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Case Report

# Progressive Neurological Decline in a Teenage Girl: A Case of Germinoma with Complex Multisystem Involvement

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**Abstract**

Germinomas are primary malignant tumours derived from neuroectodermal tissue. Their presentation can be varied based on the tumour location. This is a case of a 16-year-old female who presented with limb weakness, cognitive dysfunction, polyuria and polydipsia and menstrual disturbances. The patient's subsequent neuroimaging revealed a large lesion in the left cerebral hemisphere with extension into the frontotemporal region extending to the deep white matter, corpus callosum, basal ganglia and thalamus. There was also pituitary stalk thickening. Histological examination confirmed the presence of a germinoma. She was treated with neoadjuvant chemotherapy with bleomycin, etoposide and cisplatin followed by radiotherapy.

**Keywords:** Intracranial germinoma, diabetes insipidus, hypogonadotropic hypogonadism, Pediatric endocrinology.



## Introduction

Germinomas are primary malignant tumours derived from primordial germ cells. [1] They account for around 2/3 of intracranial neoplasms and around 2% of all brain tumours. [2] They are most commonly seen in adolescents and young adults. [3] The most common site of origin is the pineal region (45%), followed by the suprasellar region (30%) within the infundibulum or the pituitary stalk. The remaining 25% occur in other areas such as the basal ganglia and thalamus. [4] Interestingly, tumours of the pineal region account for less than 1% of intracranial neoplasms and more than 50% of pineal region neoplasms of germinoma. [5]

Symptoms and progression vary by tumour location. Germinomas in the pineal region present with a short duration of symptoms due to early compression of the cerebral aqueduct, causing obstructive hydrocephalus. Parinaud syndrome occurs in 75% of cases due to midbrain compression. [3] It is characterised by upward gaze palsy, convergence-retraction nystagmus, and pupillary light-near dissociation. Parinaud syndrome can also present with Collier's sign (upper eyelid retraction), loss of convergence and rarely, conjugate downgaze in the primary position. [3] Tumours in the basal ganglia and thalamus progress slowly, leading to extrapyramidal symptoms like rigidity, bradykinesia, and dystonia. [3] Diagnosis is sometimes delayed for years in such cases. Sellar region germinomas primarily cause endocrine issues, with diabetes insipidus (90%) being the most common. [3] Other symptoms include growth and sexual development disturbances and behavioural changes often misdiagnosed as psychosomatic. Visual disturbances occur later due to optic chiasm compression.

## Case Report

Our patient presented at the age of 16 years when she noticed weakness and difficulty in grasping objects with her right hand. Over the course of one year, this weakness ascended to involve the whole upper limb on both sides, and bilateral lower limbs as well. She had no sensory disturbances, muscle wasting, neck or truncal weakness, or symptoms suggestive of cranial nerve dysfunction. She did not experience headaches, cognitive dysfunction or behavioral changes. She gave no history of trauma to the brain or spinal cord, or of recent infection.

A year after the onset of weakness the patient developed dysarthria, with no disturbance in comprehension or reading. She also began to experience disturbances in her memory in the form of difficulty remembering factual information

learnt at school, as well as anecdotes from her childhood. There was retrograde memory loss involving both recent and remote memory. Following this, she developed polydipsia and polyuria with a urinary frequency of upto 20 times per day and disturbed sleep due to night time urination, but no involuntary passage of urine. Persistent hypernatremia on blood tests and a water deprivation test suggested central diabetes insipidus and she was started on oral desmopressin 0.1mg once daily at night. CSF analysis showed atypical cells, elevated protein with oligoclonal bands, and an AFP level of 1.83 IU/mL. She then developed oligomenorrhoea, with cycles occurring every 3 to 4 months. She attained menarche at 13 years of age and previously had cycles occurring every 28-30 days. 4LH < 0.01mIU/L and FSH < 0.5mIU/L, along with her symptoms suggested hypogonadotropic hypogonadism. MRI of the brain was done which showed a large lesion in the left cerebral hemisphere with extension into the frontotemporal region extending to the deep white matter, corpus callosum, basal ganglia and thalamus. There was also pituitary stalk thickening. In this case, basal ganglia germinoma or lymphoma was considered. As per discussions with radiologists and neurosurgeons, the possibility of germinoma was considered to be low due to significant improvement with steroids. CSF alpha feto-protein and Beta HCG were normal.

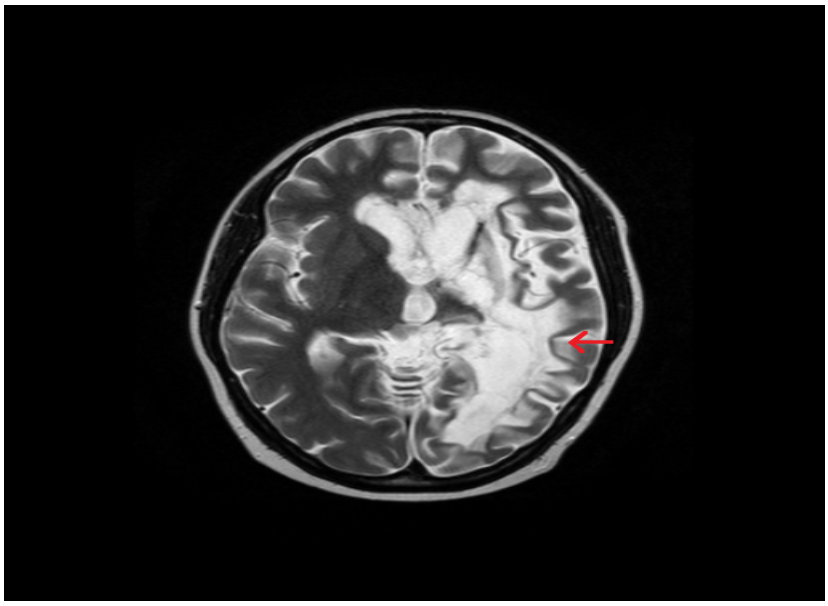

**Figure 1: This axial T2 weighted MRI shows a large hyperintense lesion involving the left cerebral hemisphere and basal ganglia with surrounding vasogenic edema**

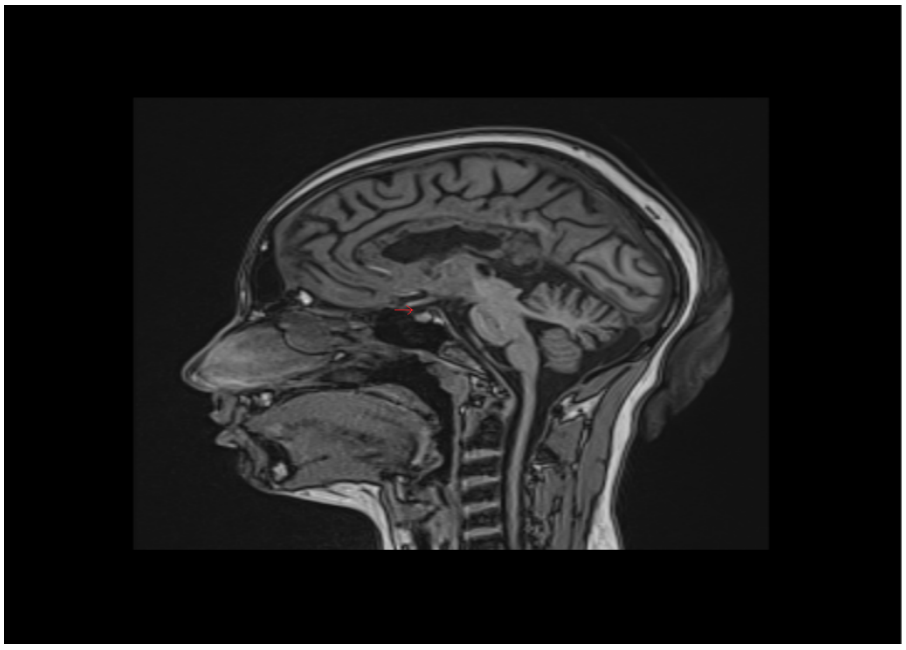

**Figure 2: Figure 2: Sagittal T1 weighted MRI**

A vario guided frameless biopsy showed: small fragments of neuroparenchyma and small fragments of a scanty tumor and clear to pale eosinophilic cytoplasm. Mitosis is evident. The intervening stroma shows mild to moderate infiltrates of lymphocytes. The parenchyma shows interstitial infiltrates of lymphocytes, edema, rarefaction and reactive gliosis. Tumour markers OCT3/4, SAL4 and MIB1 were positive. This confirmed the diagnosis of germinoma.

Tumor markers are referenced table 1.

**Table 1: Tumor markers**

| Sl No | Tumor Marker | |
|---|---|---|
| 1 | OCT 3/4 | Positive |
| 2 | SAL4 | Positive |
| 3 | PLAP | Weakly positive |
| 4 | GFAP | negative |
| 5 | P53 | negative |
| 6 | ATRX | retained nuclear expression |
| 7 | MIB1 | labels to the tumor foci |

**Legend: Tumour markers tested in the patient as per the diagnostic protocol**

She received neoadjuvant chemotherapy with three cycles of bleomycin 30 IU, etoposide 200 mg/hr and cisplatin 30 mg/hr.

This was followed by radiotherapy. Her symptoms improved following treatment. She now has minimal residual weakness with some speech and auditory deficits. Her diabetes insipidus is managed with desmopressin and serum sodium levels are regularly monitored. Her menstrual cycles are also regular following treatment. She follows up with the endocrinologist every 4-6 months. Currently she is on desmopressin 0.1 mg once a day, desogestrel 0.15 mg + ethinyl estradiol 0.02 mg once a day from day five of her cycle for 21 days, cholecalciferol 600IU once a day, elemental iron 30 mg + folic acid 200 mcg + vitamin B12 75 mcg + vitamin C 50 mg once a day.

She is also receiving physiotherapy and speech therapy and is symptomatically better and eunatremic.

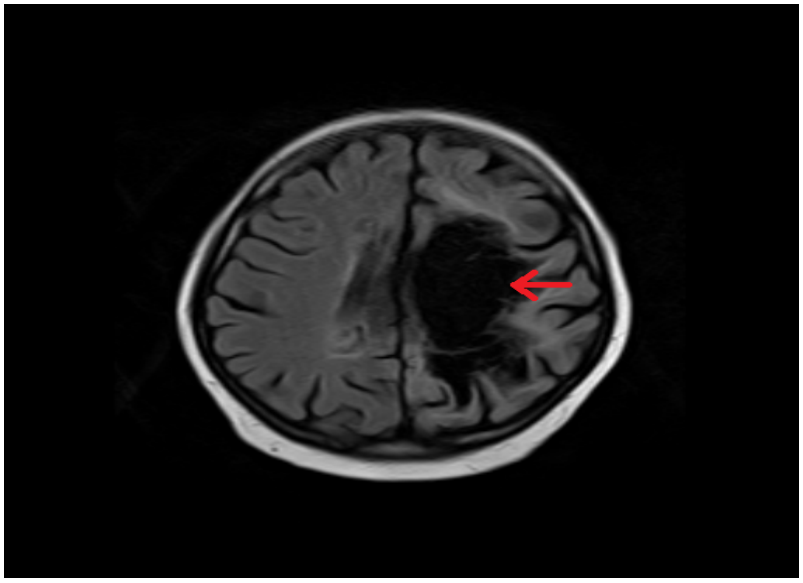

**Figure 3: Figure 3: Post chemotherapy MRI**

**Discussion:**

Germinomas occur most commonly in adolescents and young adults, and the presentation can vary widely depending on the site of the tumour: those with lesions in the sellar region or basal ganglia typically have a longer disease course than those with pineal gland involvement. [3] MRI is the preferred diagnostic modality. [3] Germinomas usually appear as well demarcated round or oval lesions. When involving the sellar region, they can present as an isolated thickening of the pituitary stalk, which has a broad differential - inflammatory (e.g., lymphocytic hypophysitis, sarcoidosis), neoplastic (e.g., germinoma, lymphoma), infectious (e.g., tuberculosis), and infiltrative conditions such as Langerhans cell histiocytosis. [6]

Serum and CSF PLAP, AFP and beta HCG are the commonly used tumour markers for diagnosis,

monitoring response to treatment and recurrence. [3] Complete staging of germinomas is important to reduce relapse. [7] Germinomas are highly radiosensitive. Various modes of radiotherapy have been attempted, such as craniospinal irradiation (CSI), whole brain/ventricular system irradiation and focal radiotherapy alone. Focal radiotherapy limited to the tumour bed is associated with a higher relapse rate than craniospinal irradiation or whole brain or whole ventricular system irradiation. [3] Combined chemotherapy and radiotherapy allows for a lower dose of radiation and has proved to be more effective than either of the two alone. [3] With high cure rates in germinomas, post-treatment quality of life is a growing concern. New endocrine dysfunction after radiotherapy is rare, though patients treated as children may experience neurocognitive issues. [7] However, studies show no significant change in IQ, social, or emotional functioning post-treatment, suggesting that other factors beyond CNS irradiation influence prognosis.

Neurosurgery was initially reserved for large tumours or those causing obstructive hydrocephalus. However, recent advances in neurosurgical techniques have allowed for multiple effective approaches to the tumours, resulting in reduced morbidity and mortality, shorter hospital stays and better postoperative quality of life. Recent developments include a automated deep learning (DL) model trained using machine learning techniques. [9] It can differentiate between different intracranial germ cell tumours based on pretherapeutic T2W MR imaging data. Such advances can reduce delays in diagnosis, improve accuracy and prognosis. [8]

An interesting aspect to consider in this case is the socio-economic factors affecting the patient's disease work-up. The first time she sought care, her family could unfortunately not afford a brain MRI, which led to a delay in diagnosis and appropriate care. Such multifaceted aspects of healthcare ought to also be considered when dealing with rare presentations in the lower-economic strata.

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