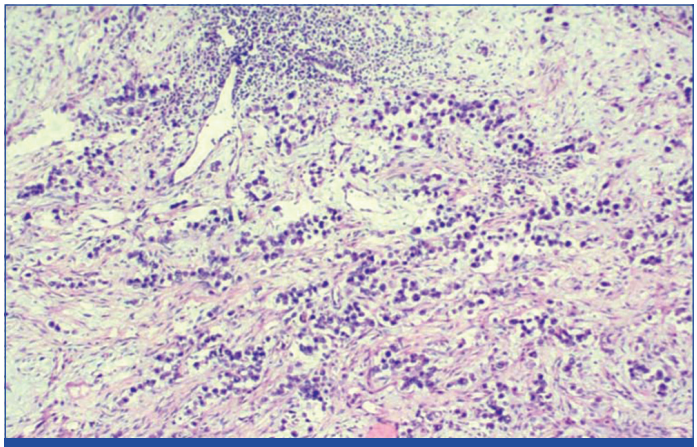


[Table/Fig-2a,b]: Non-contrast MRI brain demonstrates a suprasellar mass causing obstructive hydrocephalus- likely craniopharyngioma or germinoma.

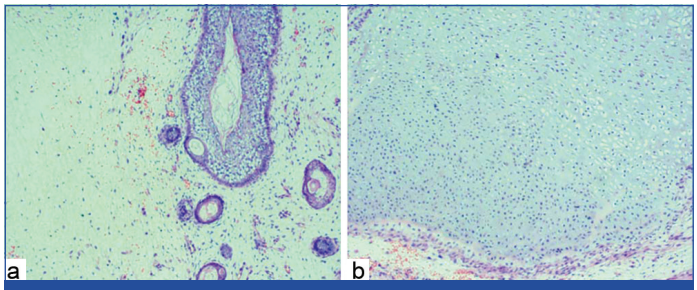
component consisted of large, uniform epithelioid cells arranged in sheets. Characterised by vesicular nuclei, prominent nucleoli, and clear cytoplasm, interspersed with lymphocytic infiltrates and syncytiotrophoblastic giant cells [Table/Fig-3]. The yolk sac component displayed a reticular and microcystic architecture featuring characteristic Schiller-Duval bodies and hyaline globules [Table/Fig-4]. Mature teratoma component showed well-differentiated tissues from all three germ layers, including squamous epithelium, cartilage, bone, adipose tissue, and nerve bundles [Table/Fig-5a,b].



[Table/Fig-3]: Germinoma component shows tumour cell with abundant eosinophilic cytoplasm & lymphocytic infiltrates (H&E stain, 400x).



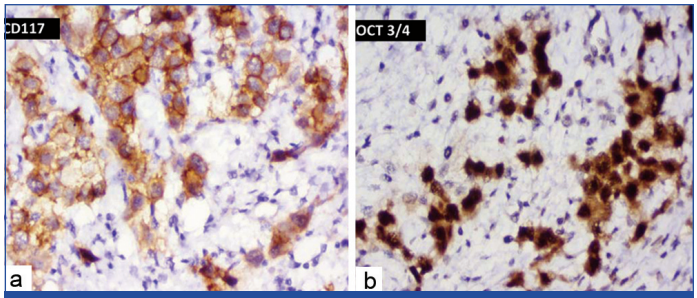
[Table/Fig-4]: Yolk sac component shows a reticular and microcystic growth pattern (H&E stain, 100x).



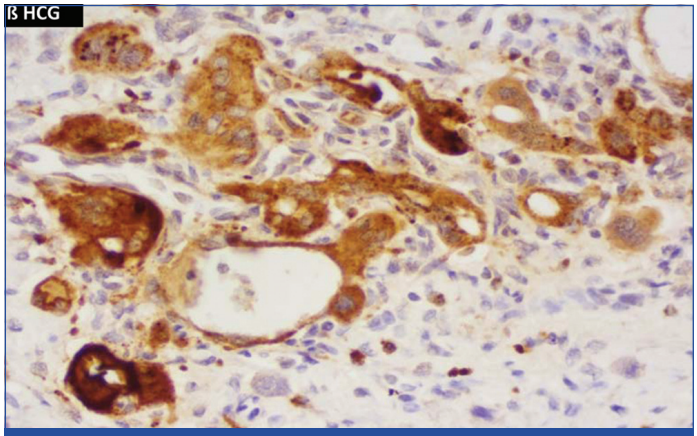
[Table/Fig-5a,b]: Mature teratoma component shows sebaceous glands, hair follicles, adipose tissue and hypercellular cartilage (H&E stain, 100x).

To confirm the subtyping, an IHC panel was performed. The germinoma cells showed strong nuclear and cytoplasmic positivity for OCT3/4 and CD117 [Table/Fig-6a,b], while the syncytiotrophoblastic giant cells were positive for β-HCG [Table/Fig-7]. The yolk sac component demonstrated cytoplasmic and membranous staining for Glypican-3 and AFP [Table/Fig-8a,b]. The teratoma component was highlighted by CK positivity in the epithelial elements [Table/Fig-9]. The Ki-67 proliferation index was measured at 59%, and markers for CD30 and GFAP were negative.

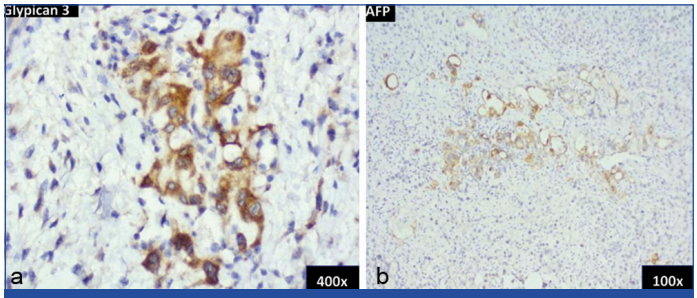
Final diagnosis: Based on the morphological findings and the IHC profile, the lesion was diagnosed as a mixed GCT of the suprasellar region comprising 75% mature teratoma, 20% germinoma, and 5%



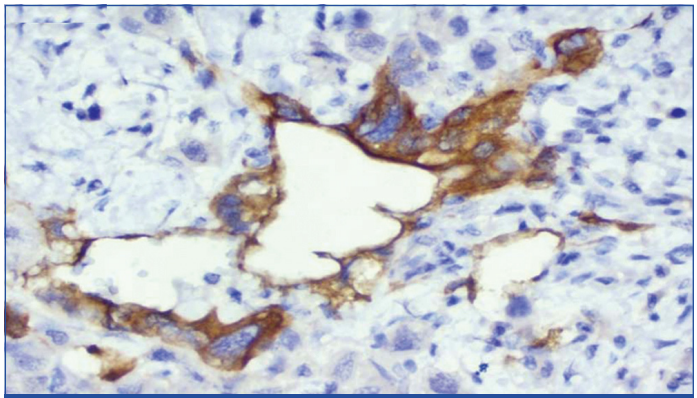
[Table/Fig-6a,b]: Immunostaining for CD 117 shows cytoplasmic and OCT3/4 shows nuclear and cytoplasmic staining positivity in germinoma component (IHC, 400x).



[Table/Fig-7]: ß HCG positivity in syncytiotrophic giant cells within germinoma component (IHC, 400x).



[Table/Fig-8a,b]: Immunostaining for Glypican 3 & AFP shows cytoplasmic and membranous staining positivity in yolk sac tumour component.



[Table/Fig-9]: Cytokeratin positivity shows in epithelial component of teratoma and yolk sac (IHC, 400x).

yolk sac tumour. The patient was critically ill and required intubation, and succumbed within 4-5 days after the diagnosis of mixed GCT. Consequently, definitive treatment and follow-up could not be undertaken.

DISCUSSION

Intracranial GCTs are rare neoplasms of the central nervous system, accounting for 0.5-3% of intracranial tumours in Western countries and up to 11% in Asian populations, such as Japan and Taiwan [1,2]. Intracranial GCTs typically arise in midline structures like the pineal and suprasellar regions due to the aberrant migration of

primordial germ cells during embryogenesis [3]. These tumours predominantly affect children and young adults, with a male-to-female ratio of approximately 2-2.5:1 and a peak incidence in the second decade of life [1].

According to the WHO Classification of CNS Tumours (2021), intracranial GCTs are classified into germinomatous and non-germinomatous GCTs, which include embryonal carcinoma, yolk sac tumour, choriocarcinoma, teratoma (mature or immature), and mixed GCTs containing two or more components [4,5]. Mixed GCTs constitute approximately 10-20% of intracranial GCTs and exhibit aggressive biological behaviour in the presence of non-germinomatous components, even when these are minor, as they critically impact prognosis and guide therapeutic decision-making. Mixed GCTs commonly consist of combinations such as germinoma with teratoma or germinoma with yolk sac tumour and exhibit marked histological heterogeneity, making accurate diagnosis essential [5].

The pathogenesis is further supported by specific molecular alterations. Germinomas are often associated with mutations in the KIT and RAS genes. In contrast, non-germinomatous germ cell tumours (GCTs) commonly exhibit isochromosome 12p [i(12p)], particularly in teratomas and yolk sac tumours [6,7].

Clinical presentation and symptoms are largely dependent on the tumour location:

- Suprasellar tumours commonly present with headache, vomiting, visual disturbances, and endocrine dysfunction, including diabetes insipidus, growth retardation, and hypopituitarism.
- Pineal tumours typically present with features of obstructive hydrocephalus and Parinaud's syndrome, resulting from compression of the cerebral aqueduct [8].

Management of GCT typically involves a multimodal approach, including maximal safe surgical resection, followed by platinum-based chemotherapy and radiotherapy, depending on tumour composition. Germinomas are highly radiosensitive and carry a favourable prognosis, whereas mature teratomas are radioresistant and need surgical removal. Non-germinomatous elements behave aggressively and require multimodal treatment. Recurrence rates are higher in mixed and non-germinomatous GCTs compared to pure germinomas. Overall, 5-year survival ranges from 65-95%, with prognosis largely dependent on tumour subtype, extent of resection, and response to adjuvant therapy [9-11].

This present case is rare as it demonstrates a malignant mixed GCT with three distinct subtypes in the suprasellar region, highlights the critical role of meticulous histopathological evaluation and IHC in identifying minor malignant components, which directly impact risk stratification, treatment planning, and outcome prediction. Accurate classification is vital, as treatment and prognosis differ markedly among components- with germinomas being highly radiosensitive, teratomas requiring surgical excision, and yolk sac tumour elements necessitating aggressive chemotherapy.

The MGCT diagnosis relies on the presence of two or more distinct germ cell components. The present case of a 12-year-old female with suprasellar mixed GCT (mature teratoma 75%, germinoma 20%, yolk sac 5%) differs from other reports by Yu Mon S et al., (2014), Nada R et al., (2000) and Isaji T et al., (2023) in age, site and histological composition. While most reported cases involved older patients or demonstrated a predominance of malignant components such as embryonal carcinoma or yolk sac tumour, the present case shows paediatric onset, female gender, and a dominant mature teratoma component, suggesting a relatively less aggressive biological behaviour. A comparative analysis of similar cases highlights the rarity and diversity of these tumours [Table/Fig-10] [12-14].

This case feature	Present case	Yu Mon S et al., (2014) [12]	Nada R et al., (2000) [13]	Isaji T et al., (2023) [14]
Age	12-year-old	23-year-old	15-year-old	50-year-old
Gender	Female	Female	Male	Female
Site of lesion	Suprasellar region	Pituitary Infundibulum	Suprasellar and Retro Sellar	Medulla oblongata
Histopathology findings	Mixed GCT: 1. Mature Teratoma (75%) 2. Germinoma (20%) 3. Yolk sac tumour (5%).	Mixed GCT: 1. Germinoma 2. Teratoma components (both mature and immature)	Malignant Mixed GCT: All three germ cell lineage: 1. Embryonal carcinoma 2. Yolk sac tumour 3. Squamous cysts.	Mixed GCT: 1. Primarily yolk sac tumour component 2. Germinoma
Serum and CSF Markers	Serum AFP and ß HCG-negative	CSF AFP and ß HCG-negative	Serum AFP-strongly positive CSF AFP-strongly positive ß HCG-negative	Serum AFP-positive ß HCG-negative
IHC markers (Positive)	OCT3/4, CD117, ß-HCG (Germinoma); Glypican 3, AFP (Yolk sac tumour), CK (Teratoma).	PLAP, OCT-3/4 (Germinoma), AFP and ß-HCG are not mentioned for tissue IHC, but serum markers are often used.	Tissue IHC is not explicitly detailed.	AFP, SALL-4, Glypican-3 (Yolk sac component); PLAP, OCT-3/4, CD-117 (Germinoma component); CD-30 (Embryonal Carcinoma component).

[Table/Fig-10]: Comparative analysis of similar cases highlights the rarity and diversity of these tumours [12-14].

CONCLUSION(S)

The comprehensive IHC panel clarified the mixed GCT nature of the tumour: OCT3/4 and CD117 confirmed the germinoma component, while AFP and Glypican-3 highlighted a minor yolk sac element. The present case is rare and demonstrates malignant mixed GCT with different subtypes in suprasellar region. In the diagnostic setting, accurate histopathological diagnosis along with IHC for subtyping of CNS GCTs is critical for estimating prognosis and planning subsequent surgical resection, chemotherapy and conventional radiotherapy.

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