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## CASE REPORT

# An Unusual Case of Pure Germinoma in a Patient With Tourette's Syndrome

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## ABSTRACT

***Tourette's syndrome is a rare, neuropsychiatric disorder of complex aetiology. Although the exact mechanism is not completely understood, neuroendocrine dysfunction is related to the pathogenesis of Tourette's syndrome. Clinical characteristics of the disorder, including motor tics and coprolalia, are associated with dysregulation of dopamine, melatonin, acetylcholine and/or endogenous opioids produced in the midbrain and epithalamus. The authors present a case of pure germinoma of the pineal gland with synchronous involvement of the nasal cavity and suprasellar region in a 20-year-old man with Tourette's syndrome. This case report illustrates the theory that alterations in the production and regulation of endogenous hormones produced by the midbrain, pineal gland, and periaqueductal grey matter may be linked to the phenotype of Tourette's syndrome.***

***Key Words:*** *Drug therapy, Germinoma, Pineal body, Radiotherapy, Tourette syndrome*

## INTRODUCTION

Intracranial germ cell tumours are rare neoplasms. Germ cell tumours are more common in children and adolescents than in adults, comprising less than 5% of all primary intracranial tumours.[1] The incidence in the USA is 30 to 40 patients per year.[2]

Germ cell tumours can be subdivided into pure germinomas and non-germinomatous tumours. Pure germinomas account for more than half of all germ cell tumours. Typically, they are well-defined non-infiltrating lesions of the midline intracranial structures, most commonly involving the pineal gland, suprasellar region, or both. Leptomeningeal spread and cerebrospinal fluid (CSF) seeding have been documented in 6% to 14% of patients.[3,4,5] Pure germinomas are extremely radiosensitive in comparison with their non-germinomatous counterparts. Long-term survival rates of 70% to 100% have been reported after radiotherapy.[3,5,6]

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The classic presentation of a pure germinoma is a pineal mass in a male adolescent who has symptoms of precocious puberty, as well as hydrocephalus and visual disturbances. Historically, if a patient had the classic findings, radiation was delivered empirically and histologic confirmation was not routinely pursued. Improved neurosurgical techniques have enabled accurate tissue diagnosis with minimal morbidity. Therefore, biopsy is currently routinely performed at many centres.[7]

Although dopaminergic dysfunction of the midbrain may contribute to the pathogenesis of Tourette's syndrome, its association with pure germinoma is not well characterised in the literature. Tourette's syndrome is a neuropsychiatric disorder that may present in up to 2% of the population.[8,9] The disorder is characterised by hyperkinesia and compulsive behaviour including motor and vocal tics. This report is of an unusual presentation of pure germinoma in a patient with Tourette's syndrome.

## CASE REPORT

A 20-year-old man had a 2-week history of diplopia and blurred vision. Impaired short-term memory, a recent episode of syncope, and a 9-month history of polydipsia were additional concerns. His past medical history was significant for the onset of Tourette's

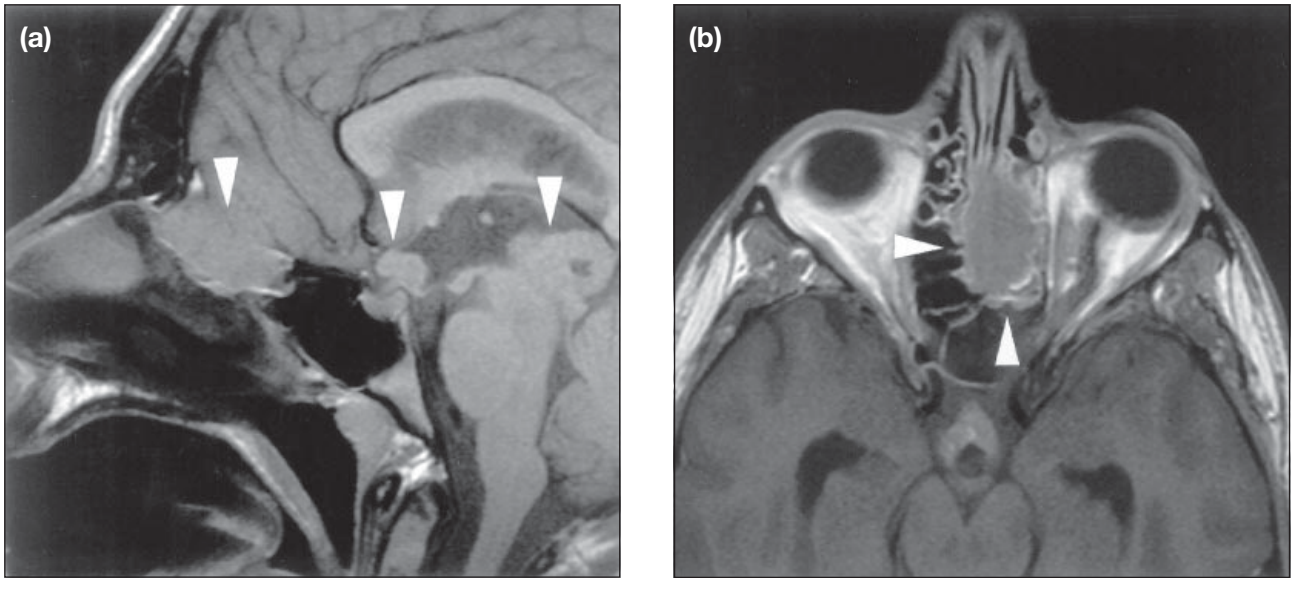


**Figure 1.** (a) Sagittal T1-weighted magnetic resonance imaging of the head demonstrates tumour growth of the pineal gland with spread to the suprasellar region and upper nasal cavity (arrowheads) and (b) axial T1-weighted magnetic resonance imaging of the head shows tumour infiltration into the left nasal cavity (arrowheads).

syndrome at the age of 5 years and recurrent severe epistaxis since the age of 2 years. Computed tomography of the head revealed a pineal mass and obstructive hydrocephalus. Magnetic resonance imaging (MRI) demonstrated an infiltrating tumour of the pineal gland with spread to the suprasellar region and the upper nasal cavity (Figures 1a and 1b). Extensive nodular subependymal spread and infiltration of the walls of the lateral and third ventricles were also present. MRI of the spine revealed subarachnoid spread throughout the spinal axis and evidence of drop metastases (Figure 2). Laboratory studies demonstrated pituitary dysfunction, including central diabetes insipidus, inappropriate antidiuretic hormone secretion, secondary hypothyroidism, low cortisol level, and elevated prolactin level. Examination of the CSF for tumour markers showed a markedly elevated human chorionic gonadotropin level (428 IU/L; normal level in serum, <3 IU/L) and normal α-fetoprotein level.

Endoscopic third ventriculostomy was performed. A transnasal biopsy specimen was obtained endoscopically from the roof of the left nasal cavity where extracranial tumour extension was evident. Histologic evaluation revealed neoplastic cells strongly immunoreactive for placental alkaline phosphatase. Cytology of the CSF demonstrated malignant cells that supported the primary diagnosis of pure germinoma.

Combination chemotherapy with cisplatin and etoposide was initiated. Upon completion of induction

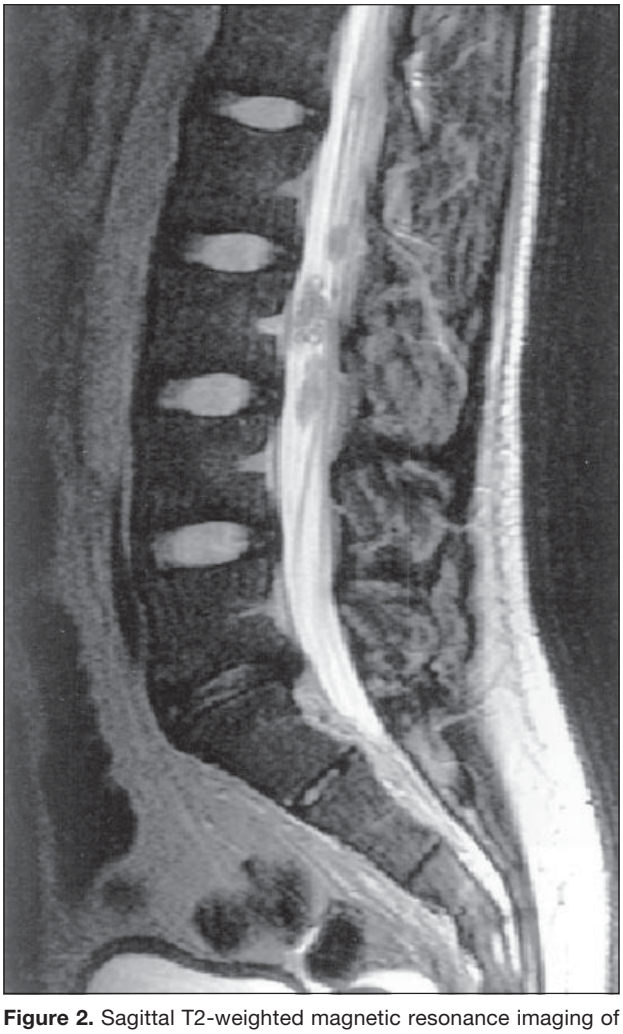

**Figure 2.** Sagittal T2-weighted magnetic resonance imaging of the lumbosacral spine reveals drop metastases within the spinal canal.

chemotherapy, low-dose irradiation was delivered to the craniospinal axis. Follow-up MRI of the brain and spinal axis 1 month after treatment demonstrated a complete response to therapy. The patient's previously stable symptoms due to Tourette's syndrome lessened in frequency and severity by 50% after the initiation of treatment. Follow-up 16 months later revealed no evidence of recurrent disease on MRI and no further change in the tic symptoms since the completion of chemotherapy and radiation.

## DISCUSSION

The differential diagnosis of the described tumour as based on radiographic findings includes esthesioneuroblastoma, pineoblastoma, lymphoma, germ cell tumour, ependymoma, rhabdomyosarcoma, and oligodendroglioma. Germ cell tumours may occur as multiple, synchronous midline masses, particularly in the pineal and suprasellar regions. In this case, extensive parenchymal infiltration and nasal cavity extension were considered atypical for primary germ cell tumour. Although elevated human chorionic gonadotropin in the CSF lent support to the diagnosis of pure germinoma, histologic confirmation was warranted to ensure appropriate therapy was delivered.

The pineal gland is an integral component of the epithalamus and is located in close proximity to critical midbrain structures. The relationship of a pineal tumour with Tourette's syndrome has been previously documented in a patient with a pinealoma.[10] However, the current patient is the only reported instance of pure germinoma associated with Tourette's syndrome. Although it may be reasonable to speculate that tumour compression of the midbrain by a pineal lesion may play a role in the pathophysiology of Tourette's syndrome, the authors recognise that the association of this neuropsychiatric disorder with a structural lesion of the pineal gland may be purely coincidental. In this case, for instance, the patient was diagnosed with Tourette's syndrome many years before he presented with evidence of a structural lesion. Additionally, the pineal tumour responded completely to treatment but there was only a 50% reduction in his tic symptoms.

Nonetheless, neuroendocrine dysfunction of the midbrain structures is likely to be related to the clinical manifestations of Tourette's syndrome. Historically, Devinsky speculated that the pathogenesis of Tourette's syndrome was due to alterations in the regulation of dopamine within the periaqueductal grey and midbrain tegmentum.[11] Pharmacologic interventions lend support to this hypothesis. The administration of dopamine receptor antagonists, for instance, tends to relieve symptoms of Tourette's syndrome, whereas dopamine agonists exacerbate them. Although Tourette's syndrome is presumed to be a predominantly dopaminergic disorder, dysregulation of the endogenous opiatergic, noradrenergic, and cholinergic systems may also play a role in its aetiology.[12,13] It has also been proposed that disturbances in melatonin secretion by the pineal gland are relevant to the pathogenesis of Tourette's syndrome.[14] Thus it appears that current understanding of the sophisticated interplay between hormonal regulation, abnormalities of the midbrain structures, and the clinical manifestations of Tourette's syndrome is lacking. Certainly there is much to be learned about the complex aetiology of this neuropsychiatric disorder.

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