Mixed germ cell tumour of the pineal region

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Abstract: Intracranial mixed germ cell tumours, particularly with the occurrence of germinoma and teratoma components, are very rare. On many occasions, the diagnosis is only reached after a second surgical resection of what is believed to be a tumour recurrence. The authors report two young adolescent males who presented with headache, vomiting, and Parinaud's syndrome. Cranial CT and MRI scans demonstrated a large heterogeneous pineal region tumour. Through a supracerebellar infratentorial approach, in both patients, a complete excision of the tumour was achieved of a histopathologically proven mixed germ cell tumour, predominantly teratoma with elements of germinoma. The patients received adjuvant chemotherapy and radiotherapy and remained tumour free during their follow-up. The authors discuss the management of this rare entity and emphasize the importance of detailed histopathological examination.

Key words: *Pineal tumours, teratoma, germinoma and germ cell tumour*

Introduction

Primary germ cell tumours (GCTs) are the commonest tumours of the pineal region. They arise from primordial germ cells that fail to migrate properly during the initial weeks of embryonic development and are invariably located in the midline, both intra-, as well as extra-cranially.[20] They are classified in the same way as their gonadal counterparts i.e., germinoma, nongerminomatous GCTs and mixed germ cell tumours (MGCTs). Teratoma is the second commonest GCT of this region, after germinoma.[18] Mixed germ cell tumours commonly have germinoma as one of its histological subtypes; the other component of the group can be a choriocarcinoma, embryonal cell tumour, endodermal sinus tumour or a teratoma.[3] The combination of teratoma and germinoma is very rarely encountered and usually the diagnosis is established after a second surgery for residual or recurrent tumour.[2,8,10,22]

The authors herein report this rare association in two young Saudi Arabian males who presented with Parinaud's syndrome who were successfully treated with complete excision, followed by adjuvant chemotherapy and radiotherapy. The optimal treatment of GCTs remains controversial and in MGCTs with a predominantly benign component such as teratoma, complete microsurgical resection is the mainstay of treatment. The literature is reviewed and the management is discussed.

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Case Reports

Case 1: A 17-year-old male presented with headache, vomiting, and visual deterioration of 6 weeks duration. On initial examination at the referring hospital, he was conscious, alert, and he had a Parinaud's syndrome with a left sixth nerve palsy and bilateral papilloedema. Computed tomography (CT) scan of the brain at that time revealed a pineal region tumour with obstructive hydrocephalus. Emergency ventriculoperitoneal shunt (VPS) was performed and he was transferred to our institution. On admission, 2 weeks after VPS insertion, his general physical and neurological examinations were normal, and the routine laboratory examinations were within normal values. A CT scan revealed a 30 mm x 30 mm heterogeneous pineal region tumour with areas of densities compatible with fat and calcifications (Fig. 1). Magnetic resonance imaging (MRI) scans of the brain revealed a 30 mm x 35 mm x 30 mm multicystic tumour of the pineal region, with heterogeneous enhancement, compressing the tectum of the midbrain (Fig. 2). Adequate decompression of the ventricles after VPS insertion was demonstrated. Spinal MRI scans were negative for tumour seeding. Cerebrospinal fluid (CSF) examination, obtained through a VPS tap, revealed normal values of cell counts and chemistry, and the culture was negative. Cerebrospinal fluid examination for malignant cells and tumour markers, including human chorionic

gonadotropin (B-HCG) and alpha-fetoprotein (AFP) were negative. Surgery was performed through a posterior fossa craniotomy and a supracerebellar infratentorial approach. Complete microsurgical resection of a greyish vascular tumour consisting of multiple cysts containing a thin, milky, non-foul smelling fluid was achieved (Fig. 3). The patient had a smooth postoperative recovery, and had MRI scans within 48 hours, which confirmed the complete resection. Histopathological examination revealed mostly mature teratoma with elements of germinoma (Fig. 4). No other germ cell component was present and immunoassaying for B-HCG and AFP was negative. The patient received adjuvant chemotherapy (cisplatinum and etoposide) and whole brain radiotherapy (4500 cGY in 25 fractions over 25 days). On the 5th year follow-up, he remained with normal neurological and radiological examinations (Fig. 5).

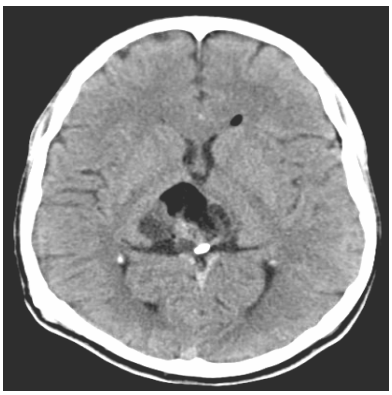

Figure 1 ← Non-enhanced cranial CT scan demonstrating 30mm X 30mm heterogeneous pineal tumour; it has densities consistent with fat and calcifications

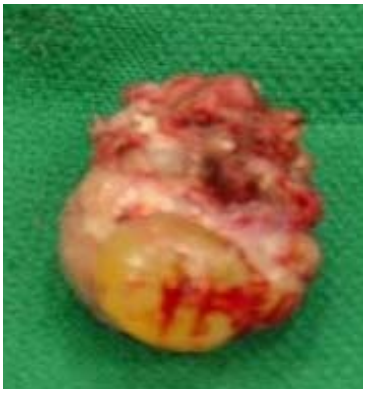

Figure 3 → Photographic image of the resected pineal tumour

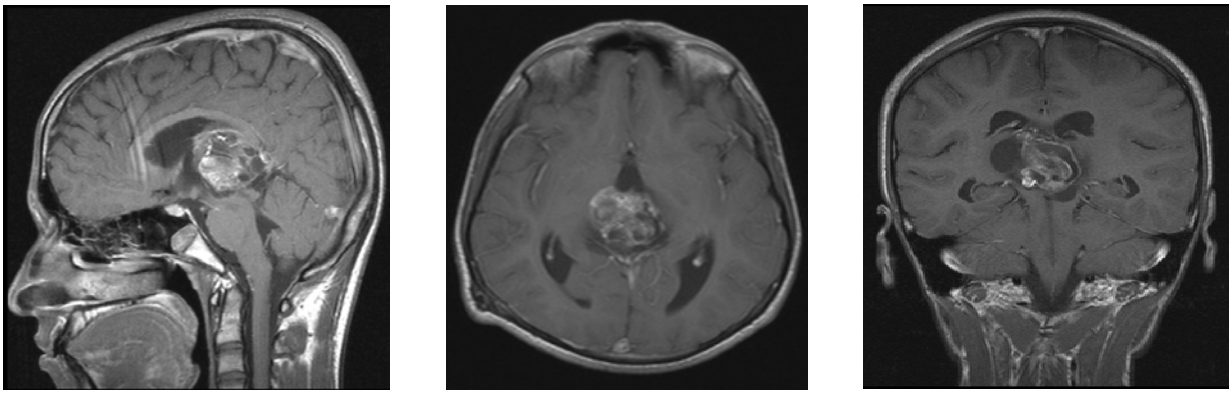

Figure 2 - Enhanced **(a)** sagittal, **(b)** axial, and (c**)** coronal MRI scans demonstrating 30 mm x 35 mm x 30 mm heterogeneously enhancing pineal region tumour.

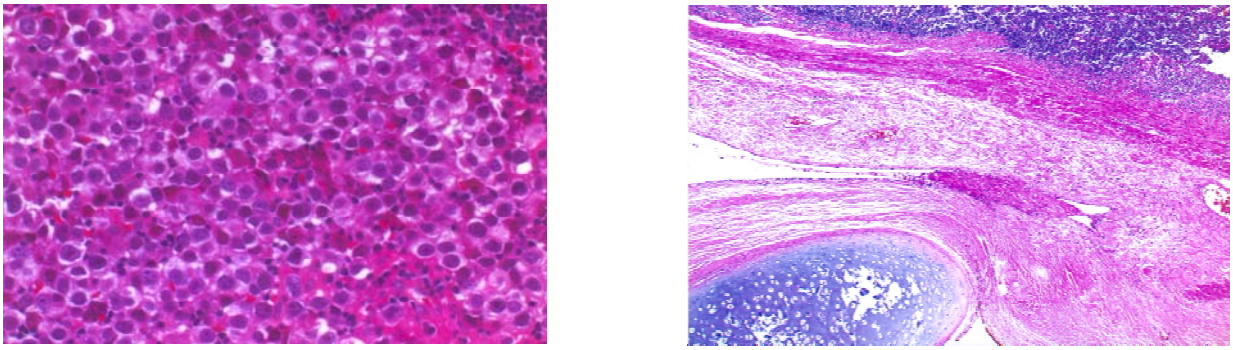

Figure 4 - (a) Section from the tumour reveals the germinoma component. A sheet of large cells with abundant clear to eosinophilic cytoplasm with distinct nucleoli; the stroma between the tumour sheets contains lymphocytes (H&E x 200). **(b)** Section from the tumour reveals the teratoma component. Mature cartilage and other mature mesenchymal components are seen (H&E x 100)

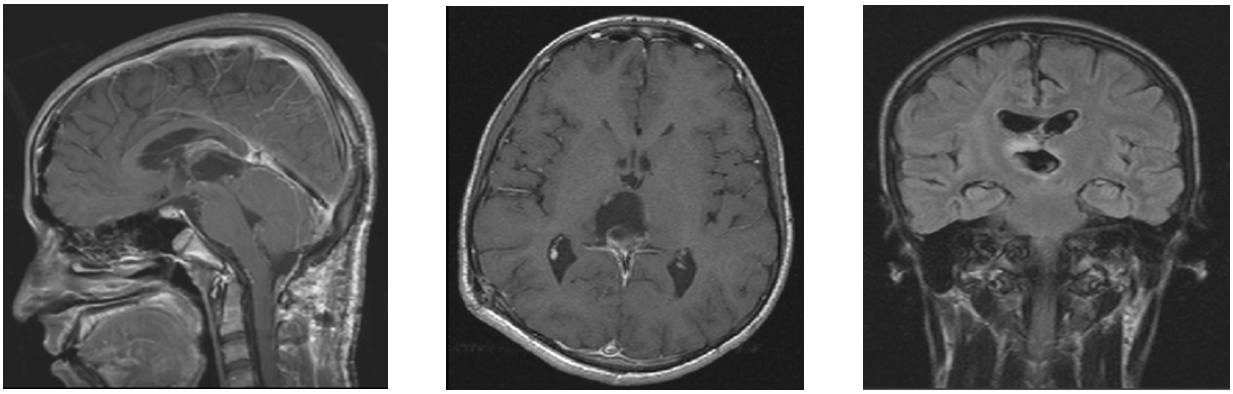

Figure 5 - Postoperative enhanced (a**)** sagittal, (b**)** axial, and (c**)** coronal MRI scans demonstrating complete resection of the tumour

Case 2: A 20-year-old male presented to a local hospital with headache, vomiting, and visual deterioration of 4 weeks duration. On initial examination, he was drowsy and confused, and he had a Parinaud's syndrome and bilateral papilloedema. Computed tomography scan of the brain at that time revealed a large pineal region tumour with obstructive hydrocephalus. Emergency VPS was performed and he was then transferred 8 days later to our institution for further management. His general physical and neurological examination was normal apart from Parinaud's syndrome and mild resolving papilloedema. Routine laboratory examinations and serum tumour markers were within normal values, but with elevated serum AFP. Cerebrospinal fluid examination, obtained through a VPS tap, revealed postoperative mild pleocytosis and normal chemistry values. Cerebrospinal fluid examination for malignant cells and culture was negative, as well as, AFP and B-HCG. Magnetic resonance imaging of the brain revealed a 60 mm x 45 mm x 35 mm multicystic tumour of the pineal region, with heterogeneous enhancement, compressing the tectum of the midbrain (Fig. 6). Adequate decompression of the ventricles after VPS insertion was demonstrated. Spinal MRI scans demonstrated no evidence of tumour seeding. Posterior fossa craniotomy through supracerebellar infratentorial approach was performed and complete microsurgical resection was achieved. A greyish vascular tumour consisting of soft component was easily removed with ultrasonic aspirator, but the hard calcified component was removed with microscissors in piecemeal fashion. There were multicystic components containing a brownish non-foul smelling fluid. The patient had a smooth postoperative recovery with transient worsening of Parinaud's syndrome. Postoperative MRI scans within 48 hours confirmed the complete resection. Histopathological examination revealed mostly mature teratoma with elements of germinoma (Fig. 7). The patient received adjuvant chemotherapy and whole brain radiotherapy as per protocol. On the 1st year follow-up, his neurological examination was normal with no tumour recurrence on MRI scan (Fig. 8).

Discussion

Pineal region tumours are rare, accounting for 0.5 to 1.6% of all intracranial tumours.[20] They are relatively more common in Asian countries than western countries, with

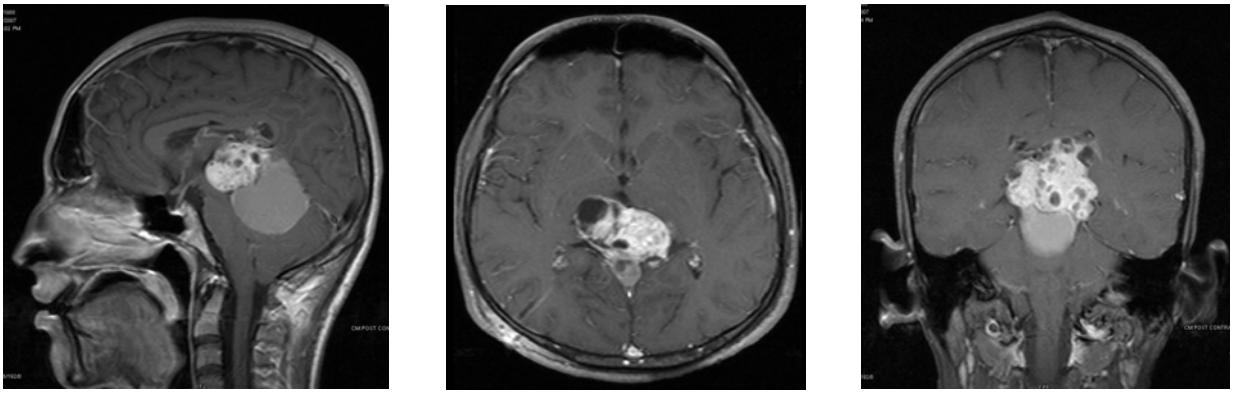

Figure 6 - Enhanced **(a)** sagittal, **(b)** axial, and (c**)** coronal MRI scans demonstrating a 60 mm x 45 mm x 35 mm heterogeneously enhancing pineal tumour

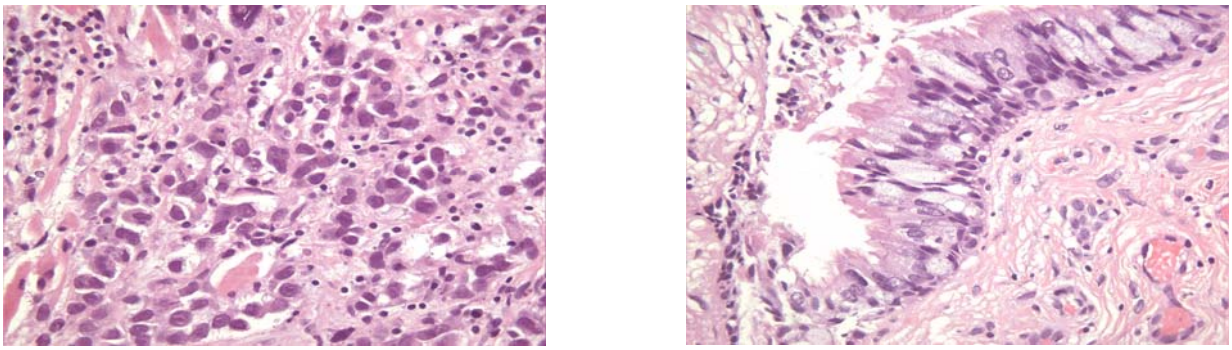

Figure 7 – (a) High power image reveals the large cells with enlarged nuclei and clear cytoplasm power represent the germinoma component (H&E x 400). **(b)** Section reveals focus of mature glandular element composed of pseudostratified ciliated columnar epithelium consistent with respiratory type epithelium represents the mature teratoma component (H&E x 400)

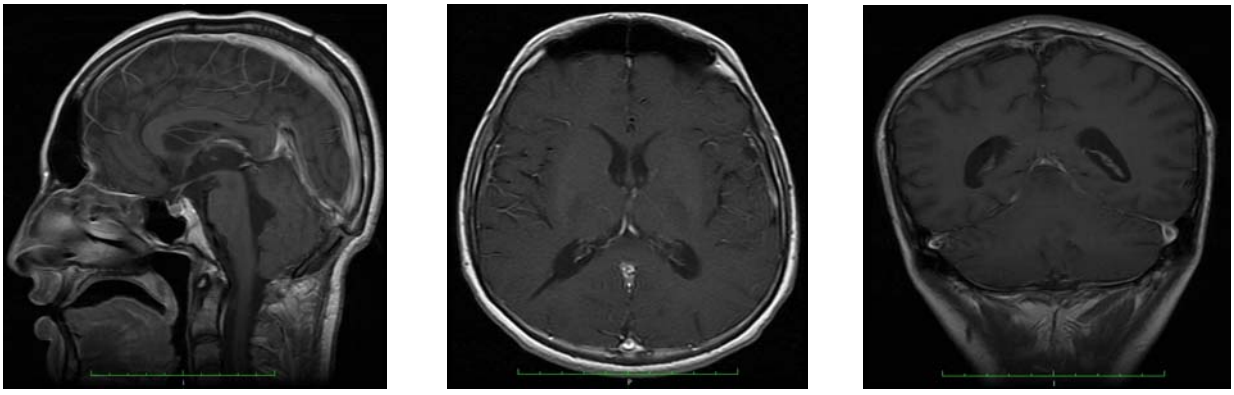

Figure 8 - Postoperative enhanced (**a)** sagittal, (**b)** axial, and (**c)** coronal MRI scans demonstrating complete resection of the tumour

marked male predominance.[18] In an epidemiological study reported by Namura et al, GCTs represent 70% of the pineal region tumours.[18] Out of those, 68% were germinomas, and teratomas represented 15%. In the reported cases in the literature, MGCTs represent 12% of all intracranial GCTs.[2,9,12-14] They usually consist of a combination of germinoma and another type of GCT that could be choriocarcinoma, embryonal cell tumour, endodermal sinus tumour, or teratoma.[3] The combination of teratoma and germinoma is very rare, accounting for 4% of these cases.[12]

MGCTs most commonly present as any tumour of the pineal region with non-specific symptoms due to raised intracranial pressure or with Parinaud's syndrome secondary to compression of the tectal plate.[15] Uncommonly, a patient may present with endocrinological manifestations such as precocious puberty, which occurs in less than 10% of patients with pineal tumors.[22]

Preoperative serum and CSF examination for tumour markers (AFP and B–HCG), which are usually secreted by mixed and non-germinomatous GCTs, and rarely by germinomas, is diagnostically important.[1] This may not only add to the diagnosis, but is important for postoperative monitoring of a therapeutic response and of potential tumour recurrence. Our patients had a mature teratoma; hence, these markers were negative.

Imaging studies with CT and MRI has narrowed the spectrum of the differential diagnosis among pineal tumours and even revolutionized their management. Germinomas usually appear as homogenous solid tumours and show isointensity on T1- and hypointensity on T2- images, while teratomas typically are multicystic tumours that show more heterogenous signal because of the various components, such as fat densities and calcification, as in our cases.[16,23] Calcification is common in teratomas, thus demonstrating a mixture of linear and nodular hyperdense areas on CT scans.[11] The MRI features of MGCTs demonstrate a considerable overlap and have not been well documented.[17] This was the case in our patient in which the MRI showed relatively homogenous intensity with intense enhancement representing the germinoma component and the multicystic component of the teratoma.

Of historical interest is the fact that patients with pineal tumours in the past were often empirically treated with radiation because of high postoperative mortality.[21] The advances in microsurgical techniques have now rendered the pineal region more accessible and surgery can be performed safely through various approaches. Complete surgical excision or debulking, or at least a histopathological confirmation through minimal invasive endoscopic or stereotactic techniques is recommended before the initiation of adjuvant radiation and/or chemotherapy.[6,7,9]

The optimum management of intracranial GCTs is still evolving.[4,5,19,24] Complete microsurgical resection is preferred over other surgical options because small pieces of tissue through stereotactic or endoscopic methods may not represent the true histology of the lesion and may affect the decision of adjuvant therapy. This is mostly true in the case of MGCTs similar to our case where one type of tumour will be diagnosed and the other will be missed. The missed component may be malignant and the patient may return later with untreatable metastatic disease. Stereotactic or endoscopic biopsy for histological diagnosis can be reserved for patients with general co-morbidity that makes them poor candidates for craniotomy. It is preferable to get tissue from more than one area in these biopsies, if possible, for better histological diagnosis. Mixed germ cell tumours, such as in our cases, are categorized as tumours of intermediate aggressiveness. Radiotherapy or chemotherapy alone has poor long-term tumour control. Currently the best strategy for MGCTs like teratoma with germinoma is microsurgical excision followed by chemotherapy and radiotherapy.[4,19] The germinoma component of this tumour is very sensitive to radiotherapy. If there is no CSF or radiologically proven dissemination of tumour, cranial radiotherapy is usually adequate.[24] Craniospinal axis radiation is controversial and recommended if the spinal MRI shows drop metastases or if the CSF analysis reveals positive malignant cells after completion of chemotherapy.[24] The five-year actuarial disease-free survival reported in literature for MGCTs after irradiation and chemotherapy following surgical resection was 60 to 70%.[4,19,24]

We herein conclude that aggressive multimodality approaches for MGCTs with microsurgical resection, radiotherapy, and chemotherapy are necessary to improve the outcome in these challenging tumours.

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