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Systematic review

Patterns of care and survival outcomes in patients with pineal parenchymal tumor of intermediate differentiation: An individual patient data analysis

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ABSTRACT

Background/purpose: Pineal parenchymal tumor constitutes less than 1% of all CNS tumors. Pineal parenchymal tumor of intermediate differentiation is a rare tumor arising from the pineal parenchyma lying between the spectrum of Pineocytoma and Pineoblastoma.

Methods and materials: We performed PubMed search with the following MesH terms: "pineal parenchymal tumor, pineal parenchymal tumor of intermediate differentiation, pineal parenchymal tumor of intermediate differentiation AND treatment, and pineal parenchymal tumor of intermediate differentiation AND survival" to find all possible publications pertaining to PPTID. Individual patient data on "age, gender, surgery, type of surgery, radiation and type of radiation, chemotherapy, recurrence, and survival" were tabulated.

Results: A total of 29 studies were found eligible with 127 patients. Median age was 33 years (range: 4.5–75 years). The male: female ratio was 1:1.6. Median MIB labeling index was 7 (range: 1–30). Adjuvant radiation was used in 46 (36.2%) of the patients and chemotherapy was used in 29 (22.8%) patients. Of the patients who had recurrence 62.5% experienced spinal or leptomeningeal recurrence while 37.5% had local recurrence. The median progression free survival and overall survival were 5.17 and 14 years respectively. Univariate analysis revealed female sex and the use of adjuvant radiation to be associated with better overall survival.

Conclusion: PPTIDs are associated with a moderate outcome with a median progression free survival of 5.17 years and median overall survival of 14 years. Patients with a sub total resection should be treated with adjuvant radiotherapy as addition of radiation is associated with better survival outcomes.

Pineal parenchymal tumor of intermediate differentiation (PPTID) is a rare tumor arising from the pineal parenchyma with limited aggressiveness lying between the spectrum of pineocytoma and pineoblastoma [1]. In 2007 WHO recognized this tumor as a separate entity of the pineal tumors. The aggressiveness of the tumor varies widely. There is some agreement that PPTID is not a single disease rather a spectrum of grade II and grade III pineal parenchymal tumors and this hypothesis may explain the wide variation in the behavior of these tumors. A surgical excision is considered standard of care and a maximal safe resection is the aim of surgery. However, even after a surgical complete tumor removal many patients experience recurrence. Hence, many centers recommend adjuvant radiation or chemotherapy or a combination of both for optimizing tumor control and to improve survival. However, owing to the rarity of these tumors most of the data are derived from institutional practice, case reports or small case series with the limitation to adopt any form of treatment with a wide range of bias. Hence, we embarked on to do an individual patient data analysis to find the optimum treatment of these tumors. So, the question we asked was "Whether adjuvant therapy has a role in the management of PPTID". We planned to derive basic patient characteristics, treatment details and survival information from all published studies of PPTID and analyzed the impact of treatment.

Search methodology

We performed a comprehensive search of the PubMed with the following MesH terms: "pineal parenchymal tumor; pineal parenchymal tumor of intermediate differentiation; pineal parenchymal tumor of intermediate differentiation AND treatment; and pineal parenchymal tumor of intermediate differentiation AND survival" to find all possible publications pertaining to

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PPTID. We also conducted a detail search of the references in the available article to retrieve missing articles and conducted a hand search in Google to find any possible publication. After a thorough search the duplicates were removed and the remaining articles were looked into detail. Articles which furnished basic demography, treatment details, and survival information were taken for the present analysis. A total of 29 articles were found eligible for the analysis. Individual patient data were then tabulated in excel chart with the headings of "age, gender, surgery, type of surgery, radiation and type of radiation (local/craniospinal radiation), chemotherapy, recurrence, duration of disease free interval, death and overall survival. The flow chart (Fig. 1) explains the data synthesis from the eligible studies.

Statistical analysis

The data were analyzed and categorical variables were summarized as frequency and percentage and quantitative variables as median and range. Progression free survival [PFS] and overall survival [OS] were calculated from the date of diagnosis to the date of documented progression or death. Univariate analysis was performed using log rank test to find the impact of prognostic variables on PFS and OS. The Kaplan–Meier method was used for survival analysis. Univariate analysis was done to find an impact of age, gender, type of surgery, use of radiation, use of chemotherapy on survival outcome. A p value of <0.05 was taken as significant. SPSS v16 (SPSS Inc. Released 2007. SPSS for Windows, Version 16.0. Chicago, SPSS Inc.) was used for all statistical analysis.

Results

A total of 29 studies found eligible with 127 patients [1–29]. Median age was 33 years (range: 4.5–75 years). Out of 127 patients 47 were male and 75 female with a male: female ratio of 1:1.6, suggestive of a female preponderance; gender of 5 patients was not available. Presenting symptom was available in 18 patients with headache being the commonest symptom (61%) followed by gait abnormality (22.2%). Radiology finding was available only for 12 patients which revealed T1-hypointense, T2-isointense mass lesion with homogenous contrast enhancement. MIB labeling index was reported for 21 cases. Median MIB labeling index was 7 (range: 1–30).

Surgery was attempted in all but one case, and nature of surgery was described in all but three cases. A gross total or near total resection was reported in 32 cases (25.2%), subtotal resection or debulking was reported in 50 cases (31.9%), Biopsy only was possible in 40 cases (31.7%), and 1 patient had diagnosis in autopsy. Information regarding adjuvant radiation was available in 65 cases, whereas it was not clearly mentioned in 62 cases. Out of these 65

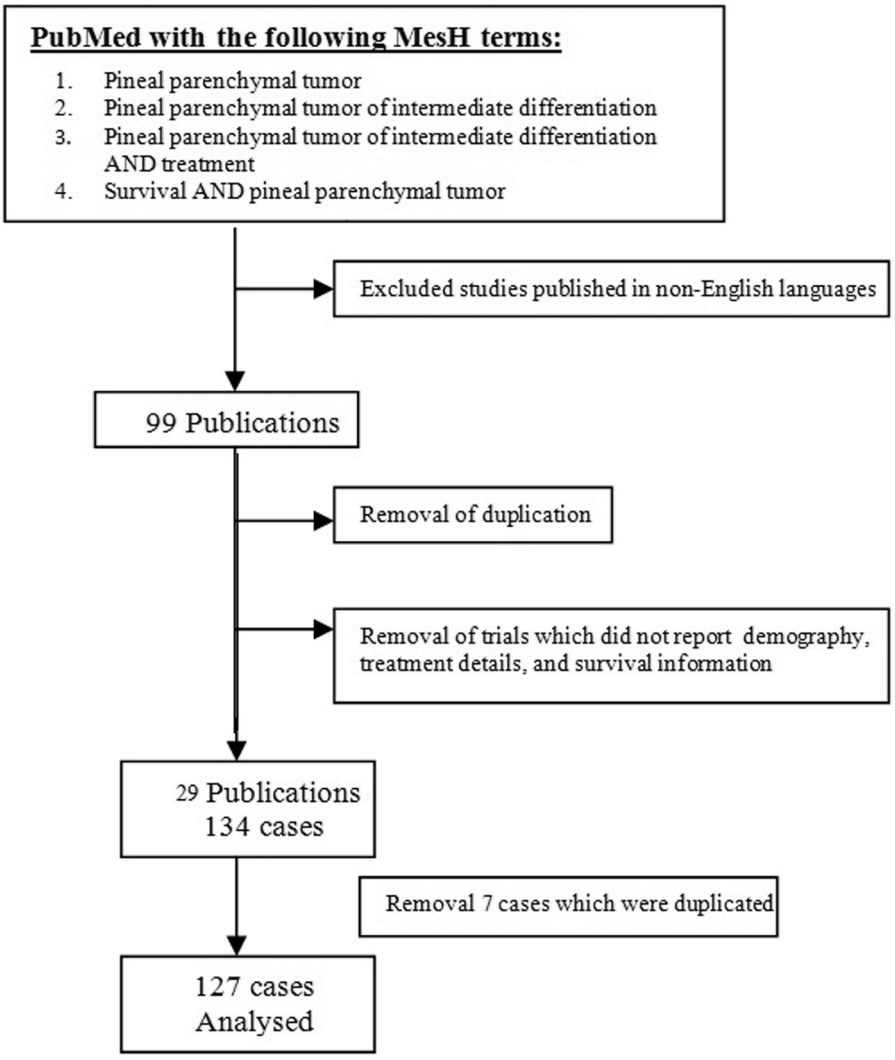

Fig. 1. The flow chart showing summary of the search methodology.