I J C R M
International Journal of Contemporary Research In Multidisciplinary

Case Report

Ependymoma: Clinic and Treatment

Virginia.Cirolla[1*] and G.Scarzello[2]
[1]MD, Ph.D. (Oncology), UOC of Oncological Radiotherapy at La Sapienza University of Rome/University of Padua, Italy
[2]Director of Radiotherapy Unit Iov/University of Padua, Italy

Corresponding Author: *Virginia.Cirolla

DOI: https://doi.org/10.5281/zenodo.12627052

Abstract

This case study focuses on a patient with a posterior cranial fossa ependymoma, highlighting its clinical presentation, treatment, and challenges. Ependymomas, more frequent in children within the cerebrum and cerebellum and in adults within the spinal cord, account for less than 3.5% of brain tumors. Infratentorial ependymomas, commonly located in the fourth ventricle, present with intracranial hypertension and focal neurological deficits due to their mass effect and hydrocephalus. The patient, following initial surgery with residual tumor, underwent external radiotherapy per the SIOP Ependymoma protocol, receiving a total of 67.4 Gy under sedation. Post-treatment, the patient exhibited significant hearing loss, dysgraphia, and dyscalculia. These symptoms, particularly the hearing impairment, significantly impacted the patient's quality of life, causing agitation and spatial orientation issues. A rehabilitation project in collaboration with AISMO ODV, Harvard University, and MIT aims to address the hearing loss using engineered molecules to stimulate ciliary stem cells. Prognostic factors for ependymoma include age at diagnosis, histological grade, disease dissemination, brainstem involvement, and extent of surgical excision. The patient's prognosis remains guarded with a 5-year survival rate between 50-64%, dependent on these variables. This case underscores the complexity of ependymoma management and the importance of multidisciplinary approaches in addressing associated morbidities.

Manuscript Information

- **ISSN No:** 2583-7397
- **Received:** 19-05-2024
- **Accepted:** 21-06-2024
- **Published:** 30-06-2024
- **IJCRM:**3(3); 2024: 190-193

- **Plagiarism Checked:** Yes
- **Peer Review Process:** Yes

How to Cite this Manuscript

Virginia. Cirolla, G. Scarzello. Ependymoma: Clinic and Treatment. International Journal of Contemporary Research in Multidisciplinary.2024; 3(3): 190-193.

KEYWORDS: Ependymoma, Pediatric Patients, Lateral Ventricle, Radiotherapy, Ponto-Cerebellar Angle

Ependymoma is a tumor of the central nervous system and is part of a group of tumors called gliomas. The central nervous system is composed of neurons (the cells that receive, process and transmit nerve impulses) and supporting cells called glial cells (or glial cells). There are four types of glial cells: astrocytes, oligodendrocytes, ependymal cells and microglial cells. Ependymal cells are cubic-shaped cells that line the cavities around the brain and spinal cord where the cerebrospinal fluid (or liquor), produced by the ependymal cells themselves, flows. However, they can also be found inside the cerebrum and cerebellum. When a healthy glial cell turns into a tumor and begins to multiply uncontrollably, it gives rise to a glioma. If the cell in question is an ependymal cell, the tumor that forms is called an ependymoma. In children, ependymomas are generally located within the cerebrum and cerebellum, while in adults they form more frequently in the spinal cord. They represent < 3.5% of brain tumors. The information comes from retrospective series, observed over long periods of time and often including both adult and pediatric patients. Ependymomas are more frequently infratentorial (60-80%), especially localized in the fourth ventricle. The second most frequent location is the lateral ventricle, followed by the third ventricle. The clinical picture varies depending on the location and size of the lesion. Intraventricular ependymomas often present with signs and

symptoms of intracranial hypertension due to hydrocephalus, due to the mass effect of the lesion or obstruction of the CSF pathway. Depending on the anatomical location, focal neurological symptoms and signs will be added. In the case of a lesion in the posterior cranial fossa, the initial symptoms may also be represented by paresis of the cranial nerves, cerebellar deficits and/or stiff neck due to infiltration of the upper portion of the cervical cord. The incidence of spinal dissemination depends on the location (1.6% for supratentorial lesions vs 9.7% for infratentorial lesions)

-peak incidence between 4 and 6 years
- approximately 1/3 diagnosed before the age of 3
- M/F=1/4:1
- Mostly benign (WHO grade II)
- Mostly benign (WHO grade III)
-Locally invasive (rarely radical surgery)
- Arises from the ependymal cells of the cerebral ventricles (IV ventricle) and the centromedullary canal
-90% of ependymoma cases are intracranial
- 1/3 supratentorial
- 2/3 infratentorial
-60% from the floor of the 4th ventricle with extension through the foramen of Magendi
- 30% from the lateral walls with extension through the foramina of Luschka and involvement of the cranial nerves of the ponto-cerebellar angle
-10% from the roof
- 10% of cases are spinal
- 5% leptomeningeal dissemination

Ependymoma with RELA fusion gene is an ependymoma that arises in a supratentorial location, is often anaplastic (grade III) and is more aggressive than forms without the fusion.

• Grade II intramedullary ependymomas are associated with NF2 (The NF2 gene is a tumor suppressor gene that controls cell replication and the integrity of the genetic heritage) appear in the second and third decades of life and are curable with surgical therapy alone. Their clinical evolution when associated with NF2 can be indolent and one can limit oneself to neuroradiological surveillance without proceeding to surgical removal. In case of suspected isolated spinal ependymoma, other manifestations of the possible genetic disease must be excluded.

FATTORI PROGNOSTICI

Age, sex, location, size of the neoplasm, Ki 67 and surgical radicality are identified as the main independent prognostic factors

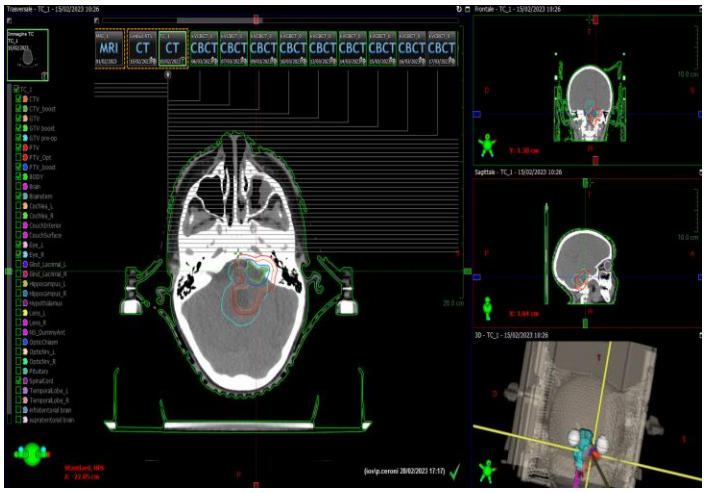
• Female patients appear to have a better prognosis than males.

• Adult patients appear to have a better 5-year survival than children (55-90%) versus 14-60%). Among adult patients, age < 40 years has been indicated as a favorable prognostic factor by some authors, while others have found no differences in survival using other age cut-offs (50-55 years)

• The location of the neoplasm is another controversial prognostic factor: the infratentorial location would be unfavorable. On the contrary, according to an analysis conducted on 1300 patients, with localization in the posterior cranial fossa they had a better survival than the supratentorial forms.

Studies on post-surgical radiotherapy of adult ependymomas are retrospective and descriptive without it being possible to know the selection criteria for treatment. No high-quality recommendations can be made on the indications for post-operative radiotherapy treatment. Numerous retrospective studies show a significant improvement in survival for patients treated with radiotherapy, going from 5-year survival values of 0.27% to 36.5%-87%. A recent analysis conducted on 1787 patients registered in the US National Cancer Database excludes the association between adjuvant radiotherapy and survival Prospective studies are ongoing and involve patients who have residual tumor after surgery. For these children it was important to verify the possibility of repeating a further operation to remove the tumor and even when this approach was not sufficient, to carry out a targeted dose of radiotherapy with precision techniques so as to exclusively target the residue. Much of these results have served as a premise for building the European treatment plan for ependymoma which is underway in 17 countries, work which concerns children with post-surgical residue as published in Neuro-Oncology, Volume 24, Issue Supplement_1, June 2022, Page i44,

The volume of radiotherapy treatment must be limited to the operating bed and any residual macroscopic disease. Craniospinal irradiation should be considered for patients with evidence of disseminated disease. Although solid recommendations on the extent of the CTV cannot be drawn from the analysis of the literature, the irradiated volume should include the operating bed and any macroscopic residues of disease with a margin of 1 cm. Due to the heterogeneity of the doses administered in the various clinical experiences it is problematic to formulate solid recommendations in this regard. In general, a total dose of 50.4-54 Gy is indicated for grade II ependymomas and >-54 Gy more often equal to 59.4/60 Gy for grade III ependymomas. Cases with leptomeningeal or spinal disseminated disease should receive craniospinal irradiation with doses ranging from 30 to 36 Gy.



Treatment of Relapses

At the onset of recurrence, patients must be restaged with MRI of the entire axis since leptomeningeal dissemination is a frequent event (up to 30%) in grade III tumors. In case of local recurrence, surgical reevaluation is indicated.

Irradiation with conventional or radio surgical techniques may be considered. Chemotherapy with regimens containing cisplatin, nitrosoureas or Temozolomide may be indicated for the treatment of relapses after surgery and radiotherapy. There are some reports of the possible effectiveness of bevacizumab

Follow up

• Follow-up with serial MRI must be performed regularly also in light of

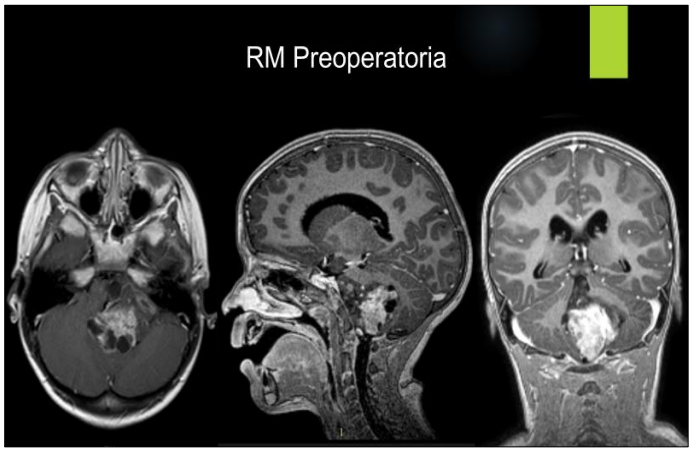
• fact that disease recurrences can be asymptomatic in up to 43% of cases.

• The frequency of follow up depends on prognostic factors such as grade of malignancy, age

• and performance status

Diagnosis

- CT and MRI + contrast medium
- Entire brain and medulla CT and MRI + contrast medium
- Cytological examination of the CSF

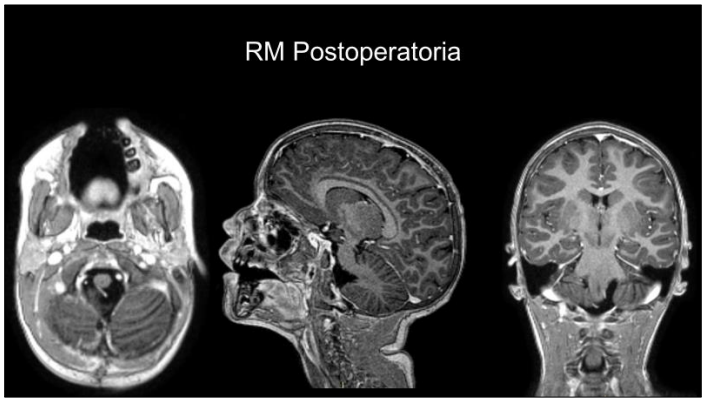


Treatment

- Surgical excision: primary treatment
  RT following surgery: Not necessary if
- Grade II ependymoma with GTR
- Intramedullary ependymoma
- Craniospinal if - leptomeningeal dissemination
- Chemotherapy-Unclear benefit
- Cisplatin as the most active drug
- It can facilitate surgical removal (second look)
- It can be useful for postponing RT

Surgical excision

- GTR: 67-80% survival to 5 years; PFS 51-75%
- Subtotal resection: 22-47% survival 5 years; PFS 0-26%
- If it recurs
- Surgery
- CHT before Surgery (to reduce vascularity).



Clinical Case

• Patient arrives in the Radiotherapy Unit with a diagnosis of EPENDYMOMA OF THE POSTERIOR CRANIAL FOSSA and has already undergone SURGERY WITH RESIDUE and CT according to the SIOP Ependymoma protocol

• Performs centering CT scan (white mould) under sedation to prepare the radiation treatment plan

• Performs external radiotherapy on the tumor bed and on the residue in the left internal auditory canal at a dose of 59.4 Gy /33 f + boost on the residue for a further 8 Gy /2 f, under sedation (Midazolam 1 mg administered pre-induction with Propofol).

• Good tolerance

• The area is inspected during the physical examination: significant hearing loss which creates agitation and makes the patient scared.

• At the request of the Specialist Doctor in Training, he carries out a drawing with numbers and a writing and the presence of dysgraphia and dyscalculia which have occurred in the patient for over 3 years and without a specific diagnosis emerges

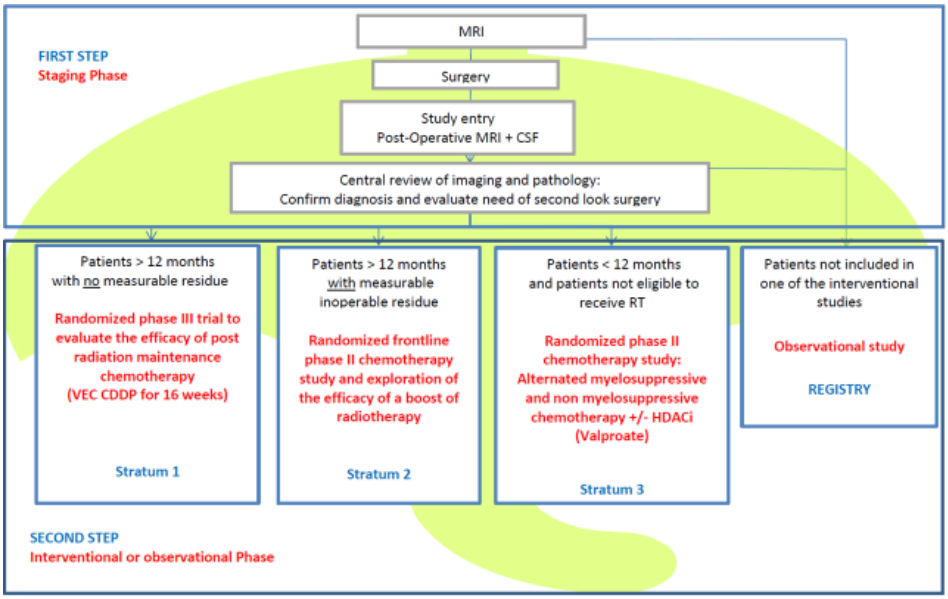
• Interview with the Iov head doctor of pediatric brain tumors, to verify whether or not the symptoms can be associated with the diagnosis of ependymoma, and the outcome of the operation.

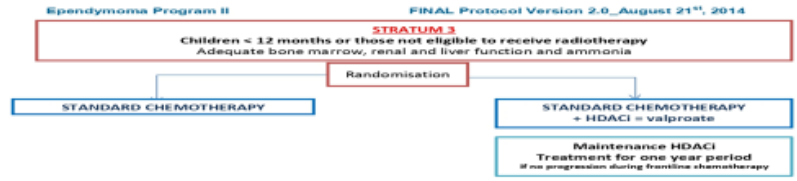
• The most uncomfortable pathology in the child is certainly hearing loss which on video creates relationship and orientation problems in space and autonomy

• In collaboration with AISMO ODV, the rehabilitation project for hearing loss associated with pediatric brain tumors starts in collaboration with Harvard University and the Massachusetts Institute of Technology (MIT), on engineered molecules capable of stimulating the ciliary stem cells of the pavilion

Prognosis

- Prognosis depends on:
-Age at diagnosis (<3 years)
- Histological grade
- Dissemination of the disease at diagnosis
- Brainstem involvement (infiltration)
- Degree of surgical excision
- Survival to 5 years: 50-64%





	CHEMO +/- HDACI**						
CYCLE N°	1	2	3	4	5	6	7
Vincristine - Carboplatin	D1	D 57	D113	D169	D225	D281	D337
Vincristine - Methotrexate	D15	D 71	D127	D183	D239	D295	D351
Vincristine - Cyclophosphamide	D29	D 85	D141	D197	D253	D309	D365
Cisplatin 2-day Continuous infusion	D43 44	D99 100	D154 155	D211 212	D267 268	D323 324	D379 380
+/- Valproate (*)	Initial dose: 30 mg /kg/day for two weeks in 2 divided doses (BID 15mg/Kg) Increasing weekly up to 40->50->60 mg /kg/day in 2 divided doses until serum target level of 100-150 µg/ml achieved.						

Dosing schedule according to age	Dose > 12 months (m²)	Dose for infants 6 to 12 months (m²)	Dose for infants < 6 months (m²)
Vincristine	1.5 mg/m² x 1	1.125 mg/m² x 1	0.75 mg/m² x 1
Carboplatin	550 mg/m²x 1	412.5 mg/m² x 1	275 mg/m² x 1
Methotrexate	8000 mg/m² x 1	6000 mg/m² x 1	4000 mg/m² x 1
Cyclophosphamide	1500 mg/m² x 1	1125 mg/m² x 1	750 mg/m² x 1
Cisplatin	40 mg/m² x 2	30 mg/m² x 2	20 mg/m² x 2
Valproate * (BID)	30 mg/kg/day*	30 mg/kg/day*	30 mg/kg/day*

* Initial dosing then according to monitoring
** If residual disease please consider for further surgery at each reassessment point.

REFERENCES

1. Gerstner ER, Pajtler KW. Ependymoma. InSeminars in neurology 2018 Feb (Vol. 38, No. 01, pp. 104-111). Thieme Medical Publishers.
2. Acquaye AA, Vera E, Gilbert MR, Armstrong TS. Clinical presentation and outcomes for adult ependymoma patients. Cancer. 2017 Feb 1;123(3):494-501.
3. Merchant TE. Current clinical challenges in childhood ependymoma: a focused review. Journal of Clinical Oncology. 2017 Jul 20;35(21):2364-9.
4. Schild SE, Nisi K, Scheithauer BW, Wong WW, Lyons MK, Schomberg PJ, Shaw EG. The results of radiotherapy for ependymomas: the Mayo Clinic experience. International Journal of Radiation Oncology* Biology* Physics. 1998 Dec 1;42(5):953-8.
5. Wright KD, Gajjar A. Current treatment options for pediatric and adult patients with ependymoma. Current treatment options in oncology. 2012 Dec;13:465-77.