

## Pineal region tumors: A retrospective analysis

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### Abstract

Pineal region tumors are rare comprising 0.4% to 0.1% of all primary tumors of the central nervous system<sup>1,2</sup> and constitute 3% to 11% of childhood brain tumors.<sup>3-5</sup> These tumors are classified into tumors of germ cell origin, which clearly account for the majority of tumors in this region and those originating from pineal parenchymal cells.<sup>1</sup> The latter include pineoblastomas, pineocytomas, and tumors of glial origin. These retain the potential for neuronal or glial differentiation.<sup>1,6</sup> Approximately three-fourths of tumors in this area are malignant with the propensity for seeding<sup>(3,7,8,9,10)</sup>. Retrospectively we have analyzed 47 cases of pineal region tumors and have discussed the clinical features, histopathology, management and outcome.

**Keywords:** Pineal tumors, Central nervous system, Tumors of glial origin.

### Introduction

The clinical syndromes associated with posterior third ventricular region tumors relate directly to normal anatomy as well as tumor histology. Headache, nausea, vomiting and alteration of mental status are the usual presenting features. These symptoms are due to obstructive hydrocephalus caused by compression of the aqueduct of Sylvius. Compression of superior colliculi either directly or due to tumor invasion results in the syndrome of vertical gaze palsy or Parinaud's syndrome. In pineal germ cell tumors-precocious puberty, diabetes insipidus or hypogonadism may be the presenting features. In some of these tumors surgery offers cure, while others need adjuvant therapy. Adequate tissue sample for histological diagnosis is important for treatment planning. Before the development of contemporary microsurgical techniques, surgical therapy was associated with an operative mortality of 30% to 70% and morbidity of up to 65%.<sup>11-16</sup> Most neurosurgeons performed only ventricular shunting for obstructive hydrocephalus followed by fractionated radiation therapy, which allowed an overall mortality of less than 5% and a five year survival rate of 60 to 75%.<sup>17-19,29</sup> Recent advances in Neuroradiology [computed tomography (CT), magnetic resonance imaging (MRI)], micro neurosurgical techniques, modern neuroanaesthesia and postoperative intensive care have led to more encouraging surgical results. The mortality of direct surgery has been reduced to less than 5% and morbidity to a minimal level.<sup>16,21-26</sup> Presently surgical extirpation of pineal tumors is the main approach for pineal region tumors. Chemotherapy coupled with irradiation is needed to treat malignant pineal tumors.

Remissions have been reported in many cases in which mostly cisplatin based chemotherapy in conjunction with radiation therapy was delivered.<sup>27-32</sup> Retrospectively we have analyzed 47 cases of pineal region tumors and have discussed the clinical features, histopathology, management and outcome.

### Materials and Methods

This is a retrospective study carried out in the department of surgery, Career institute of medical sciences and hospital, I.I.M road Lucknow, (U.P).

Data was obtained from departmental records, patient files, operation notes and follow up files. From these records patient's demographic profile, pre and post-operative neurological status, management, complications, hospital course and follow up was analyzed. Appropriate statistical methods were used to analyse the data.

### Result

#### Observation

Forty seven cases of posterior third ventricular tumors were reviewed. There were 35 males and 22 females between the age group of 1-87 years. Majority of cases were in their second and third decade. Male to female ratio was 2.9:1.

**Table 1:** Study of the symptomatology

S. No.	Symptom	Numbers	%
1	Headache	42	89.3
2	Vomiting	22	46.8
3	Visual deterioration	16	34
4	Diplopia	8	17
5	Generalized seizures	6	12.7
6	Memory and behavioral changes	7	14.8
7	Altered sensorium	8	12.7

**Table 2:** Neurological deficits

S. No.	Symptom	Number	%
1	Hemiparesis	5	10.6
2	6th paresis	6	12.6
3	Perinaud's syndrome	27	57.4
4	7th nerve paresis	3	6.3
5	3rd nerve paresis	2	4.2
6	Altered sensorium	6	12.6
7	Gait ataxia	11	23.4

**Table 3:** Radiological findings

S. No.	Diagnosis	Total	MRI			CT Scan
			T1W	T2W	Others	
1	Epidermoid	12	Hypointense	Hyper intense	Non contrast enhancing ADC* similar to brain	Hypodense, non enhancing
2	Cavernoma	2	Mixed signal surrounded by hemosiderin ring	Low signal more prominent	Homogenous enhancement	Isodense, contrast enhancing
3	Arachnoid cyst	2	Hypo intense	Hyper intense	Non contrast enhancing, ADC* similar to water	Resemble to CSF, nonenhancing
4	Pinealocytoma	4	Hypo to iso intense	Hyper intense Occasional area of hypo intense on T2W	Contrast enhancing	Isodense enhancing
5	Pinealoblastoma	5	Hypo to iso intense	Hyper intense	Contrast enhancing	Isodense enhancing
6	Astrocytoma	1	iso to hypointense	Heterogeneous	Irregular enhancement	Mixed density
7	Glioblastoma	1	Heterogenous ment	Heterogeneous	Inhomogenous contrast enhance	Mixed density
8	Immature teratoma	3	Mixed signal	Mixed signal	Mixed contrast enhancing	Mixed density
9	Germinoma	2	Isointense	Isointense	Contrast enhancing	Mild hyper dense and homogenously contrast

						enhancing
10	Papillary pineal tumor	1	Hypo intense	Hyper intense	Mild contrast enhancing	
11	Acellular biopsy	2	Isointense	Isointense	Contrast enhancing	Mild hyperdense and homogenously Contrast enhancing

ADA: \*Apparent Diffusion Coefficient

Surgery was performed in 35 cases (74.4%). Out of these 35 cases, 24 cases required ventriculoperitoneal shunting prior to surgical excision. In 30 cases infratentorial supracerebellar approach was used and in 4 cases transcortical transventricular approach was used (Table 4). One patient was operated endoscopically and ETV and cystoventriculostomy was performed.

Gross total excision was achieved in 17 cases. Near total excision in 6 cases and subtotal excision was performed in 12 cases.

**Table 4**

S. No.	Surgical Route	Numbers and Percentage
1	Infratentorial supracerebellar approach	30(8s.7%)
2	Transcortical transventricular approach	4(11.4%)
3	ETV and cystoventriculostomy	1(2.8%)

Treatment modalities in non operative cases (12) cases

**Table 5**

S. No.	Diagnosis	ETV and bx*	VP shunt	Total
1	Pinealoblastoma	1(bx)	-	1
2	Astrocytoma	1(bx)	-	1
3	Acellular biopsy	1(bx)	-	1
4	Presumptive Radiological diagnosis of germinoma	-	9	9

\*bx-biopsy

### Complications

Postoperative complications were observed in 9 cases (18.3%). CSF leak and pseudomeningocele were present in 2 and 1 case respectively. They were managed by lumbar CSF drainage. Transient up gaze palsy was seen in 3 cases and bilateral 6th and up gaze palsy was seen in one case. These cases improved subsequently on steroid therapy. Operative site extradural hematoma and seizure were noted in one case each and were treated successfully.

### Discussion

Pineal region tumors are uncommon deep seated tumors of brain and comprise 1% or less of all intracranial neoplasms.<sup>1,2</sup> These tumors are approximately ten times more common in children as compared to adults and constitute 3% to 11% of childhood brain tumors<sup>3,5</sup> and commonly seen in 2<sup>nd</sup> decade of life.<sup>33,34</sup> In our series 61.7 % cases were present in 2<sup>d</sup> and 3<sup>d</sup> decade. Approximately three-fourths (75%) of Pineal

tumors are malignant in nature with the tendency for seeding.<sup>3,7-10</sup> A higher incidence of pineal region tumors in Asian countries compared to Western countries has been reported. In the Brain Tumor Registry of Japan (BTRJ), there were 38,273 primary brain tumors except those of unknown histology (1123 cases) registered in the period between 1984 and 1993. There were 807 pineal region tumors (with 104 unknown histology) who were registered in BTRI. Of these pineal region tumors, germ cell tumors had highest frequency (70.3%), followed by pineal parenchymal tumors (12.0%), pineocytoma 7.8% and pineoblastoma 4.2%. Limited to germ cell tumors germinoma had highest incidence (68.0%), followed by teratoma (including malignant teratoma) with frequency of 14.7% in pineal region.<sup>35</sup> In Ojemann et al, Regis et al and Alexander N. Kononov et al series, germ cell tumor were commonest pineal region tumor.<sup>33,34,36</sup> Gliomas were second commonest tumors in the series of Regis et al<sup>36</sup> and Alexander N. Kononov et al<sup>34</sup> but pineal: parenchymal tumors were second most common in Ojemann

et al series.<sup>33</sup> In a study from India, Pragati Kumar et al found highest incidence of pineal parenchymal tumors 33.8% followed by gliomas in 37%. They found germ cell tumors in only 7.4% and miscellaneous tumors in 16.6%.<sup>37</sup> In the present series, benign lesions were present in 16 cases (34%) and malignant lesions were present in 31 (65.9%) cases. In benign lesions, epidermoids were commonest (12 cases). In malignant lesions, Germ cell tumors were most common (16 cases), followed by pineal parenchymal tumors (8 cases) and gliomas (7 cases). Majority of pineal region tumors present with symptoms of intracranial hypertension because of obstructive hydrocephalus due to compression or direct infiltration of the aqueduct of sylvius. Approximately 90% of patients with pineal region tumors have symptoms of intracranial hypertension at the time of presentation.<sup>3a</sup> In our series 89.3% cases had symptoms of raised intracranial features. Headache was present in 42 cases (89.3%) and it was associated with vomiting in 22 cases (46.5%). Perinaud's syndrome was seen in 27 (57.4%) cases. In a study carried out by Alexander N. Konovalov et al found eye movement disorders in 76% cases.<sup>30</sup> Magnetic resonance imaging and Computed tomography are important diagnostic tools in the detection of these tumors. CT scan easily detects tumor calcification. MRI is the investigation of choice for pineal region tumors. It gives accurate information about size, extent of tumor, anatomical relations to surrounding neurovascular structures. Establishing histological nature of the tumor and extent of tumor resection are important prognostic factors. These two factors appear dominant in predicting outcome.<sup>25,38-40</sup> Before the development of microsurgical techniques, treatment strategy usually involved ventricular drainage followed by fractionated radiation therapy because of high operative mortality of 30% to 70% and morbidity of up to 65% after surgery.<sup>11-16</sup> Ventricular drainage followed by fractionated radiation therapy had overall mortality of less than 50% and a 5-year survival rate of 60 to 75%.<sup>17,18</sup> Nowadays with the introduction of modern microsurgical techniques and technology, development of neuroanesthesiology and neuro-radiological techniques, surgical treatment of pineal region tumors can be carried out. The mortality of direct surgery has been reduced to under 5% and morbidity to a minimal level.<sup>16,21-26</sup>

In the present series, ventriculoperitoneal shunting was performed in 33 cases (70.2%). In 9 cases, only VP shunt was done and in 24 cases definite surgery was done after VP shunt. Nowadays the endoscopic third ventriculostomy is good alternative to normalize CSF circulation for hydrocephalus in pineal region tumors. In patients with malignant germ cell tumors or pineoblastomas, there is risk of peritoneal metastasis following shunting.<sup>42,43,49</sup> Infection,

malfunction or peritoneal metastasis associated with ventriculoperitoneal shunts are eliminated by third ventriculostomy. In the present series ETV and biopsy was done in 3 cases. ETV itself can potentially facilitate dissemination of the neoplasm.<sup>44,45</sup> Haw and Steinbok<sup>47</sup> reported metastatic deposit of the pineal germinoma at the ventriculoscope tract. There was no dissemination in ETV group in the present series.

Presently, surgical excision remains the treatment of choice for pineal region tumors and a wide variety of lesions can be safely excised.<sup>7,23-26,48,49</sup> Many approaches for removal of pineal region tumors can be adopted. Supracerebellar-infratentorial and occipital-transtentorial approaches are commonly used surgical approaches for this location.<sup>3a</sup> In 1971, Stein popularized the infratentorial supracerebellar approach, originally described by Krause.

Germinomas are highly radiosensitive and radiation is the primary treatment modality. There is no significant difference between the outcome of patients irradiated after direct surgery and those receiving radiotherapy alone.<sup>8,17,50</sup> The patients with definite radiologic features do not require direct surgery or stereotactic biopsy for pathologic confirmation of diagnosis and can be irradiated directly. In the present series direct radiotherapy was given to 11 cases on the basis of radiological diagnosis of germinoma and these patients responded very well. Three cases were lost to follow up. The tumor disappeared in other with no recurrence in available follow up.

Aggressive tumors like malignant germ-cell tumors, pineal parenchymal cell tumors tend to invade surrounding structures and have a risk of CSF dissemination.<sup>27,29-32,51</sup> There is controversy about the extent of radiation. At present craniospinal irradiation is indicated only in patients with clinical or radiologic evidences of dissemination of tumor because myelopathy is a serious late complication of craniospinal irradiation.<sup>38,52-54</sup> In the present series, one case of pinealocytoma had leptomeningeal seeding. Platinum-based multiagent chemotherapy has improved the outcome in patients with nongerminomatous germ cell tumors and anaplastic pinealocytomas.<sup>30,31,43,55,56</sup> The benefits of this approach are still debated,<sup>29,51</sup> although patients with pineoblastomas are often treated with adjuvant systemic chemotherapy after craniospinal irradiation. The incidence of pineal region epidermoid tumors is approximately 3% to 4% of all intracranial epidermoids.<sup>57</sup> The incidence of epidermoid tumors in the pineal region varies from 3.4% to 10% in different series.<sup>57,58</sup> In present series, epidermoid was present in 12 cases (25.5%) out of 47 cases. Exact pathogenesis of epidermoids in general is still under discussion. Defect in the cleavage of the neural tissue from

the cutaneous ectoderm, embryonic inclusions, differentiation from multipotential cell rests, and epithelial remnants are the various other mechanisms implicated in the origin of epidermoid tumor. The seedling of the subarachnoid space by the irritant component of the epidermoid cyst results in aseptic chemical meningitis. The incidence of recurrence after radical excision is uncommon.<sup>57-60</sup>

Pineal region cavernomas and arachnoid cysts are rare and only case reports are available in the literature.<sup>61-63</sup> In present series 2 cases of arachnoid cysts and 2 cases of cavernomas were noted. There was no recurrence in available follow up.

### Conclusion

Pineal tumors are a heterogeneous group of mass lesions originating in and around the pineal gland and represent a spectrum of neoplasms. Direct surgical excision remains the treatment of choice for pineal region tumors with minimum mortality and morbidity. Complete excision should be the goal for majority of these lesions. For germinomas, radiation therapy good long term recurrences free survival and outcome. Endoscopic biopsy and ETV offers histological diagnosis and CSF diversion in many of such lesions and further treatment can be planned accordingly.

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### Conflict of Interest

None.

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