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Case Report

# Case Report of Symmetric Parkinsonism Secondary to a Pineoblastoma

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## Abstract

**Objectives:** In order to identify and classify the types of a secondary Parkinsonism related to intra-axial tumors, a unique case involving a 17-year-old patient diagnosed with pineoblastoma is presented. This case highlights the rare secondary Parkinsonism symptoms associated with intra-axial tumors and emphasizes the need for comprehensive assessment and early intervention in uncommon brain tumor cases. **Material and methods:** A comprehensive literature search was conducted using PubMed, a widely recognized and authoritative database for scientific publications. The search encompassed articles published between June, 01 and July 26, focusing on pineoblastoma-related studies. Inclusion criteria comprised papers reporting clinical cases, diagnostic criteria, and treatment modalities. **Results:** We found the case of an adolescent with headaches, hydrocephalus and parkinsonian symptoms due to a pineal germ cell tumor who was treated with chemotherapy and levodopa/carbidopa resulting in clinical improvement. **Conclusions:** Secondary Parkinsonism due to brain tumors is rare but can mimic idiopathic Parkinson's disease. Delayed diagnosis can lead to severe deficits. Timely imaging and diagnosis are crucial for management.

**Keywords:** Intra-axial tumors, germ cell tumors, pineoblastoma, secondary Parkinsonism, movement disorders

## Introduction

The majority of germ cell tumors originate in the testes, although they can occasionally develop primarily in the retroperitoneum, mediastinum, or extremely rarely, in the pineal gland on the roof of the diencephalon [1]. The primary types of brain tumors that have been reported in conjunction with Parkinsonism include: Meningioma's, Gliomas, Ependymomas, Craniopharyngiomas, pituitary adenomas, and metastases [2]. In the present case, a 17-year-old young male was referred to the esteemed Neurology department subsequent to a thorough evaluation conducted by a distinguished neurosurgeon, who discerned the presence of a pineoblastoma. The patient had been experiencing sporadic frontotemporal headaches, which exhibited a self-limiting and did not appear to be connected to auras or any identifiable triggers. Notably, during the physical examination, apart from the aforementioned headache, the presence of parkinsonism was astonishingly observed, which is typically an uncommon symptom in individuals with brain tumors. It is worth highlighting previous consultations and services consulted before reaching the Neurology department had not, in fact, identified any signs of parkinsonism in the patient, as detecting it symmetrically in individuals with this type of tumors is often a challenging endeavor.

**Narrative:** Germ cell tumors predominantly originate in the testis, although they can sporadically emerge as primary tumors in unusual locations like the retroperitoneum, mediastinum, and exceptionally, the pineal gland, giving rise to extragonadal germ cell tumors. Among the spectrum of brain tumors associated with secondary parkinsonism due to tumor-related effects, diverse

entities emerge, including meningiomas, gliomas, ependymomas, craniopharyngiomas, pituitary adenomas, and metastases. In this context, we present a compelling case study of a 17-year-old male patient, whose clinical journey led him to the Neurology department subsequent to assessment by a neurosurgeon. Remarkably, the neurosurgeon's evaluation unveiled an unexpected pineoblastoma, a rare and aggressive neoplasm arising in the pineal gland. The patient's medical narrative was further marked by intermittent frontotemporal headaches, characterized as self-limited and devoid of associated aura or triggers. Upon physical examination, a noteworthy facet emerged, adding complexity to the clinical presentation: parkinsonism. This motor disorder, often synonymous with neurodegenerative conditions like Parkinson's disease, manifested in the context of a brain tumor an uncommon convergence. Parkinsonism, encompassing a constellation of movement-related symptoms, is an atypical feature in individuals harboring brain tumors, evoking a distinctive clinical scenario.

In summary, germ cell tumors, typically rooted in the testis, can occasionally manifest as extragonadal tumors, triggering intricate clinical presentations. The coexistence of brain tumors and parkinsonism, as witnessed in our 17-year-old patient with a pineoblastoma, underscores the enigmatic interplay between neuro-oncology and movement disorders. This case serves as a poignant illustration of the diverse and intricate manifestations that may arise in the intricate realm of neurological pathology, prompting continuous exploration and understanding.

**Case:** A 17-year-old male patient started with intermittent headaches of one month and a half duration, frontotemporal, self-limited, of variable intensity, predominantly at night, not associated with aura or triggers. On physical examination the data to be highlighted are: fundus with low-degree papilledema Frisen II, visual acuity 20/30 bilateral, last but not least, limitation to supraversion in conjugated gaze. The Magnetic Resonance Imaging (MRI) shows a hyperintense lesion with respect to the surrounding parenchyma in the pineal region (Figure 1), which causes hydrocephalus with dilatation of the third ventricle, as well as the lateral ventricles, with transependymal edema towards the occipital horns, as well as decreased definition of grooves and arachnoid mantle towards the convexity (Figure 2). Therefore, he underwent placement of Ventriculoperitoneal Shunt (VP) + endoscopic fenestration with surgical risk ASA I by the neurosurgery service.

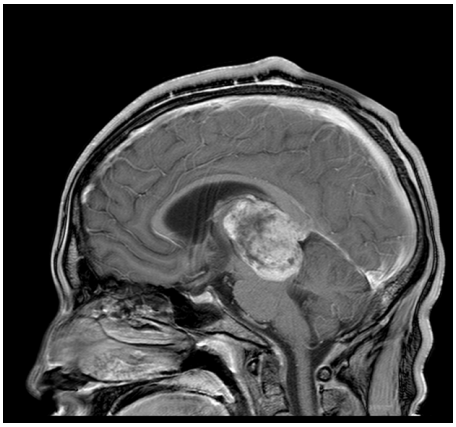

**Figure 1:** Sagittal magnetic resonance imaging in T1 sequence with gadolinium contrast showing a hyperintense heterogeneous lesion in the pineal region.

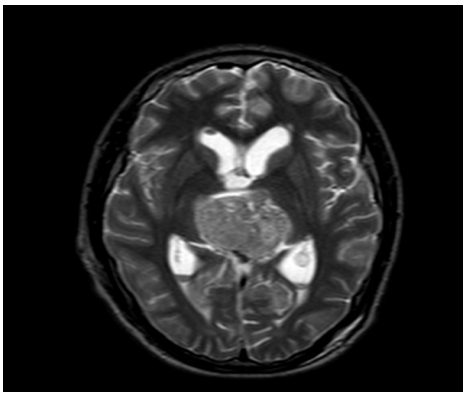

**Figure 2:** Axial T2-weighted magnetic resonance imaging showing an intra-axial brain lesion with dilation of the third ventricle, as well as the lateral ventricles

Upon clinical assessment by the Neurology service, the patient was awake, alert, oriented to person and circumstance, amimia; hyporeflective pupils, on primary gaze left palpebral ptosis was observed with right endotropia; ocular movements with limitation towards supra and infraversion of the gaze; as well as bilateral abduction, decreased bilateral corneal reflex, normal masseter reflex, facial diparesis, bilateral hearing loss, nerves IX, X, XI, XII without alterations. Extremities with symmetrical

mobilization. Muscle stretch reflexes ++/++ in all extremities, absent Hoffman and Tromner signs, left extensor plantar response. Non-assessable gait. He presented global rigidity of all four extremities with the presence of symmetric upper extremities bradykinesia, with rest tremor ++, postural tremor +, without kinetic tremor which meets the symptom of parkinsonism in addition to a total score of 43 pts in Unified Parkinson Disease Rating Scale [3].

The histopathological study reported gliosis and traces of bleeding without evidence of neoplasia. Positive germ cell markers were performed, not seminoma, so it was classified as a non-seminoma stage III extragonadal germ cell pineal tumor (TXNXM 1B) IIIC. Due to the location of the tumor, the oncology service proposes management with systemic chemotherapy with a BEP scheme (Bleomycin, Etoposide and Platinum) with a good clinical response. A testicular USG was performed, in which no apparent alteration was observed. (Figure 3).

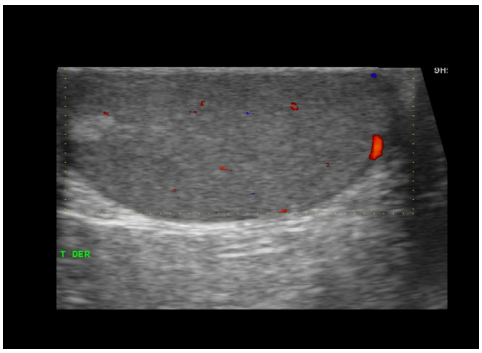

**Figure 3:** Longitudinal gray-scale ultrasonography with internal vascular flow on color Doppler imaging of the right testicle without any mass or abnormality.

After initiating management with low doses of levodopa/carbidopa (62.5 mg TID); the patient presented improvement in parkinsonian symptoms; especially in rigidity.

**Material and methods:** An extensive and thorough exploration of existing scholarly literature was undertaken, employing the renowned and highly regarded PubMed database renowned for its credibility in the realm of scientific publications. This meticulous search encompassed a time frame spanning from the first day of June to the twenty-sixth of July, with a deliberate concentration on studies directly associated with pineoblastoma. The established parameters for inclusion in this analysis consisted of scholarly papers that elucidated clinical cases, delineated diagnostic criteria, and expounded upon various approaches to treatment.

**Results:** The study encountered a complex medical case involving an adolescent who presented a constellation of symptoms, including recurrent headaches, hydrocephalus, and clinical manifestations reminiscent of Parkinson's disease. The symptoms of secondary parkinsonism in this case were unusually peculiar and included bradykinesia, rigidity and resting tremor. Upon investigation, these symptoms were attributed to the presence of a germ cell tumor situated within the pineal gland. In response to this challenging scenario, a comprehensive therapeutic approach was carefully crafted. This multifaceted strategy encompassed the administration of chemotherapy, complemented by medication containing levodopa/carbidopa. The implementation of this combined treatment regimen yielded substantial improvements in the patient's clinical condition. These results underscore the remarkable effectiveness of this therapeutic approach when applied to similar cases within this particular clinical context.

## Discussion

The discussed case revolves around a young patient who displayed clinical signs that resembled those of Parkinson's disease. A comprehensive treatment approach was employed, which included chemotherapy and the administration of levodopa/carbidopa medication. This combination of therapies resulted in a significant improvement in the patient's clinical condition, demonstrating the effectiveness of this therapeutic strategy in similar cases.

Existing literature has reported instances where parkinsonism, a neurodegenerative disorder characterized by motor symptoms like tremors and rigidity, can be triggered by several mechanisms. One such mechanism involves the direct compression of critical brain regions, including the basal ganglia and midbrain, by tumors [4]. Additionally, parkinsonism can be induced indirectly when a herniated temporal lobe exerts pressure on these specific brain structures, or when tumors cause the displacement of the brainstem [5].

It's worth noting that the majority of cases of secondary parkinsonism are associated with extra-axial tumors, which means that the tumors develop outside the brain's neural tissue. Among these, meningiomas, a type of tumor arising from the meninges (the protective membranes surrounding the brain and spinal cord), are the most frequently observed culprits [6]. Nevertheless, it's important to highlight that instances of intra-axial tumors, meaning tumors originating within the neural tissue and affecting the basal ganglia or midbrain directly, have been rarely documented in the available scientific literature [6].

In this patient the entity was a non-germinoma pineal tumor which usually requires surgical resection, chemotherapy, and radiation with the exception of mature teratomas; frequently curable with surgery alone. Germinomas have a favorable prognosis with a greater than 90% overall survival, while non-germinoma tumors only have survival rates ranging from 40–70% [7].

Benign lesions arising within the pineal gland that can be mistaken for neoplasms include pineal cysts, vascular malformations, and vein of Galen aneurysms [8]. Parkinsonism resulting from intracranial tumors typically falls into a category known as akinetic-rigid syndrome. This form of parkinsonism often does not show a positive response to levodopa treatment and is characterized by unilateral symptoms, alongside neurological deficits such as impaired eye movement, pyramidal signs, and issues with cerebellar function [9]. In our patient, the primary distinguishing feature was the presence of pure bilateral parkinsonism without any accompanying neurological abnormalities, setting it apart from other forms of secondary parkinsonism.

Parkinsonism is a clinical syndrome presenting with a combination of bradykinesia with resting tremor or rigidity. The most common form of parkinsonism is Parkinson's Disease (PD), a chronic and progressive condition resulting from the gradual degeneration of dopaminergic neurons in the brain. Clinically, it is identified by the presence of asymmetric parkinsonism [10,11]. Bradykinesia is described as reduced movement speed, often accompanied by a decrease in the size or speed of movements, as well as gradual pauses or interruptions during continued movement. Rigidity refers to resistance against passive movement of major joints, which is not dependent on movement speed, while the patient is in a relaxed state. Resting tremor is a tremor with a frequency of 4 to 6 Hz observed in a limb when it is completely at rest and stops when movement is initiated [12].

Unlike neurodegenerative parkinsonism, which is often characterized by the aggregation of specific proteins, most secondary or symptomatic forms of parkinsonism, with the exception of chronic traumatic brain disease, do not exhibit a propensity for protein aggregation [6,13,14]. Among the patients studied by Polyzoidis et al. up to 1985, it was observed that 42 out of 49 individuals with parkinsonism induced by a tumor had tumors located supratentorially with basal ganglia involvement, while the remaining seven cases were associated with tumors affecting the substantia nigra [6,15].

In patients with brain tumors, parkinsonism can occur, particularly when the tumors infiltrate or exert pressure on the midbrain. It's important to note that this symptom is relatively uncommon among individuals with brain tumors. Most cases linking tumors to parkinsonism involved meningiomas as the most prevalent, followed by gliomas. In contrast, ependymomas, craniopharyngiomas, pituitary adenomas, and metastases appear to be less frequent causes of this condition [16,17] (Figure 4).

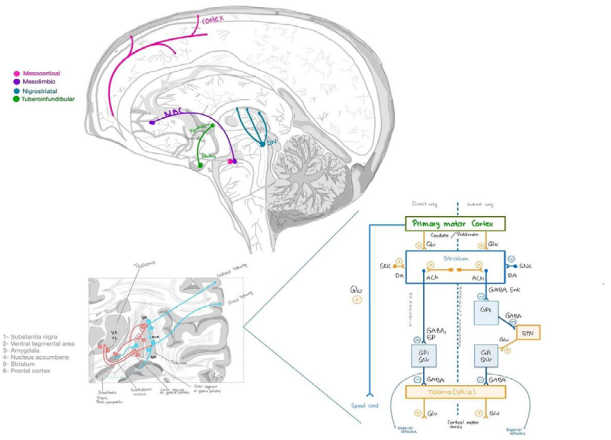


**Figure 4:** Via cortico-thalamic-striatal pathway. It begins in the regions of the cerebral cortex that are related to the control of movements (supplementary motor area, premotor cortex, motor cortex, somatosensory cortex) and goes to the motor portion of the putamen in the form of a topographically organized pathway. From the putamen exit pathways to the globus pallidus, the substantia nigra, the subthalamic nucleus, and the thalamus. From this nucleus (anterior ventral and lateral nuclei of the thalamus) the circuit returns to the supplementary motor area and the premotor area. There is thus defined a feedback organization in this circuit.

The three primary histologic tumors that predominantly occur in the pineal gland are germ cell neoplasms. While most of these tumors originate in the testis, they can occasionally arise primarily in the retroperitoneum, mediastinum, and, very rarely, within the pineal gland itself; this is referred to as extragonadal germ cell tumors. Typically, these tumors are categorized based on the specific cell types they derive from, including seminoma (constituting 40-70% of cases) and non-seminoma tumors, which encompass embryonic cell carcinoma (15-20%), teratoma (5-10%), and choriocarcinoma (less than 1%) [18].

## Study Limitations

Follow-up was challenging due to scheduling appointments activities in both neurology and oncology services. The reasons behind the lack of postoperative imaging remain somewhat unclear including the patient's financial situation and the high demand of the hospital consultation. It is known that the patient was discharged by the oncology service, where they received outpatient chemotherapy and radiotherapy as part of their treatment plan. However, during the hospital stay, the patient exhibited improvement in the mentioned parkinsonian symptoms

after being evaluated and treated by the neurology service. Gathering additional information from the patient after discharge was complicated due to these circumstances.

**Clinical Implications**

Understanding the clinical implications of our findings is crucial for guiding medical practices and clinical decision-making. Based on the results of this study on pineal gland tumors, we can highlight the following clinical implications:

1. Early diagnosis and personalized treatment: Prompt recognition of pineal germ cell tumors is vital for tailoring effective treatments based on histology, improving patient outcomes. Physicians should consider the possibility of these tumors when evaluating patients with movement disorders and perform appropriate diagnostic tests such as brain magnetic resonance.
2. Long-Term monitoring: Patients require ongoing surveillance to detect recurrences and late treatment effects, ensuring continued care.
3. Interdisciplinary collaboration: Collaborative efforts among specialists, including neurosurgeons and oncologists, are crucial for comprehensive and personalized treatment plans.
4. Further research: Continuous research is needed to enhance understanding of tumor pathogenesis and develop more effective therapeutic strategies.

**Recommendation for future research**

Neurological impact and functional outcomes: Future research should delve into the neurological impact of pineal germ cell tumors and assess long-term functional outcomes in patients following different treatment approaches. This includes paying special attention to potential movement disorders that may arise as a result of these tumors. Understanding the neurological consequences and functional recovery can aid in optimizing neurosurgical and neurorehabilitation strategies for these patients.

**Conclusion**

In summary, pineal germ cell tumors pose significant challenges in both clinical and neurological contexts. Understanding their neurological impact and the potential presentation of parkinsonian symptoms, whether symmetric or asymmetric, is of paramount importance. This clinical manifestation may resemble idiopathic Parkinson's disease, emphasizing the need to consider the possibility of secondary parkinsonism, especially in young patients with evidence of intracranial lesions, notably intra-axial brain tumors.

Failure to suspect secondary parkinsonism may result in diagnostic delays and subsequent development of more severe permanent neurological deficits. It is imperative to underscore that, despite the rarity of secondary parkinsonism due to brain tumors, a timely and accurate diagnosis plays a pivotal role in managing and prognosticating this complex pathology. Conducting imaging studies and histopathological identification are critical components to ensure appropriate care and enhance the quality of life for affected patients. Encouraging future research efforts that focus on evaluating long-term functional outcomes, with special attention to neurological aspects and potential movement disorders, is imperative. This approach will contribute to advancing the understanding and management of this intricate clinical condition.

**Author Contribution**

We confirm that all authors contributed equally and significantly to the conception or design of the work, the acquisition, analysis, and interpretation of data. They either drafted the article or provided critical revisions for important intellectual content. The final version for publication was collectively approved. Each author participated sufficiently and takes public responsibility for the relevant content.

**Ethical Considerations**

A written informed consent was obtained from the patient's nearest relative by their next of kin, with the understanding that there would be no recognition or compensation provided, and that all their data would be kept completely anonymous, for the publication of this case report and any accompanying images.

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**Conflict of interest**

The authors wish to clarify that there are no conflicts of interest to be disclosed concerning the research, the article, or its publication. They have no financial, personal, or professional affiliations that might impact or introduce bias to the content of this study or its presentation in any manner.

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