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Clinical study

Grade II Pleomorphic Xanthoastrocytoma; a meta-analysis of data from previously reported 167 cases

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ABSTRACT

Pleomorphic Xanthoastrocytoma [PXA] is a rare low grade glial tumor commonly affecting young adults. We did this systematic review and meta-analysis to identify prognostic factors and optimal treatment in these patients. A thorough search of the PubMed, Google scholar was made to find all possible publications related to grade II PXA. A total of 167 patients from 89 articles were included in the analysis. Median age of the entire cohort was 20 years. Headache was the most common presentation in 49.1% of the patients followed by seizure in 27.9%. Temporal lobe was the most common location of the tumor. 63% patents underwent a gross total resection [GTR] and 26.7% underwent a sub total excision [STR]. Adjuvant radiation was given to 17.6% of patients. Median follow-up for the entire cohort was 33 months. Estimated median overall survival [OS] for the entire cohort was 209.0 months [96% CI: 149.7–268.3]. Estimated median progression free survival [PFS] was 48 months [95% CI: 31.9–64.0]. In univariate and multivariate analysis younger patients and patients who underwent a GTR had a significantly better survival outcome. Use of adjuvant therapy was not found to be a significant factor affecting PFS or OS. Radiotherapy was used in salvage treatment in 76.1% of the patients. Younger patients and patients who undergo a GTR, have better survival outcomes. There is inadequate evidence to recommend routine adjuvant radiation or chemotherapy in all patients with grade II PXA.

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1. Introduction

Pleomorphic Xanthoastrocytoma [PXA] is a low grade glial tumor and commonly affects young adults. Kepes et al in 1979 identified this as a distinct entity [1], later WHO recognized these tumors as grade II and III tumors. These tumors are usually present as localized disease, but isolated reports of early leptomeningeal dissemination have been reported [2]. Surgical resection is considered the cornerstone of therapy and remains so. However, there is debate regarding the extent of resection with few reports suggesting a prolonged survival in patients treated with a gross total resection [GTR] alone. The role of adjuvant treatment in grade II Pleomorphic Xanthoastrocytoma has been not been agreed upon and practice varies widely. The greatest limitation is the sporadic reporting of PXA in the literature owing to its rarity. Hence, in the absence of a robust data, we did this systematic review and individual patient's data analysis to identify prognostic factors and optimal treatment in these patients.

2. Materials and methods

2.1. Search methodology

A thorough search of the PubMed, Google scholar was made with the MesH terms: "Xanthoastrocytoma; Pleomorphic Xanthoastrocytoma, Xanthoastrocytoma AND treatment; and Xanthoastrocytoma AND survival" to find all possible publications related to grade II Pleomorphic Xanthoastrocytoma. We retrieved full length articles of those remaining to complete articles for data extraction. In addition, we searched the references in articles to fetch any missing article in our search strategy. After duplicates were removed, the remaining articles were looked into detail. We extracted individual patient data in excel chart with the headings of "age, gender, presenting complaint, surgery, type of surgery, radiation, chemotherapy, recurrence, duration of progression free interval, overall survival and salvage treatment. Articles which described only the pathological, molecular and other factors unrelated to treatment and outcome were excluded from the data extraction. Once the data extraction was completed it was rechecked by the authors independently to rule out any error and duplication. A total of 89 articles were retrieved on grade II

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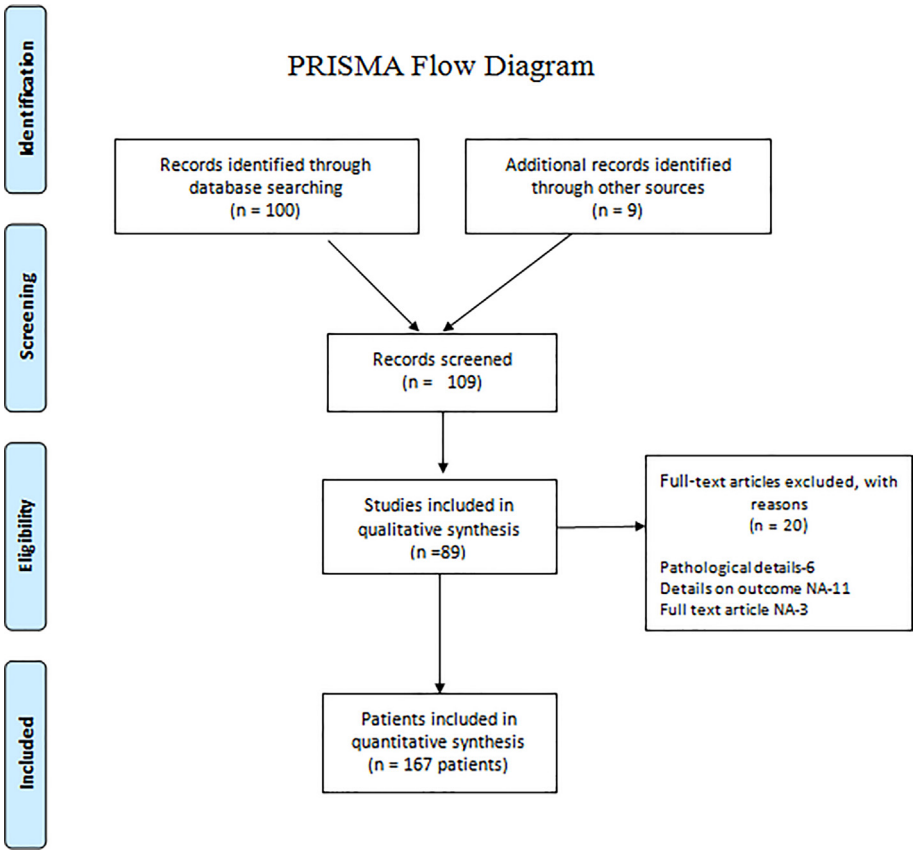

Fig. 1. The PRISMA flow chart showing summary of the search methodology.

PXA with 167 patients [2–89]. The PRISMA flow chart [Fig. 1] explains the data synthesis from the eligible studies.

2.2. Statistical analysis

The data was analyzed, categorical variables were summarized as frequency and percentage and quantitative variables as the 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. Kaplan-Meier method was used to for survival analysis. Univariate analysis was performed using log-rank test to find the impact of age, gender, type of surgery, use of radiation, use of chemotherapy on survival outcome. Multivariate analysis was performed using Cox regression test to further evaluate factors significant on univariate analysis. A p value of <0.05 was taken as significant. SPSS v16 [SPSS for Windows, Version 16.0 Chicago, SPSS Inc.] was used for all statistical analysis.

3. Results

3.1. Demography

We retrieved data of 167 individual patients from a total of 89 publications pertaining to grade II PXA. Of these only 3 had a sample size more than 10. The median age of the entire cohort was 20 years [Range 1–84 years]. Interestingly, 30% patients were diagnosed in second decade of life making it the most common age group affected [Fig. 2]. PXA was equally distributed among males and females. Symptom at presentation was available in 71% of the patients of whom headache was the most common presentation in 49.1% followed by seizure in 27.9% of the patients. Temporal lobe was the most common location of the tumor seen in 42.6% of the patients. 7.7% of the patients had a tumor location in the infratentorial part with 3.9% having it in the spinal cord. Two patients had leptomeningeal dissemination at diagnosis. Median MIB-1 labeling index was found to be 2 [Range: 1–10]. BRAF mutational analyses were performed for 14 cases, and mutations were identified in 10/14 (71.4%.)

3.2. Treatment

Surgical details were available for 157 cases. Of these 99 [63%] patients underwent a gross total resection [GTR] and 42 [26.7%] patients underwent a subtotal excision [STR]. Adjuvant radiation details were available in 142 patients of whom only 17.6% received adjuvant radiation. One patient received radiation therapy with palliative intent. In the available reports, all patients received local radiation alone. Adjuvant chemotherapy was used in 8 patients. Chemotherapy regimen varied widely within this cohort. Patient characteristics and treatment details are summarized in Table 1.

3.3. Survival outcome

Median follow-up for the entire cohort was 33 months. Estimated median OS for the entire cohort was 209.0 months [96% CI: 149.7–268.3]. In univariate analysis younger patients [$\leq$30 years] found to have better OS compared to elder patients [>30 years] [Hazard ratio 4.4, p-0.001]. Patients that underwent a GTR had a significantly better OS than those treated with a STR only [Hazard ratio 3.7, p-0.006] [Fig. 3]. Locations of the tumor, use of adjuvant radiation or chemotherapy were not found to be significant factors affecting OS. Multivariate analysis confirmed that age and extent of surgery were significant factors affecting

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