

HSOA Journal of Neonatology and Clinical Pediatrics

Research Article

Outcome of Children with Ependymoma: The Children's Cancer Institute of Lebanon experience

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Abstract

Introduction or Background

Ependymoma is ranked as the third most common childhood brain tumors after astrocytoma and medulloblastoma. No specific data describing in our region or the Middle East indicated the incidence, and the prevalence and outcome of childhood ependymoma in our region and the Middle East is scarce. The World Health Organization (WHO) classifies ependymal tumors into three grades (grade I–III). Surgical resection of the tumor and radiation therapy are considered the standard of care for childhood eEpendymoma, while chemotherapy, induction or myeloablative hematopoietic stem cell transplant areis still a conflicting matter debating their benefit. Shedding the light of the obstacles in the management of ependymoma in a limited-source country such as Lebanon, and evaluating on the 5- years survival rate, and comparing it to data published internationally and regionally are, were the target goals for this investigation.

Methods

This study it is a retrospective chart review with anonymized patient data. All medical charts for the patients diagnosed with eEpendymoma at thein American University of Beirut Medical Center between January 2004 and June 2020 were reviewed. All patients below the age of 21 years old were included in this investiga-

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Citation: Fahad N, Hamideh D, Borghol R, Ahmed MA (2023) Outcome of Children with Ependymoma: The Children's Cancer Institute of Lebanon experience. J Neonatol Clin Pediatr 10: 114.

Received: October 10, 2023; Accepted: October 25, 2023; Published: November 1, 2023

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tion. Ethical approval was obtained from study by the Institutional review board (IRB) of American University of Beirut.

Results

29 patients were enrolled in the study matcheding the inclusion criteria and were enrolled in the study. According to the WHO classifications, most of the eEpendymoma in our investigations were staged as stage III. Only five5 patients only presented with were staged as grade I and II ependymoma, while 24 patients (82%) were at stage III. Making them the majority with 82%. None of the patients had a confirmed underlying syndrome in both groups in our study.

Discussion

During the study period, 329 children were diagnosed with brain tumors. Only 29 patients were diagnosed with childhood ependymoma, accounting for 8.8% of all childhood brain tumors. Cases were 29 cases, out of all the 329 Brain tumor cases, making it 8.8% of all the brain tumors. This incidence rate goes along with the international incidence rate reported in literature. Posterior fossa eEpendymoma has shown superior outcome in terms of 5- years' survival over the supratentorial ependymoma, with (88.2%) to 75% in sequence. Moreover, organ metastasis has been documented in the literature as one of major complications affecting prognosis of Ependymoma. None of our patients had distant metastasis at the initial presentation or during the course of during treatment. Also however, all these this results may need to be confirmed with a larger sample size.

Conclusion

The role of chemotherapy and targeted therapy needs to be addressed in more prospective well-defined protocols to achieve better survival rate. Molecular staging should be implanted more often depending upon specialized labs. The emphasis of the role of specialized rehabilitation centers must be acknowledged.

Keywords: Astrocytoma; Cancer; Ependymoma; Medulloblastoma; WHO (world Health Organization)

Introduction

The complexity of the structure of the brain has always been considered as one of the greatest mysteries and miracles yet to be solved. Although we can simplify it in two major cells constituting the majority of most of the brain: The neurons, also known as nerve cells, and glial cells also known as neuroglia [1]. Upon understanding the basic components of the brain, hence the classifications of the brain tumors developed over the years. With the development of the genetic and molecular advances noticed in the last two decades, newer classifications compelled scientists to modify most of the brain tumors staging. Ependymoma is no different from most of other tumors.

Ependymoma is ranked as the third most common brain tumor in children's after astrocytoma and medulloblastoma [2]. No specific data in our region or the Middle East indicated the incidence and the prevalence of eEpendymoma. Only recently two recent studies have been conducted in Egypt and Saudi Arabia which have enlightened the characteristics of Ependymoma in their studies [3,4]. The World Health Organization (WHO) classifies ependymal tumors into Citation: Fahad N, Hamideh D, Borghol R, Ahmed MA (2023) Outcome of Children with Ependymoma: The Children's Cancer Institute of Lebanon experience. J Neonatol Clin Pediatr 10: 114.

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three grades (grade I–III) [5]. Other classifications opted to sub classify those grades depending on the molecular characteristics, while of childhood Ependymoma and many others depended on the tumor site to optimize treatment guidelines. Classification of eEpendymoma as supratentorial, posterior fossa and spinal relies depended on the site of the tumor, with posterior fossa site being the most common [6]. Molecular cClassifications with RELA and YAP fusions further subdivided the supratentorial entity, yet while many tumors without genetic features still could be identified [7,8]. When it comes to posterior fossa ependymoma, two important characteristics help in classifications of the posterior Fossa or the infratentorial tumors [9]. Spinal cord tumors are more known with tanycytic [10].

Many syndromes were associated with eEpendymoma, most notably with Neurofibromatosis Type II (NF2) being the most common [11]. Hereditary predisposition syndromes, such as Li Fraumeni and Turcot's syndrome haves also been reported to be linked with incidence of ependymoma [12,13]. Even though Ependymoma generally develops sporadically, other genetic disorders such as down syndrome haves been reported in few case reports [14].

Surgical resection of the tumor and radiation therapy are considered the standard of care for childhood eEpendymoma [15]. On the other hand, while the role of chemotherapy, induction or myeloablative hematopoietic stem cell transplant remain is still a conflicting matter debating their benefit? [16]. Complete resection, or gross total resection, can be is achieved through with one surgery or multiple surgeries. Many patients need to undergo multiple surgeries to achieve this goal [17]. Depilating consequences of surgical resection of debulking of eEpendymoma, and social life burden, from being wheel chair bound to visual complications had to be explored with no sufficient data in literature specified to our region. Shedding the light of the obstacles in the management of Ependymoma in a limited-source country such as Lebanon, and evaluation the 5- years survival rate, comparing it to data published internationally and regionally, were the target the target goals for this investigation.

Patients and Methods

After securing the approval of the initially, obtaining Approval for the study by the institutional review board (IRB) at the American University of Beirut, a retrospective revision of charts was performed. Patients aged younger than 21 years, and who presented to the American University of Beirut Medical Center (AUBMC) with a diagnosis of brain tumor between January 2004-June 2020 were identified. Patient consent is not required for this study, which is a retrospective chart review with anonymized patient data. All medical charts only for the patients diagnosed with eEpendymoma in American University of Beirut Medical Center within the study period were included. between January 2004 and June 2020 were reviewed Patients' charts including progress notes, laboratory testing, imaging results, procedures and follow up notes were all reviewed.. All patients below the age of 21 years old tumor histology, eEpendymoma molecular type, tumor site, drop metastasis, number of surgeries needed for resection of the tumor, radiation and chemotherapy received were collected and analyzed. All documented finally, our in the study charts. Findings were test association between the main outcomes and independent variables, t-test was used for continuous variables and Chi-square for categorical variables. Any P-value less than 0.05 considered significant. All the this analysis was conducted through SPSS V 20.

Results

Baseline demographic characteristics: A total of 29 patients matched the inclusion criteria and were enrolled in the study. Matching the inclusion criteria. The demographic and tumor characteristics of these patients are shown in table 1. The median age at presentation was 3 years. Patients were divided into two groups based on age at presentation: 3 years or younger, which constituted 32% (9 patients) of the study population, or above 3 years of age which included most patients (68%). Classifications according to the location of the tumor were grouped into two groups.

	Ependymoma Tumor Location, number of patients (%)			Total	P value
	Posterior fossa + Spine	Supratentorial		N	
Age					
<3	4(44.4%)	5 (55	5 (55.6%)		0.422
≥3	13(65.0%)	7(3:	5%)	20	
Gender					
Male	8(40.0%)	12(60).0%)	20	0.003*
Female	9(100%)	0(0	0(0%)		
WHO grade					
1 and 2	5(100%)	0(0	0(0%)		0.059
3	12(50%)	12(5	0%)	24	
Clinical presen- tation					
Headache	7(70%)	3(30%)		10	0.449
Seizure	0 (0%)	5 (100%)		5	0.007*
Vomiting	11(73.3%)	4(26.7%)		15	0.139
Abnormal Gait	9(75%)	3(25.0%)		13	0.251
Number of sur- gery					
One Surgery	9(69.2%)	4(30.8%)		13	0.451
Multiple Sur- geries	8(50%)	8(50%)		16	
Type of 1 st Surgery					
Partial Resection	4(44.4%)	5(55.6%)		9	0.422
Complete Resection	13(65%)	7(35%)		20	
Type of 2 nd Surgery					
Partial Resection	1(16.7%)	5(83.3%)	6		
Complete Resection	7(70%)	3(30%)	10		
Molecular tests if available	2 (25.0%)	6(75.0%)	8		
Radiation thera- py Received	14(56.0%)	11(44.0%)	25		
Received Che- motherapy	4(50%)	4(50%)	8		
Complications of the Tumor					
Vision affected	7(70.0%)	3(30.0%)	10		
Feeding affected	1(33.3%)	2(66.7%)	3		

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Neurogenic bladder	1(100%)	0(0%)	1	
Wheelchair bound	1(100%)	0(0%)	1	
CSF Metastasis	1(100%)	0(0%)	1	
Associated syndrome	0(0%)	0(0%)	0	
Survival after 1 year	17(60.2%)	11(39.3%)	29	
Survival after 5 years	15(60%)	10(40%)	25	
Death	2(40%)	3(60%)	5	

Patients in this study were divided into two groups based on the location of the ependymoma: Supratentorial, and infratentorial group. Infratentorial includes tumors in the consisted of (Posterior fossa and spine as one entity). The infratentorial masses were the most common, present in presentation with 17 patients (58%) while the supratentorial were 12 patients (41%) exhibited supratentorial masses. Males were predominant in our population, with the male to female ratio of were 2.2: 1 making male as the predominate gender. Interestingly, all the females (9 patients) included in the study had 9 patients (100%) were all from posterior fossa and spinal tumor group with no females getting affected with supratentorial tumor infratentorial tumor, whereas, supratentorial tumor accounted for the majority of tumors in males (60%)., while 12 patients (60%) of all the males had supratentorial tumors. As the median age at presentations was 3 years. Age at presentation was classified to below and above 3 years. 20 patients (68%) presented above 3 years of ages. According to the WHO classifications, most of the eEpendymoma in our investigations were staged as stage III. Only five 5 patients had only were staged as grade I- and II ependymoma at presentation, while 24 (82%) patients were stage III making them the majority with 82%. The most frequent presenting clinical manifestations were Vomiting, Ataxia and Headache. Patients frequently presented with vomiting (51%), ataxia (44%) and headache (34%) as their initial chief complaint. Only five (17%) patients presented with seizure as the primary complaint. Notably, all the five patients were 51%, 0.44% and 34% in sequence. Although 5 patients (17%) only had seizures during first diagnosis, but had significantly 100% of them were supratentorial tumors (P-value = with p value 0.007). None syndrome in both groups in our study.

Ependymoma molecular characterization

All of the patients underwent surgical resection. Many patients had to go for multiple surgeries (more than one) during the course of treatment. Unfortunately, 16 out 29 patients (55%) suffered from multiple surgeries although 20 patients (68%) of our patients managed to have a complete (Gross total resection) during their first surgery. However, 10 patients (62%) of all the patients who had a second surgery managed successfully to have gross total, or complete, resection again.

Course of treatment and outcomes

Table 2. Summarizes the tumor characteristics, course of treatment and outcome of the included patients. All the patients in this investigation underwent surgical resection. Gross total resection through a single surgical intervention was successful in 20 patients (68%). Unfortunately, 16 out 29 patients (55%) suffered from multiple surgeries although 20 patients (68%) of our patients managed to have a complete (Gross total resection) during their first surgery. However, 10 patients (62%) of all the patients who had a second surgery managed successfully to have gross total, or complete, resection again.

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	Ependymoma Tumor Location, number of patients (%)		Total	P value			
	Posterior fos- sa + Spine	Supratentorial	N				
Number of surgeries			-				
One Surgery	9 (69.2%)	4 (30.8%)	13	0.451			
Multiple Sur- geries	8 (50%)	8 (50%)	16				
Type of 1 st Surgery							
Partial Resection		4(44.4%)	5(55.6%)	9	0.422		
Complete Resection		13(65%)	7(35%)	20			
Type of 2 nd Sur- gery							
Partial Resection		1(16.7%)	5(83.3%)	6	0.039*		
Complete Resection		7(70%)	3(30%)	10			
Molecular tests if available		2 (25.0%)	6(75.0%)	8	0.038*		
Radiation therapy Received		14(56.0%)	11(44.0%)	25	0.622		
Received Chemotherapy		4(50%)	4(50%)	8	0.683		
Complications of the Tumor							
Vision affected		7(70.0%)	3(30.0%)	10	0.678		
Feeding affected		1(33.3%)	2(66.7%)	3	0.543		
Neurogenic bladder		1(100%)	0(0%)	1	1		
Wheelchair bound		1(100%)	0(0%) 1		1		
CSF Metastasis		1(100%)	0(0%)	1	1		
Associated syndrome		0(0%)	0(0%)	0	1		
Survival after 1 year		17(60.2%)	11(39.3%)	29	0.414		
Survival after 5 years		15(60%)	10(40%)	25 1			
Death		2(40%)	3(60%)	5	0.622		
Table 2: Course of treatment and outcome.							

Since radiation therapy is considered the standard of care with childhood eEpendymoma, 25 (86%) patients received radiation. Six6 patients of them (24% of all the ones who required radiation) were less than< 3 years of age, while 19 patients were above 3 years (76% of all the ones who required radiation). None of the patient received proton therapy due to unavailability of this modality of treatment. On the other hand, chemotherapy is still a debatable issue in the treatment of childhood eEpendymoma. Eight8 patients (27%) received chemotherapy during the course of during treatment. All of all these patients had aim were for patients with WHO grade III ependymoma. Impairment of the visual fields and squint are common complications expected during the course of during treatment that might occur secondary to the, due to complications of the surgical interventionery or secondary due to the nature and location of the tumor. Visual field was affected in 10 patients (34%). Most of these patients (90%) had of them were from WHO Grade III classification, and 70% had a were due to Posterior fossa masses. Other complications that might heavily affect the affecting social life, such as like feeding difficulties, neurogenic bladder, refractory seizures, and becoming wheelchair bound were faced in four4 (14%) of the patients, all of whom had and all of

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them where with WHO grade III tumor. The overall prognosis of the ependymoma in our study was 82% after 5 years from diagnosis. Out of all the patients who died secondary due to eEpendymoma, 80% survived were able to manage to survive at after 1 year from of diagnosis.

Discussion

Data from the national cancer registry in the region is quite limited and missing updated information, especially when it comes to brain tumors. Show ever, since the initiation opening of the Children Cancer Center of Lebanon (CCCL) in 2002, 29 cases of childhood eEpendymoma cases were encountered accounting for 29 cases, out of all the 329 Brain tumor cases, making it 8.8% of all the brain tumors in children. This incidence rate goes along with the international incidence rate reported in literature [2].

Childhood Ependymoma occurs more frequently in males, as was also noted. It was noticed in our statistics. As the ratio between male: female was 2.2: 1 with a significant p value. Regionally and internationally ratios were almost consistent [3,4,7]. Until now, clear explanation couldn't be reached clarified.

Needless to comment on the fact that of molecular diagnosis is a new advanced technique in classifications of patients with ependymoma. A, the lack of complete molecular evaluations specifications of the molecular specificity of the tumors could have predicted prognosis and recurrence. Posterior fossa eEpendymoma with chromosome 1 q gain carries a bad omen as being classified with poor, intermediate and good prognosis [18]. Detecting only two2 patients with only with chromosome 1 q gain on the posterior fossa group tumors in our sample is considered a backflow step in the clinical management especially that none hat all of them didn't survived. Lack of specialized labs as most of them were overseas, coupled with severe and, limitations in lack of financial coverage, especially that such and as it is considered a new technological diagnosis are expensive, were the main reasons for the little number of the lack of molecular profile in most patients molecularly diagnosed patients. Since comparison of chemotherapy versus radiation is an unjustified able comparison to the effect of chemotherapy on Ependymoma. None of our patients had myeloablative hematopoietic stem cell transplant, neither as adjuvant or neoadjuvant chemotherapy. Besides, hhematopoietic stem cell transplant has provided no historical superiority over conventional chemotherapy [16].

The option of targeted therapy was experienced in one patient, who received dasatinib, sirolimus and tretinoin with unfortunate success and the disease progressioned. Perruccio et al [19]. has tried trial of sirolimus and nivolumab, which were well was tolerated, however, the trial was also well by the patient but trial had to be aborted due to evidence of disease the progression of the disease. In our study, posterior fossa eEpendymoma has shown superior outcome in terms of 5- year's survival compared to over the supratentorial eEpendymoma, with (88.2%) vs. to 75% 5-year survival rate respectively in sequence. Our data goes as our data is going along with that obtained by Hammad et al [3], while it is contradicting other reports. The dilemma of considering the depending on tumor location, as supratentorial or posterior fossa, as a prognostic factor requires broader studies could be finalized with larger population broader sample size and wider variability, or a with future prognostic cohort study.

The fact of relatively low that a relatively small number of the patients became were wheelchair bound or bed-ridden secondary to the due to direct complications of surgical or radiation therapy provide encouraging data treatment, give an encouraging optimistic hope regarding on the current pathway of treatment. Even though, the sample size was limited, especially the spinal type eEpendymoma, different international investigators reported similar low rate of ly with minimal complications [20]. Moreover, organ metastasis has been documented in the literature as one of major complications affecting prognosis of eEpendymoma [21,22], none of our patients had distant metastasis at the initial presentation or during the course of treatment. Also this result may need to be confirmed with a larger sample size.

Conclusion

The 5-year survival rate of prognosis of eEpendymoma in this study compared to other studies reported in the region and other international investigators were in our investigation was 82%. After 5 years from diagnosis. The role of chemotherapy and targeted therapy need to be addressed in more prospective well-defined protocols to achieve better survival rate. Molecular staging should be implanted more often, with further extensive investigation of the role of the molecular characterization in determining the prognosis of the disease depending upon specialized labs. The emphasis of the role of specialized course and outcome of childhood ependymoma in the region, however further larger and time-extended studies are definitely required.

Funding and Conflict of Interest

The authors declare that there is no conflict of interest and the study was not funded by any institution.

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