Case series: Pediatric Pineoblastoma (PNETs)-Radiological, and clinicopathological studies

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Case series: Pediatric Pineoblastoma (PNETs)-Radiological, and clinicopathological studies

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ABSTRACT

A rare type of brain tumor, pineoblastoma (PNET) is found in young adults and children. PNETs are rarest representing under 1% of all cerebrum cancers. The most common type of this type of tumor starts at the pineal glands, a small gland located at the base of the brain. Pineoblastomas make up approximately 50% of all pineal gland tumors. These tumors can be challenging to treat because of their location in the brain. The five-year endurance of patients of PNETs or pineoblastoma is around 50-60%. Infants and children who have had partial surgical removal and a poor response to radiation therapy have less favorable outcomes.

Keywords: Pediatric, Pineoblastoma (PNETs), Pineal gland, Whole Brain Radiation Therapy (WBRT)

INTRODUCTION

An uncommon and rare Pineoblastoma (PNET) supratentorial highly malignant is found in pediatrics and grown-up youths. PNETs are rarest addressing less than 1% of all frontal cortex diseases or pineal glands. The pineal glands, a small gland at the base of the brain secretes melatonin hormone that is responsible for sleep, and are the starting point for the most common form of this type of tumor.

As of late integrative epi/genomic investigations have uncovered that pineoblastoma more common tumors of CNS cancers, pineoblastoma is naturally heterogeneous and is made out of 5 center particular atomic infection subgroups with exceptional clinical elements and different outcomes [1,2].

A recent study revealed that the pineoblastoma patients treated at St Jude Youngsters' Exploration Clinic, depicted 5-year Progression-Free Survival (PFS) and overall Survival (OS) (100%) in 20 patients with confined sickness treated with 23.4 Gy CSI [3]. Published study uncovered the A novel finding, that the pediatrics of the male gender who are <3 years are significantly associated with lower PFS than female pediatrics. Likewise, medulloblastoma also shows that male pediatrics were associated with lower PFS than female pediatrics [4].

Pineoblastoma is difficult to treat and requires different treatment approaches, such as surgical resection, radiation therapy, chemotherapy, and other possible interventions used to treat pediatrics with pineoblastoma, and the study showed that all interventions are intervened undependably in pediatric pineoblastoma patients remained unclear, and unable to identify appropriate treatment protocol in these patients [5].

One of the studies described that only older pediatric pineoblastoma patients showed an improved survival rate after aggressive tumor resection. Patients who have undergone surgery improved higher from radiotherapy. Age-based interventions will bring much higher health improvement in pediatric pineoblastoma patients [6].

The other study narrates that the Cranio Spinal Irradiation (CSI) intervention was very harmful to very younger pediatrics', and other therapies led to toxicities thus prolonging the Complete Remission (CR) in these pediatric pineoblastoma patients. [7] As there are recurrences in pediatric pineoblastoma patients lesser toxic Radio Therapy (RT), and proton therapy have a limited impact on better outcomes [8].

For the best outcome, the clinicians treated the pediatric pineoblastoma patients with IT Topotecan and Intra-Ventricular (IVT) which protects the patients from leptomeningeal disease, but declined efficacy was found with intraparenchymal tumors [9]. Another study explained that their patients with pediatric pineoblastoma tolerated well the combination therapy IT topotecan and metronomic therapy, and also showed health improvement [10]. Recent study showed that nortriptyline was found to be a potential therapy effective for nortriptyline-induced disruption of lysosomes, and cell death due to autophagy-induction [11].

Data Collection of Case Series Patients

The case series of 12 pineoblastoma pediatric patients were evaluated for 11 years from 2004-2015 for the clinical outcomes at 2 years and 5 years of follow-up after multimodality treatment with surgery, radiotherapy, and chemotherapy. The case series pediatric patient's ages ranged from 5-17 years with a mean age of 10. 3 years.

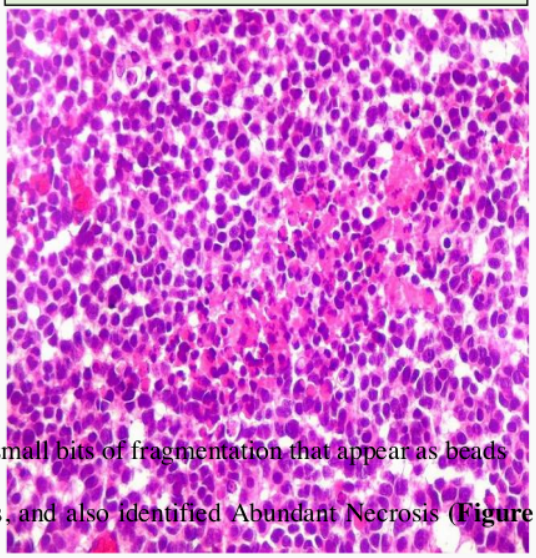
Data collected includes age, sex, initial symptom, VP shunt procedures, CSF analysis, type of surgery, radiotherapy, chemotherapy regimen, failure pattern, recurrence follow-up, death rate, and toxicities. The study endpoints included PFS and OS at 2 years and 5 years of follow-up.

Initial Identification of the Case Series Patients

Symptoms found in the Case Series Patients Lead for the Suspecting of Pediatrics Pineoblastoma

Headache (83.3%), Vomiting (75%), Diplopia (33.3%), Fever (16.7%), Papilledema (8.3%), Abdominal pain (8.3%), Deviation of eye (8.3%), Involuntary muscle action (8.3%), Giddiness (8.3%).

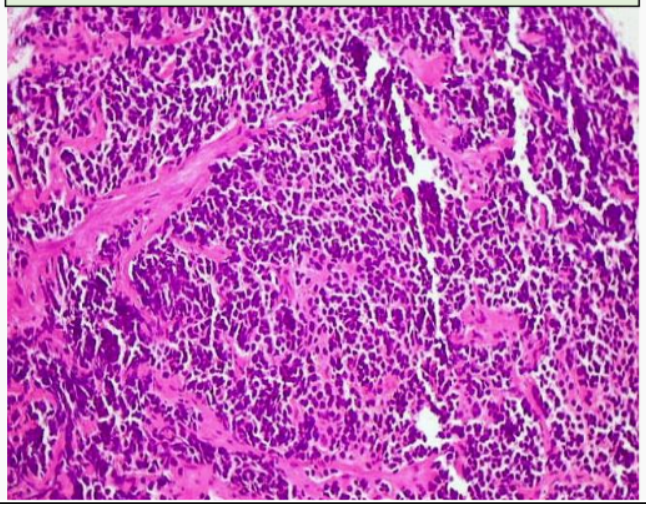
Figure 1: Karyorrhexis and Abundant Necrosis



Pathological Presentation of Case Series

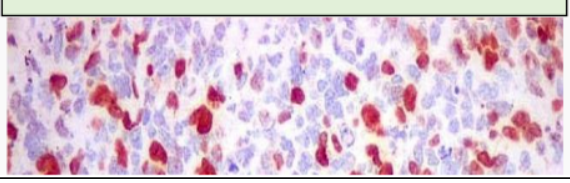
The pathological presentation of case series patients Showed evidence of Karyorrhexis (nuclear fragmentation), degenerative transpose, breaking down of the nucleus into small bits of fragmentation that appear as beads with damaged chromatin, identified in the aseptic exudates, and also identified Abundant Necrosis (**Figure 1**).

Figure 2: Cellular Cerebrospinal Fluid containing a small blue cell Neuroepithelial Malignant Tumor



Immunostaining for glial fibrillary acidic protein (GFAP) showed numerous positive large cells, Ki-67 proliferation protein and moderately cellular cerebrospinal fluid with a small blue cell neuroepithelial malignant tumor (**Figure 2**).

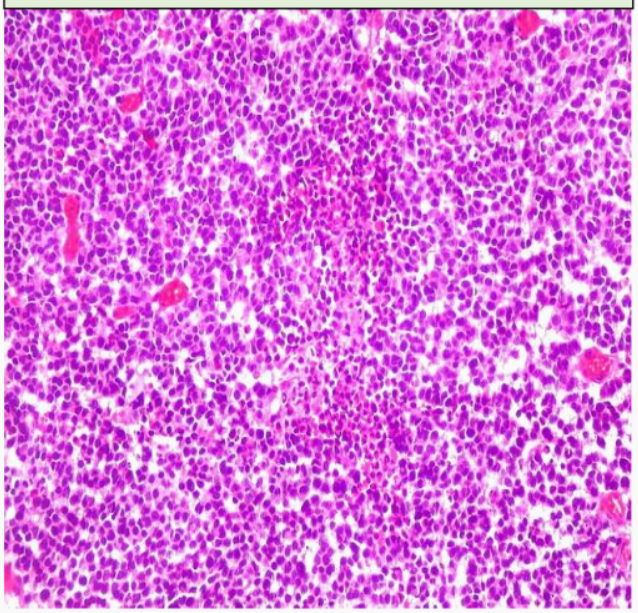
Figure 3: Pleomorphic Large Hyperchromatic Nuclei-Immunostaining



Microscopic Evaluation

The eosinophilic staining of the case series patient's sample showed the presence of clusters of highly atypical cells, some large with pleomorphic large hyperchromatic nuclei,

Figure 4: Immunostaining-Brain Pineoblastoma

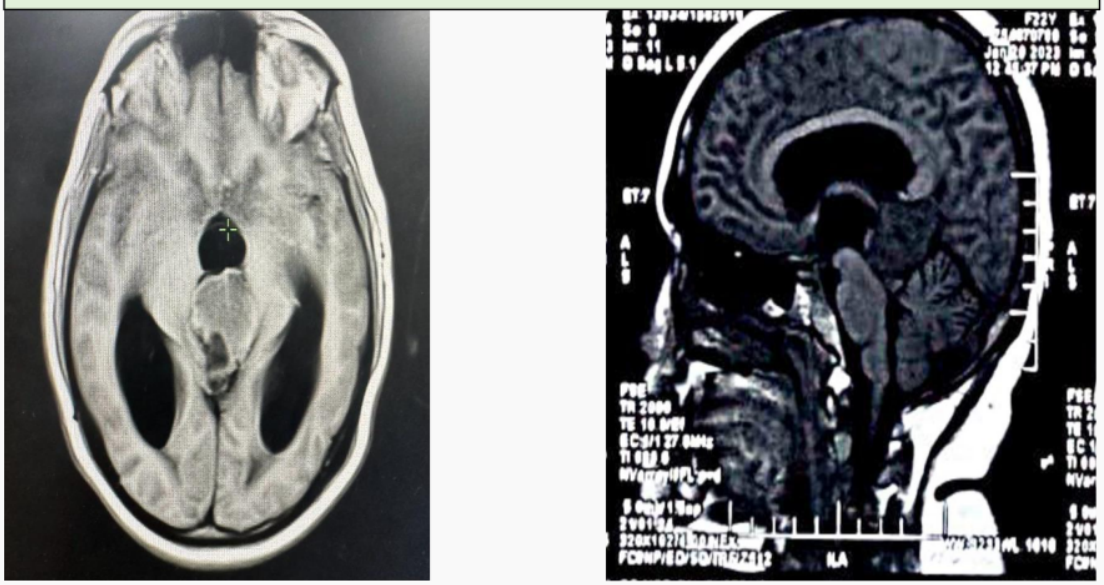


moderate amounts of eosinophilic cytoplasm and inconspicuous nucleoli. Scattered small cells with dense small nuclei were also observed and identified in the samples of case series patients **(Figure 3, 4)**.

Radiological Confirmation (MRI)-Pediatrics Pineoblastoma

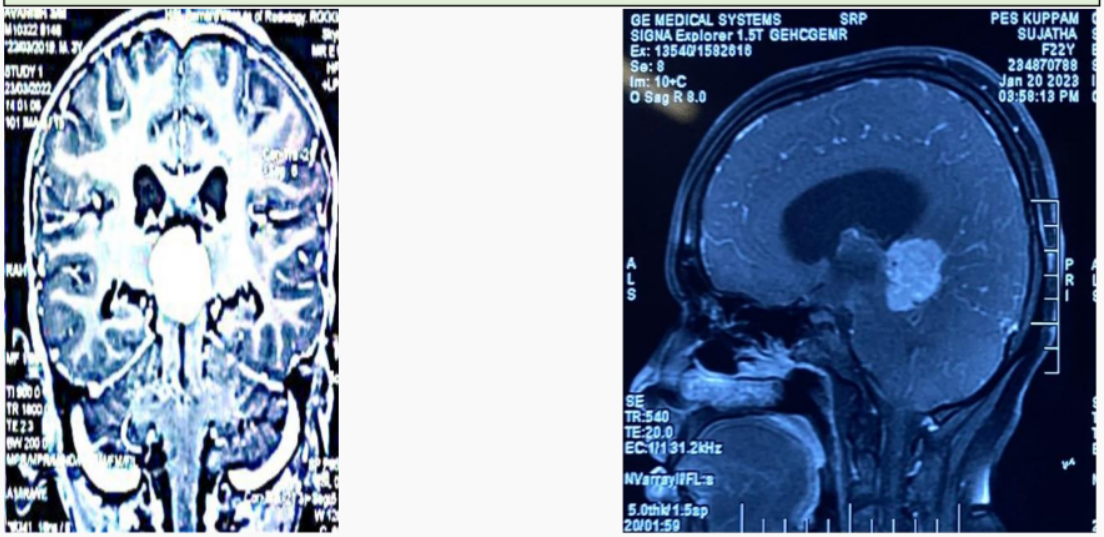
The case series patients were further confirmed their Pineoblastoma by MRI imaging, and found with tumors in the Pineal region. Around n=7 (58.3%) of case series patients were found with drop metastases.

Figure 5 (a, b): MRI Imaging of Pediatrics Pineoblastoma



(a) (b)

Figure 6 (a, b): MRI Imaging of Pediatrics Pineoblastoma



(a) (b)

Treatment for the Case Series Pineoblastoma Pediatric Patients

Out of 12 case series pineoblastoma pediatric patients, 10 patients received Chemotherapy, 2 did not receive chemotherapy, and chemotherapy was 6 cycles of vincristine for 4 patients (33.3%), 6 cycles of PCV (33.3%) for 4 patients, vincristine, etoposide, cisplatin (16.7%) for 2 patients, and cisplatin, vincristine, oral lomustine

(16.7%) for 2 patients were administrated. Out of 12 case series pineoblastoma pediatric patients, 6 underwent surgery, and 6 did not underwent surgery.

All patients underwent postop radiotherapy with the 2D technique using a C0-60 machine. CSI dose was 36 Gy + localized boost up to 54 Gy and the Whole Brain Radiation Therapy (WBRT) dose, and near-total excision was (n=6) 50%, subtotal was (n=6) 50%, Cranio-Spinal Irradiation (CSI) was (n=10) 83.3%, and WBRT was (n=2) 16.7%.

Follow-up of the Case Series Pineoblastoma Pediatric Patients

In the follow-up of case series pineoblastoma pediatric patients, local recurrence of tumors was most common in (n=8) (66.7 %) of patients, presenting with headache (n=8) (66.7 %), paraparesis (n=2) (16.6 %), and diplopia (n=2) (16.6 %).

Among 2 case series pineoblastoma pediatric patients who received WBRT, 1 patient developed recurrence and passed away at 2 years, and the other developed paraparesis at 7 years of follow-up and expired subsequently. The earliest death was as early as 1.5 years on follow-up, whereas long-term survival of 8 years of follow-up was also found, and among the long-term survivors, 1 patient had decreased height for age on follow-up.

In the follow-up of 2 years, out of 12 case series pineoblastoma pediatric patients, 7 were normal, 3 were alive with recurrence, and 2 passed away. In the follow-up of 5 years, out of 12 case series pineoblastoma pediatric patients, 4 were normal, 3 were alive with recurrence, and 5 passed away. The Overall Surveillance (OS) in 2 years of follow-up was 83.4%, and 58.6% in 5 years of follow-up, and Progression-Free Survival (PFS) was 58.7% in 2 years of follow-up, and 34.3% in the 5 years of follow-up.

DISCUSSION

Pediatric Pineoblastoma was present in our case series in 5-17 years with a mean age of 10.3 years, and symptoms such as headache along with vomiting were found in the higher number of case series patients. Our study of the patient's symptoms was compatible with the study of Huo XL et al study, [12]. This present study reported that 83.35 of the study pediatric pineoblastoma patients suffered from headaches, and 75% suffered from vomiting, whereas Rodriguez S et al study showed that 48% of study patients suffered from headaches, and 31% suffered from vomiting, [13]. In this current study, pediatric pineoblastoma patients also suffered from Diplopia (33.3%), and Shimony N et al also described that Diplopia is a chief symptom present in pediatric pineoblastoma patients, [14].

In the present case series study 7 (58.3%) of patients were reported with "Drop metastasis", and studies were evident that stage IV of the cancer of case series patients was identified as "Drop metastasis", otherwise called

intramedullary spinal string metastasis (ISCM), which is an uncommon intricacy of malignant growth, influencing 0.1%-0.4% of all disease patients [15,16].

CONCLUSION

In conclusion, the present study reported a case series of patients with pineoblastoma and found long-term survival can be achieved for patients who received near-total excision and completed radiotherapy and chemotherapy. Since pineoblastoma is aggressive in growth and requires an accurate diagnostic tool, an extensive work-up, and an appropriate treatment, further studies with better cohort size are needed.

Conflict of Interest: None

Author's Contribution

First Author- Sangitha. R- *Study design, Data Collection*

Second Author- Giridharan. R - *Approval*

Third Author- Vijayasree. T.N - *Literature Review, Critical revision*

Corresponding Author- J Janifer Jasmine - *Manuscript preparation*

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