

Intracranial Ependymomas in Children the Role of Surgery and the Adjuvant Therapy

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Abstract

The purpose: The management of intracranial ependymomas represents a real challenge and the perfect treatment modality remains controversial. The goal of this study is to highlight the role of tumour removal and the adjuvant therapy in the survival rate of children presenting with intracranial ependymomas.

Patients and methods: This retrospective study of 56 children presenting with non-metastatic intracranial ependymomas treated in the period between 2015 and 2020. The age varies from 3 months to 15 years while the mean age was 8 years. The infra tentorial location was found in 67.8%.

Result: The total resection of the tumour was achieved in only 42.8% of cases, whereas the subtotal resection was performed in 35.7%. More than 50% of tumours were grade I and II of the WHO classification (grade I: 12 cases, grade II: 18 cases). 44.6% were anaplastic ependymomas (grade III: 25 cases). More than half of our cases had initial adjuvant radiotherapy (55.3%) and 21.4% had chemotherapy. 4 children had both radiotherapy and chemotherapy. Complications that were found in our series were 6 cases of CSF fistula in the origin of 4 cases of meningitis, 9 cases of neurological deterioration with 2 cases of post-operative seizures and 2 other cases of intra ventricular haemorrhage. The mortality rate after 38 months was 7.1% (4 cases). The Follow-up length was 5 years.

Conclusion: The role of surgery and the extent of resection in the intracranial ependymomas in children remains the most important factor in the global management of this type of intracranial tumour. adjuvant radiotherapy helps achieving a survival rate for the anaplastic types and recurrences.

Keywords: Anaplastic ependymomas; Ependymomas; Radiotherapy

Introduction

Ependymomas are neuro epithelial tumours derived from a neoplastic transformation of ependymal cells that line the ependymal cavity and take part in the glial group of tumours representing 2-9% of all intra cranial tumours and more than 12% of intra cranial tumours in children. 75% of these tumours are located in the posterior cerebral fossa [1-3]. The first histological description of ependymomas was performed by Virchow in 1864. Bailey and Cushing in 1926 classified ependymomas among the glial tumours [1]. Ependymomas of the posterior cerebral fossa affect particularly young infants, whereas the supra tentorial location affects older children, adolescents and adults [1-3]. These tumours manifest clinically with a high intra cranial pressure cerebellar syndrome and focal neurological symptoms. The insertion of posterior fossa ependymomas adhere to the floor of the 4th ventricle (in 80%) and more precisely in the bulbar triangle in contact with vital neurological structures. In this location, ependymomas can develop through the magendie hole to gain size in the cervical subarachnoid space or toward the ponto cerebellar angle and distal cranial nerves through the luschka hole. The upward extension toward the 3rd ventricle is exceptional through the sylvius aqueduct. Their treatment is surgical and can be completed by radiotherapy and/or chemotherapy as an adjuvant therapy [2-5]. In addition to the problem of the extent of

resection, which is usually incomplete due to their location, the prognostic of ependymomas is difficult to predict due to their risk of recurrence and the possibility of distant metastatic implantation through CSF pathways [5]. Radiotherapy has an important role in the treatment of recurrent ependymomas as well as the anaplastic types [2,6].

Patients and Methods

We are presenting a retrospective study of 56 patients operated in the period between 2015 and 2020 at chercell specialized hospital in Algiers. Female predominance was found in our serie (29 females and 27 males). The mean age was 8 years with extremes varying from 3 months to 15 years.

Result

Location

The infratentorial location of intracranial ependymomas in children was found in 36 cases (67.8%) whereas the supra tentorial location concerned 18 patients (32.2%). In detail, the infra tentorial location reflects many precise locations of these tumours (Table 1):

- 18 cases of ependymomas of the floor of the 4th ventricle (Figure 1).
- 4 cases of ependymomas with extension toward the bulbo medullar junction and the second cervical vertebra.
- 12 cases of the roof of the 4th ventricle.
- 7 cases of the lateral recess with extension toward the homolateral cerebellar pontine angle (Figure 2).

Table 1: Number of the main clinical symptoms. Clinical features are multiform.

Semiology	Number
Intracranial Pressure	50 cases
Cerebellar Syndrome	28 cases
Hemiparesis	11 cases
Macrocrania	12 cases
Seizures	4 cases
Frontal Syndrome	2 cases
Coma	8 cases

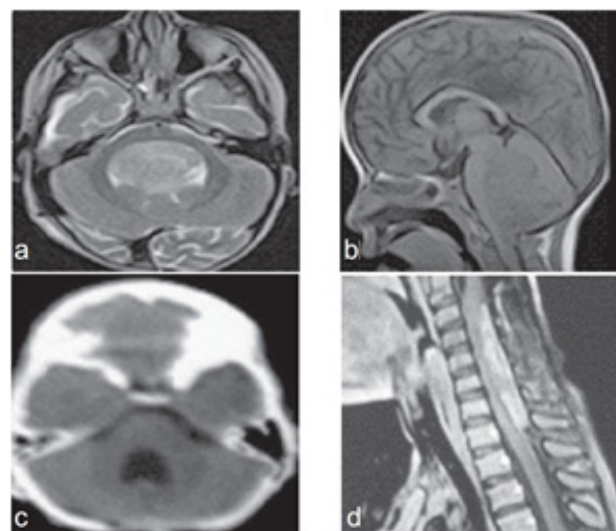


Figure 1: a, b: Preoperative MRI in sagittal and axial views show an important ependymomas of the Posterior cranial fossa with cisternal extension.
c: Early post-operative CT scan showing the extent of the tumour removal after Radiotherapy.
d: Image of cervical MRI in sagittal view show a cervical ependymoma in the same patient after 3years follow-up.



Figure 2: a, b: preoperative CT scan showing an ependymoma of the roof of the 4th ventricle with extension toward the cerebello pontine angle.
c: MRI in sagittal view showing the quality of resection after radiotherapy and two years follow up.

The supra tentorial location involved

- i. 11 cases of lateral ventricle (Figure 3).
- ii. 1 case was para ventricular.
- iii. 6 cases were para and intra ventricular (Figure 4).

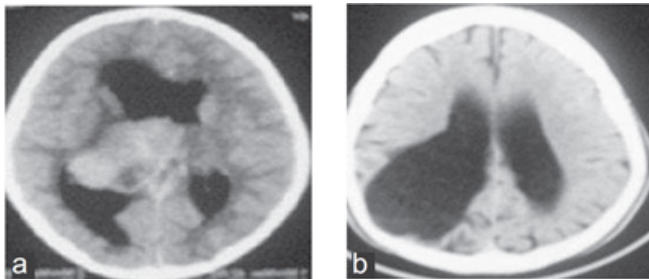


Figure 3: CT scan of intraventricular ependymoma (a) and the extent of the resection after 4 years follow up (b).

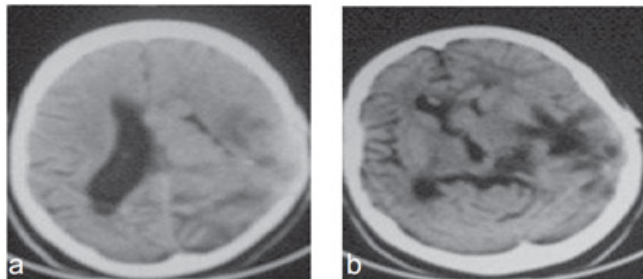


Figure 4: Preoperative CT scan (a) of an intra ventricular ependymoma and post-operative image showing the resection quality (b).

Extent of tumour removal

Post-operative imaging (CT scan and MRI) were used to assess the extent of the tumour removal. The majority of our patients underwent CT scan immediately after surgery (Table 2). MRI was performed after a few weeks to evaluate the extent of the tumour resection. The Gross total resection was achieved in 42.8% of patients (25 cases), whereas 25 others had a subtotal resection of infra tentorial locations of the studied ependymomas in Children.

Table 2: Patients features with treatment modality.

Patients	Number
Gender	
Male	27
Female	29
WHO Classification Grade	
Grade I	13
Grade II	18
Grade III	25
Tumour Location	
Infra Tentorial	38
Supra Tentorial	18

Extent of Tumour Resection	
Subtotal/Partial resection	31
Total resection	25
Chemotherapy	12
Radiotherapy	31
Radio-chemotherapy	4

Histological grade

More than half of tumours were ependymomas myxopapillary or sub ependymomas of grade I and II of the WHO classification of CNS tumours. 12 cases were grade I and 18 were grade II. The grade III anaplastic ependymomas were found in 44.6% of cases (25 cases).

Adjuvant treatment

More than half of our patients (55.3%) have had radiotherapy as a complementary treatment initially, whereas 21.4% of them received chemotherapy. 4 children received both radiotherapy and chemotherapy.

Morbidity

In the post-operative period, we have recorded complications listed below:

- i. 6 cases of CSF fistula after surgery of 6 cases of infra tentorial ependymomas. 4 cases presented meningitis and were treated with targeted antibiotics.
- ii. One case presented with a cervical metastasis was re-operated few months after the first surgery with anatomical pathological finding showed an ependymoma.
- iii. Two patients presented with post-operative intra cranial pressure due to mal function of VP shunt, they improved after revision.

Prognostic

All our patients were followed up regularly after 36 months especially those for which the tumour removal was not complete and who have had radiotherapy or chemotherapy. The residual tumour was unchanged and was followed up by oncologists and neurosurgeons. Two cases of supratentorial ependymomas show a late recurrence and were re operated on with an adjuvant chemotherapy. 4 cases of mortality were recorded in the period of 38 months after surgery.

Discussion

The intra cranial ependymomas represent the third more frequent tumour of the central nervous system in children. Although these tumours can affect patients of every age, 50% of intra cranial ependymomas involve children under 5 years old affecting particularly the infra tentorial compartment in 70-80%. The

intracranial ependymomas affects the supra tentorial compartment in adults [6-8]. In our Serie, the infratentorial location was found in 67.8%. In the infancy, Ependymomas are particularly malignant which is different from tumours diagnosed in older children of 10-15 years of age which have a lower grade. The surgical removal of ependymomas is difficult due to its close relationship to the brainstem, cranial nerves. This feature reflects a dilemma between a total resection with a high risk of morbidity and partial resection with high risk of recurrence and a good post-operative outcome. Many studies argue that the total resection offers a better long-term control. Ikezaki [9] consider that the location and the size of infra tentorial ependymomas were important factors for long term prognosis. The infratentorial ependymomas are then classified into: ependymomas of the roof, floor and the lateral recess of the fourth ventricle. In the latter, the tumour encases cranial nerves IX, X, XI, XII and adhere to the brainstem [10].

The majority of authors agree that the anaplastic type has a poor prognosis whereas the prognosis is variable for the other types of ependymomas. Also, less than 5% of ependymomas are infiltrative at the time of diagnosis which was not taken into account in the classification of patients. In the other hand biomarkers under study could be good prognosis predictors. One of the most important challenges in the management of intra cranial ependymomas is to determine the most optimal multimodal therapy for these tumours. Surgery has an important role in the treatment of intracranial ependymomas and the extent of resection influence highly the overall prognosis. Nowadays, majority of authors agree to perform surgery on these patients and tend to achieve the most complete resection followed by radiotherapy. In series published by Sutton et al., the survival rate after 5 years was 60% for patients who had a total or subtotal removal against 21% for children who had partial removal or biopsy [11]. However, surgery is rarely curative and recurrences are mainly local.

In our Serie the total resection was achieved in 42.8% of cases (25 cases) with a partial resection in 35.7%. The survival rate after 5 years was 88% after surgery followed by radio therapy. Shu et al. [7] report a survival rate of 40.7-66.2% with a mean

survival length of 110.2 months according to a Serie of 49 infants treated at university hospital in Pennsylvania [10]. Mansur, et al. followed up 60 patients in 10 years and had a survival rate of 49.5-55% at Washington university school of medicine with a mean survival length of 12.5 years [12]. Paulino [8] followed up 49 children for 9.6 years and had a survival rate of 60.3-71.4% with 5 years of local control. The conventional radiotherapy has good tumour control after total resection. Radiotherapy should include brainstem and cervical medulla and has less effects on neurocognitive function according to the literature [13-16]. There is no consensus concerning the age to receive radiotherapy, certain authors used radiotherapy in children of 1 year. The benefit of chemotherapy is far from being proved. Some studies suggested that there is no benefit to add chemotherapy concomitant or after radiotherapy. On the other hand, other studies show the efficiency of chemotherapy in anaplastic ependymoma before radiotherapy [17]. Other authors tried to use chemotherapy to delay the need of radiotherapy particularly for vulnerable patients who cannot handle the effect of radiotherapy such as children younger than 3 years old. Ependymomas in children is one of the most frustrating pathologies that the neurosurgeon face from the prognosis point of view. Factors such as age, location, extend of the resection, histological type and the efficiency of complementary treatment are not sufficient to predict the prognosis. Nowadays, molecular biology is interesting for many authors and can identify a group of a poor prognosis with poor global survival. The therapeutic strategy could be then targeted better [18].

Conclusion

Ependymomas are relatively aggressive and resistant to adjuvant therapies. The severity observed during evolution of ependymomas is related to risk of recurrence and CSF metastasis. The total removal of ependymomas is particularly difficult due to their situation inside the ventricular cavity but that remains the best option to achieve a long survival [19-23] (Table 3). In the opposite, the attempt to a total resection exposes the patient to serious morbidity. Adjuvant radiotherapy for patients with a low risk who had complete resection is reasonable option.

Table 3: Survival rate of children after surgical resection followed by radiotherapy according to different series of the literature.

Serie	Number of Patients with Total Resection	Radiotherapy Dose (Gy)	Survival Rate After 5 Years (%)
Mansur & al	14	50	69
Massimino & al [13]	46	70	82
Perilongo & al [12]	53	>45	57
Rousseau & al [3]	38	50	51
Robertson & al [19]	15	54	79
Schroeder & al [20]	17	54	82
Shu & al [7]	13	Variable	83
Hukin & al	4	No	100 (3years)

Palma & al	6	No	83 (3years)
Awaad & al	10	No	71 (3 years)
Paulino & al [8]	21	54	75
Our Serie	25	54	88

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