Pineal Body Tumor: An Overview of the Pathophysiology

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Authors’ contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJMAH/2022/v20i1030507

Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/88634

Received 27 April 2022
Accepted 03 July 2022
Published 06 July 2022

ABSTRACT

The pineal gland is a small endocrine gland in the brain that regulates the circadian rhythm in humans. It is responsible for melatonin production, also produced by parenchymal and glial cells. Pineal region tumors account for 3–11% of pediatric brain tumors, and 1% of adult brain tumors according to World health Organization (WHO). These tumors arise from the germ cells, pineal cells, and adjacent structures. It is fundamental for medical knowledge (clinical and laboratory) to differentiate and identify the various types of pineal gland tumors and thus facilitate accurate diagnosis with crafted therapeutic management of the pathology accompanying its incidence. There exist different histological subtypes of pineal body tumors and various management options like surgery, chemotherapy and radiotherapy. The review article is a student’s project on integrated learning, aiming at understanding the pathophysiology of the rare pineal body tumor.

Keywords: Brain neoplasm; pineal body tumor; pineoloma; pineal gland; pineocytoma; melatonin.

1. INTRODUCTION

Pineal body is part of the circumventricular organ of the brain that produces melatonin, an endocrine hormone responsible for the regulation of sleep-wake pattern (Circadian rhythm) in humans [1]. In the pineal gland, information on environmental lighting conditions that is encoded by the retina is responsible for the synthesis of melatonin at night involving both biochemical and
neuronal input. It is evident that pineal body may harbor neoplastic growth which can be primary or secondary (rare) metastatic lesions. Tumors are generally rare in the pineal gland [1,2].

Pineal body tumors are rare brain tumors accounting for approximately 3–11% of pediatric brain tumors and approximately 1% of adult brain tumors. They are mostly asymptomatic, but few symptomatic ones are usually mild and there are reported cases of aggressive subtypes.

The management of Pineal gland tumors are generally less discussed in most literatures because of the rarity. There exist a few histopathological subtypes of primary pineal body tumors with varying level of differentiations, thus requiring a multi-disciplinary approach in the management [3,4]. There is evidence of varying response to therapy depending on multiple factors with fairly good prognosis for some of the subtypes [4,5].

2. EMBRYOLOGY AND ANATOMY

The pineal gland begins as an evagination in the diencephalic roof of the ventricle prenatally and flanked by posterior and habenular commissures below the splenium of the corpus callosum. It continues to grow after birth in response to rhythmic sympathetic innervation from the superior cervical ganglia [1,2,3].

Anatomically, the gland is described as a pinecone shaped, a neuroendocrine gland part of the thalamus. The structure connecting to the pineal and dorsal suprapineal recesses with anatomic boundaries that include the posterior wall of the third ventricle forming the gland’s base, the splenium of the corpus callosum superiorly, and the thalamus surrounding both sides [4]. The gland calcifies with age, with most of its cells comprising pinealocytes.

3. PHYSIOLOGY

In lower vertebrates, the pineal gland participates in the biological circadian rhythm by receiving information through its light-sensitive cells, with its primary responsibility being the production of Melatonin. However, in higher vertebrates, light is picked up by the eye’s retinal cells, which transports this information to visual and non-visual areas of the brain, the pineal being one of such areas. The gland works hand in hand with the suprachiasmatic nucleus (SCN), which secretes GABA if the light signal is positive, inhibiting melatonin synthesis. When there is no light signal, the SCN secretes glutamate, driving paraventricular nucleus (PVN) transmission to the pineal gland. The PVN also communicates with the superior cervical ganglion that acts on the pineal gland through sympathetic fibers releasing norepinephrine (NE). The presence of NE is a major trigger for the pinealocytes to synthesize and secrete melatonin [6]. There are documented studies showing that in blind subjects, melatonin secretion occurs through independent rhythm [7].

The precursor of melatonin is tryptophan, which is hydroxylated inside the pinealocytes to 5-hydroxytryptophan (5-HT). The aromatic L-amino corrosive decarboxylase then decarboxylates 5-hydroxytryptophan into serotonin. Serotonin then, at that point, gets changed into melatonin due to the methyltransferase-0-hydroxy-indole protein (HIOMT) [8,9]. This biochemical response chain suggests the presence of N, N-dimethyltryptamine (DMT) in pinealocytes.

![Fig. 1. Melatonin biosynthesis.](https://www.researchgate.net/figure/SYNTHESIS-IS-OF-MELATONIN_fig1_6198068)
4. PATHOLOGY

Pineal gland tumors are remarkably uncommon cancers, predominantly occurring as childhood malignancies representing 3–11% of all pediatric brain tumors compared to <1% of brain tumors in adults [4]. Another study demonstrated that the pineal body tumors represent 1.5 to 8.5% of the pediatric brain tumors and 1.2% of all brain tumors [10]. A study analyzed 633 patients with pineal gland tumors between 1973-2005 showed predominance in males (3–11.8:1) for those with a germ cell tumor variant. The cohort’s 5-year overall survival (OS) was 65% ± 2.1%. Those with germ cell tumors experienced the best survival (OS = 78.9% ± 2.3%), followed by those with gliomas (OS = 61% ± 9.3%), and those with pineal parenchymal tumors (OS = 47.2% ± 4.2%) [11].

The pineal gland tumors are grouped as germ cell tumors (germinoma, choriocarcinoma, teratomas, yolk sac tumors), pineal parenchymal tumors (pineocytomas, pineoblastomas), and tumors derived from structures adjacent to the gland (Fig. 2).

Practically speaking, the determination of pineal gland neoplasms depends on the clinical features, imaging study, and histopathology results. Serum and cerebrospinal liquid (CSF) biomarkers supplement these standard indicative strategies by giving extra information before intrusive techniques are performed. This review will explore the clinical features and relevance of the main pineal gland tumors, highlighting the importance of triggering causes of the masses and effective primary diagnosis with subsequent management.

4.1 Germ Cell Tumor

Germ cell tumors are derived from primordial germ cells that, although developed primarily in the gonads, can migrate to the pineal gland, mediastinum and other part of the brain. These tumors are commonly found in male patients and accounting for about 50% of germ cell tumors in the brain, seemingly more common in Asian populations [12]. There are six types of germ cell tumors: germinomas, choriocarcinomas, teratomas, embryonal carcinomas, yolk sac tumors, and mixed germ cell tumors.

4.1.1 Germinoma

Germinomas are the most common pineal gland tumor type, accounting for almost 50% of pineal body tumors in Europe, United States, and Asia (Japan). Germinomas are not encapsulated and find it easy to invade adjacent brain structures while also disseminating along the brain surface through the CSF. Histology reveals homogenous germinoma cells with large round nuclei, prominent nucleoli, clear cytoplasm with connective tissue septal bands, capillaries and lymphocytes proliferation and, infrequently, granulomas [12, 13]. Germinomas showing heterogeneous features on imaging, are usually appearing as solid or solid/cystic masses with calcifications. Imaging alone is not sufficient in distinguishing between the tumors; therefore, a complete and thorough evaluation is needed. Germinomas diagnosis are aided using serum and CSF markers with the expression of oncoproteins like alpha-fetoprotein(AFP), lactate dehydrogenase(LD), and beta-human chorionic gonadotropin(beta-hCG) [14].

Fig. 2. Pineal tumor classification
Source: https://www.mdpi.com/2072-6694/13/7/1547/htm
Furthermore, corticosteroid treatment seems to be able to modify the patient’s immunological defense, empowering the immune system to suppress cancer.

4.1.2 Choriocarcinoma

Choriocarcinomas are relatively uncommon neoplasms, they have the most aggressive (anaplastic) form of gestational trophoblastic disease (GTD). They have a very poor prognosis concerning other germ cell tumors.

Young men (3–22 years old) with premature puberty are more likely to develop primary cerebral choriocarcinoma. There may be reports of headaches, nausea, vomiting, visual impairment, polydipsia, polyuria, and rarely endocrinological manifestations [15, 16]. Syncytiotrophoblasts and cytotrophoblasts characterize the histology without forming definite placental type villi. On imaging, choriocarcinomas may appear as ovoid, heterogeneous, and slightly hyperdense tissues/masses. Choriocarcinomas can be linked with elevated plasma and CSF human chorionic gonadotropin levels.

4.1.3 Teratomas

Teratomas (Intracranial) account for up to 50% of fetal brain neoplasms, comprising 33% of intracranial tumors in neonates, but only 2%–4% of intracranial tumors in patients aged <15 years [17]. Teratomas are histologically classified as mature (cystic), immature, and teratomas with malignant transformation. This tumor is made up of multipotential cells that can transform to normal organ-producing mechanisms, usually producing tissues that showcase two or more layers of germ cells (ectoderm, mesoderm, and endoderm). Teratomas can be encapsulated or not capsulated (invasive) [18].

These pineal tumors present with foci of fat, calcification, and cystic (and non-cystic) regions on imaging.

4.1.4 Pineal Parenchyma Tumors (PPD)

Pineal parenchymal tumors (PPD) are neuroepithelial-derived neoplastic tissues emerging from pinealocytes. These growths are phenomenal, representing less than 1% of all primitive central nervous system cancers and comprising 15% to 30% of pineal gland tumors. These tumors present with varying and distinct features, tumor grades, and levels of invasiveness. The World Health Organization (WHO) recognizes pineal parenchymal tumors in four distinct categories (see Fig 6) namely: pineocytomas, pineoblastomas, papillary pineal tumors, and pineal parenchyma tumors of intermediate differentiation [19].

Pineal parenchyma tumors are highest in children with no sexual predominance [20]. PPTs are negative for the three most commonly evaluated tumor markers (AFP, b-HCG, ALP).
4.1.5 Pineocytomas

Pineocytomas are slow-growing low grade I neoplasms that are histologically characterized by benign-appearing cells (uniform size and intact membrane) and the presence of neurocytic rosette. On gross pathology, pineocytoma is characterized by solid, sometimes with focal areas of cystic change, gray, well-circumscribed mass with or without hemorrhage [21]. Pineocytomas may be seen in all age group, but have higher frequency in adults aged 30-60 years.

4.1.6 Pineoblastomas

Pineoblastomas are aggressive, grade IV neoplasms derived from the neuroectoderm. They are undifferentiated embryonal tumors with poor prognosis and sometimes clinically aggressive due to the invasion of adjacent structures and metastasis to the ventricular system (CSF) [22]. Incidence is highest in children under two years, where retinoblastomas can also be combined with pineoblastomas [23].
Fig. 6. Classification of CNS tumors
Source: WHO (2021)

Pineoblastomas and can be detectable in the serum or CSF [4]. Pineoblastomas are histologically characterized by hypercellular appearance, packed small round blue cells (which indicates a high nucleus to cytoplasm ratio), Homer-Wright rosettes, and oval, angulated nuclei with atypia. Gross pathology reveals solid, large, poorly defined masses.

4.1.7 Papillary tumors

Papillary tumors are rare grade I or II tumors that occur within a broad spectrum of patients with the age of patients presenting with papillary tumors ranging from 1 year and 3 months to 67 years with higher female prevalence [24]. The major clinical manifestation of this condition is headache related to obstructive hydrocephalus. Histological examination shows distinct solid finger-like growth patterns with a lining of the papillae by multi-layered cuboidal to columnar cells, distinct perivascular rosette, and foci ependymal formation (true rosette). Cells may have moderate amounts of eosinophilic, non-fibrillary cytoplasm, and ill-defined borders, with large pleomorphic nuclei displaying a dense chromatin pattern and occasionally prominent nucleolus. A lot of apoptotic structures can also be seen [25,26].

Fig. 7. Pineocytoma H&E stain showing moderate cellularity with low mitotic rate and pseudo rosettes
Source: The ISPN Guide to Pediatric Neurosurgery
Pineal papillary tumors often present with increase proliferative activity (Ki67/MIB1 proliferation index) [27], in which the presence is synonymous with a poor prognosis. Immunohistochemistry of papillary tumors (Pineal) are also positive for CAM 5.2, prealbumin and S100 [26,27].

Pineal parenchymal tumors of intermediate differentiation are often considered as a part of spectrum of grade II and III pineal parenchymal tumors [28,29]. Although there is yet to be a grading criterion for differentiating PPTIDs. The WHO classification of CNS tumors considers that an approach to classification/stratification adopted by Jouvet et al. based mainly on two criteria, mitoses index and immunoreponse to neurofilament protein, with less immunoreponse in higher grade tumors [5]. PPTIDs show moderate cellularity, mild-moderate atypical nuclei, low-moderate mitosis, occasional Homer Wright rosettes, lack of small, primitive appearance, and necrosis.

Fig. 8. Pineoblastoma H&E stain showing a sheet of small round blue cells tightly packed with nuclear atypic and frequent mitotic figures
Source: The ISPN Guide to Pediatric Neurosurgery

4.1.8 Pineal parenchymal tumors of intermediate differentiation [PPTIDs]

These are rare tumors that present features found in pineocytomas and pineoblastomas [28]. It can be seen in any age and commoner in women, teenagers, and middle-aged patients.

4.2 Pineal Metastasis

Metastatic cancer of the pineal tumor is highly uncommon and is almost always associated with lung carcinoma. This usually occurs in end-stage of the disease, and treatment of pineal gland metastases depends on the type of tumor, systemic conditions, and presenting neurological symptoms [30].
Fig. 10. Pineal Parenchymal Tumor of Intermediate Differentiation with presence of small rosettes (grade II-III)

Source: WHO

Fig. 11. Pineal metastasis from lung adenocarcinoma. Brain MRI sagittal (A), coronal (B), and transverse (C) sections show the pineal gland metastatic mass. Computed tomography shows a lung nodule over the left hilar region in the lower right corner (D). Image from Abdallah et al. (2020)-Ochsner Journal
5. CLINICAL MANIFESTATIONS

The clinical complications resulting from pineal gland tumors are related to the gland’s anatomy and histology.

Migraines, nausea, and vomiting caused by aqueduct of Sylvius compression leading to obstructive hydrocephalus with raised ICP. Hydrocephalus that is left untreated may lead to lethargy, altered sensorium, and death. Visual changes occur due to the involvement of the rectal region (a region responsible for dictating eye movements). Diplopia is a common feature, along with difficulty in accommodation [20,31,32].

Parinaud Syndrome is compression of the superior colliculus and pretectal area or tumor invasion, resulting in a syndrome of vertical gaze palsy associated with pupillary or oculomotor nerve paresis, pupillary light-near dissociation, lid retraction, and convergence-retraction nystagmus (Collier's sign) [30,33].

Ataxia and dysmetria are motor neurons impairment results from compression of the cerebellar efferent fibers (superior cerebellar peduncle) [33].

Pseudo precocious puberty caused by beta-human chorionic gonadotropin (b-hCG) can be seen in germ cell tumors (Pineoloma) in the pineal body or suprasellar region [33]. Hormonal disturbances lead to secondary amenorrhea and growth arrest. Children with pineal region tumors can present with hormonal malfunctions, hydrocephalus or concurrent suprasellar tumors leading to diabetes insipidus [31]. Pineal apoplexy (bleeding into the tumor area of the pineal gland) is a rare but possible manifestation [34,35].

The relative 5-year survival rate for pineal region tumors is 69.5%. There are many factors that can affect the prognosis and these factors include the tumor grade and type, cancer traits (phenotypes), age and general health status (presence of co-morbidity) when diagnosed, and general response to treatment. Talk to your doctor if you want to understand your prognosis [4,36,37].

6. DIAGNOSTIC MODALITIES

Diagnosis is based on the following:

Clinical presentations (outlined in presenting signs and symptoms), Magnetic Resonant Imaging study (MRI), Excisional biopsy and molecular/histopathological analysis.

Serum and CSF biomarkers complement the above standard diagnostic techniques [34,38,37].

Stepwise Pineal mass workup presently entails imaging which is followed by serum and CSF laboratory workup for germ cell tumor markers. The common markers are alpha-fetoprotein, β-hCG, and placental alkaline phosphatase. They are somewhat helpful for diagnosis but are more helpful for monitoring response to therapy [37]. The presence of biomarkers, in conjunction with clinical and radiographic evidence of a pineal region tumor, may help in making decision to either undertake stereotactic biopsy, surgical excision or whether to proceed straight to medical treatment [37,39].

Comparing CSF and serum β-hCG levels is a crucial step in the management of a pineal tumor. Patients with metastatic disease do not benefit from resection of the primary tumor [40]. Endoscopic biopsy offers another means of obtaining tissue for diagnosis without open resection and can be used as an alternative to stereotactic biopsy, depending on the physician’s level of expertise [41,42,43,45]. Endoscopic tumor biopsies are safe as a minimally invasive procedure, and highly effective strategy for the initial treatment of pineal body tumors. The procedures help in making definitive tissue diagnosis and provide a tentative solution to the hydrocephalus frequently encountered in patients with Pineal body tumor [44,45,46].

Surgical resection without tissue biopsy would expose many patients to unnecessary risk. Primary biopsy of pineal lesions should precede attempted surgical resection in children because a third of patients need surgical resection once the histological diagnosis is confirmed. The inability to control bleeding and limited tissue sampling are the limitations of endoscopic technique.

Studies have reported up to 94% yield, although many patients may require a second procedure [42]. A single burr hole for endoscopic third ventriculostomy and an endoscopic biopsy of the pineal region is usually impossible because of anatomic considerations.
7. MANAGEMENT

7.1 Tumor Resection

Microsurgical excision is still the basis of treatment for most pineal area malignancies today except Germ cell tumor [43]. Pineal region tumors surgical management comprise various microsurgical and endoscopic options, with benign pineal tumors curable with surgery alone.

Evidence suggests that surgical debulking may improve the response to postoperative adjuvant therapy in patients with malignant tumor components. Gross complete tumor excision also offers the neuropathologist adequate tissue specimens for diagnosis. This avoids the concerns of sampling mistakes and incorrect diagnosis that stereotactic biopsy can cause due to the little volume of tissue available.

Malignant pineal body tumor Patients presenting with hydrocephalus and radiographic evidence of the disease may have their hydrocephalus treated with a third ventriculostomy or ventriculoperitoneal (VP) shunt before biopsy or resection. The staged procedure allows for definitive control of the hydrocephalus before surgical resection [46].

7.2 Radiotherapy

Radiotherapy is being used to treat malignant pineal area tumors in children over three years. Early clinical trials of radiation patients revealed considerable mortality. Low doses radiation can have long-term effects on a cognitive development especially in children. Radiation-induced complications are important considerations because many children with pineal body tumors have good prognosis [31, 29].

Although the advent of more sophisticated surgical procedures inspires a periodic renewal of enthusiasm for extirpation, radiotherapy remains the approved primary care treatment for pinealoma and ectopic pinealoma [44]. In most published series, germinomas are among the most radiosensitive cancers, with patient response rates and long-term tumor-free survival rates above 90%. Conventional radiation therapy alone can cure pure germinomas, which are highly radiosensitive. Malignant tumors should be treated with aggressive resection followed by radiation and chemotherapy [45,47].

Equally complex are the treatment options with microsurgery as the standard modality, but stereotactic radiosurgery, an alternative and adjunctive treatment to surgery for selected cases, also holds promise. Patients with malignant and/or residual grade II/grade III tumor benefit from adjuvant therapy after surgery. Intensive multimodal adjuvant therapy is recommended for patients with evidence of neuraxial dissemination, and prophylactic multimodal adjuvant therapy is recommended for all patients with PB and PPTIDs [46].

7.3 Surgical Therapy

The literature has thoroughly argued the pros and cons of performing a biopsy versus an open operation for a pineal tumor. The choice of procedure to be done is based on physician/surgeon’s skills and distinct
advantages and disadvantages exist for each procedure.

7.4 Chemotherapy

Chemotherapy has emerged as a promising way to adequately decrease the quantity of radiation required to treat children with pineal tumors. Chemotherapy response for patients with pineal area tumors varies according to tumor histology, just like radiation. Pineal cell cancers have traditionally been more resistant to chemotherapy than germ cell tumors [40].

Patients with pineal gland tumor can be given platinum-based regimens, where response rates for germinomas and non-germinomatous germ cell cancers have ranged from 80 to 100%. Nongerminomatous (extracranial) germ cell tumors respond well to treatment with various chemotherapeutic agents.

Some regimens have shown response rates as high as 78 percent in patients with nongerminomatous germ cell tumors.

The Einhorn regimen, which comprises cisplatin, vinblastine (Oncovin), and bleomycin and later swapped VP-16 for vinblastine (Oncovin) and bleomycin. The latter has shown some promise. Numerous studies are underway to determine the best adjuvant therapy sequence for children with non-germinomatous germ cell tumors. The children are now undergoing chemotherapy before receiving radiation treatment [37, 39].

The success of radiotherapy in treating germinoma has precluded extensive consideration of chemotherapy as a first-line treatment in older children. Chemotherapy should be considered as the first-line treatment only in very young children [47]. Chemotherapy before radiation is advocated by some authors to reduce radiation exposure and associated morbidity.

Patients with recurring or metastatic germinomas, most clinicians now recommend a variant of the Einhorn regimen as an alternate treatment. After diagnosing nongerminomatous germ cell tumors, some doctors recommend chemotherapy and radiotherapy. Children with nongerminomatous germ cell tumors who were treated with radiation alone had a 5-year survival rate of 30-65%, which prompted the introduction of chemotherapy to these patients [47].

The effectiveness of chemotherapy treatments for children with pineal cell tumors has only been described in anecdotal case reports and small case series. Treatment regimens have included various combinations of vincristine, lomustine, cisplatin, etoposide, cyclophosphamide, actinomycin D, and methotrexate [39].

High-dose cyclophosphamide has been advocated in some quarters as a single-agent protocol for treating pineoblastomas, with evidence of stable or declining illness, according to a report by Ashley and colleagues. The adverse consequences were pulmonary dysfunction and thrombocytopenia.

8. COMPLICATIONS

Extraocular movement dysfunction, ataxia, and altered mental status are the most commonly seen following surgery on Pineal gland tumor regardless of the skills and techniques [48]. Neurologic symptoms, such as extraocular movement dysfunction and ataxia, are present before surgery and progressively worsen before improving or resolving completely. Treatment with radiotherapy in the past, significant preoperative neurologic deficiency, malignant tumor (Anaplasia) and stage of the tumor are all factors that are linked to an increased risk of surgical complications.

The most devastating postoperative complication of pineal region tumor is hemorrhage usually into a sub resected tumor bed. Pineal cell tumors are vascular tumors and are mostly associated with hemorrhage after surgery, which can be early or delayed for several day. Another serious consequence is venous infarction, which can occur with or without bleeding. Malfunction shunts, bleeding during the third ventriculostomy following fenestration of the third ventricle floor, ventriculostomy closure, and aseptic meningitis are less common postoperative complications. Seizures, hemianopsia, and hemiparesis are possible side effects of supratentorial methods.

Hypothalamic and endocrine dysfunction, cerebral necrosis, secondary tumorigenesis, and disease progression are possible complications. 35 cases of radiation-induced meningioma have been reported in children after radiotherapy for pineal region tumors since 1953. A known standard radiotherapy protocols for malignant pineal cell tumors in pediatrics is the use of 4000 cGy (whole-brain radiation) which is followed by
1500 cGy to the pineal region. The daily dose of 180-cGy daily fractions is administered [47,49].

Whole-brain radiation can cause significant damage to the body especially in prepubescent patients, limiting the recommended initial extended field to 2500-3000 cGy. An additional dose specific for the tumor bed can be administered afterwards. Several studies show that individuals who receive less than 5000 cGy are more likely to have a recurrence, implying this is the ideal total dose of radiation [47]. The typical treatment pediatrics is focused irradiation, then followed by ventricular field radiation. The histology of the tumor being treated determines how radiation is used [4,49].

The use of prophylactic radiotherapy for the spine is controversial. Reports demonstrating that drop metastases in the spine are generally low have precluded early recommendations for postoperative spinal irradiation. The likelihood of a pineal tumor metastasizing to the spine varies depending on the tumor's histology. Pineoblastoma has higher spinal seeding to the spine compared to pineocytoma, with overall estimate incidence of seeding of pineal body tumor to the spine is 10 to 20%.

9. CONCLUSION

Pineal body tumors are rare group of brain tumors commoner in children with varying degrees of manifestations. Confirmation of the definitive diagnosis of pineal body tumors often involve multiple investigative procedures employed over the years. However, it is established that in order to confirm the incidence of pineal body tumor inclusion of the patient’s clinical presentations, combined with investigations like MRI, CT scans, and pathological biopsy are essential. An increase in alpha-fetoprotein (AFP) and Beta-human chorionic gonadotropin hormone in either serum or CSF will aid the diagnosis of a secreting tumor. It is advisable that once the histological diagnosis is confirmed with a primary biopsy of pineal body lesion in children, surgical resection should follow [30,42,49].

It has been established that endoscopic tumor biopsies are considered safe and minimally invasive, thus an effective strategy for the initial treatment of pineal gland tumors. Furthermore, benign pineal tumors can be cured with surgery intervention alone, while irradiation and chemotherapy will be effective for malignant pineal tumors.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/88634