

# Solid Tumour Section

## Mini Review

## Nervous system: Ependymomas

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### Identity

**Note:** Ependymomal neoplasms are tumors of children and young adults, originating from the cerebral ventricle or from the spinal canal. In the central nervous system (CNS), they account for 3,9 % of all neuro-epithelial tumors.

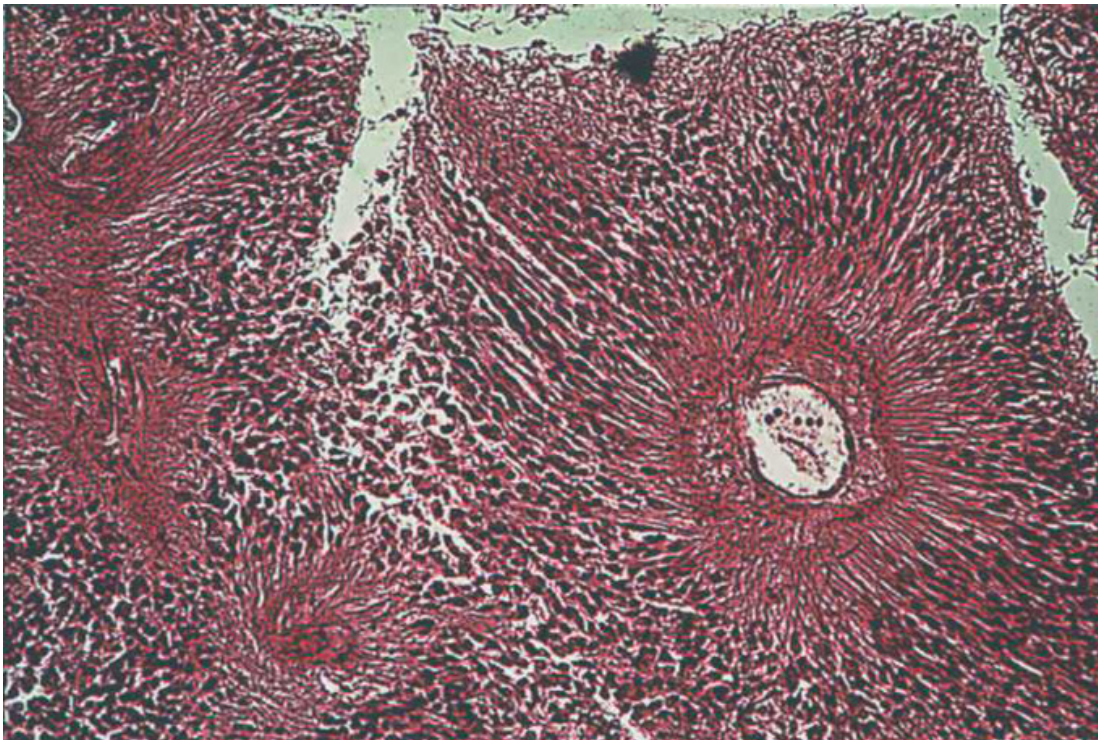
### Classification

Ependymomas are well-delineated moderately cellular gliomas. Histological features are perivascular

pseudo rosettes and ependymal rosettes. WHO classification differentiate four major types:

#### 1. Ependymoma and variants (grade II):

- Cellular ependymoma: a variant of ependymoma with conspicuous cellularity but often less prominent pseudo-rosette or rosette formation.
- Papillary ependymoma: a rare variant which looks like choroid plexus papilloma.
- Clear cell ependymoma: a rare variant which may be confused with oligodendroglioma neurocytoma or metastatic renal cell carcinoma.



Histological feature of ependymoma: perivascular rosettes - Anne Marie Capodano.

2. **Anaplastic (malignant) ependymoma (grade III):** An ependymoma with histological evidence of anaplasia.

3. **Myxopapillary ependymoma (grade I):** It occurs almost exclusively in the conus-cauda-filum terminale region, with a generally favourable prognosis.

4. **Subependymoma (grade I):** Benign tumor composed of nests of ependymal cells in a dense glial fibrillary matrix.

## Clinics and pathology

### Epidemiology

In children, 30 % of ependymomas appear before the age of 3 years and are more aggressive than in adults. Nearly 90 % of pediatric ependymomas are intracranial: they occur in supratentorial or posterior fossa locations, and only 10 % are intraspinal. Ependymomas account for 6 to 12 % of brain tumors in children and represent the third most common central nervous system neoplasms in this age range, following astrocytoma and medulloblastoma.

In adults, 60 % of ependymomas are tumors of spinal cord and only 40 % are intracranial. Intramedullary spinal ependymomas can be seen in patients with neurofibromatosis type 2 (NF2), a hereditary disease. Clustering of ependymomas has been noted in some families suggesting inheritance of a genetic susceptibility to this type of tumor.

### Clinics

Clinical manifestations of these tumors are localization dependent.

### Pathology

**Immunohistochemistry:** The great majority of ependymomas display GFAP immunoreactivity. It is usually observed in pseudo-rosettes, but GFAP is not specific of ependymomas. It is observed in all gliomas. Ependymomas typically express S 100 protein and Vimentin. In ependymomas WHO grade II, epithelial membrane antigen (EMA) immunoreactivity has been reported.

### Treatment

The treatment of ependymomas is mainly exeresis of tumor and radiotherapy after exeresis.

### Prognosis

Ependymoma is a recurrent tumor. The identification of parameters with prognostic value in ependymomas is very important, but controverted. By order of importance the following factors are considered:

Age and extent of resection

Prognosis in children is significantly worse than in adults. The children's cancer group reported a 5 year progression-free survival of 5 % in children with intracranial ependymomas. A retrospective analysis of 83 pediatric ependymomas revealed are below 3 years

incomplete tumour resection as indication of a poor outcome.

In adult patients survival at 10 years is 45 %.

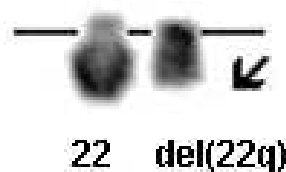
Complete or near complete resection emerged as an independent prognostic factor.

**Localization**

Supratentorial ependymomas are associated with better survival rates compared to posterior fossa tumors.

Spinal ependymomas are associated with better outcome than cerebral tumors. Cerebrospinal localization shows a poor prognosis.

## Cytogenetics



Partial karyotype of a cell of ependymoma: 46, XX, del(22)(q11) with R-banding - Anne Marie Capodano.

### Cytogenetics Morphological

No specific cytogenetic abnormality has been described but ependymomas with 30 % incidence of aberrations involve chromosome 22 as the most frequent change. Monosomy 22 as well as deletions or translocations involving 22q can appear.

Less frequent are structural abnormalities of chromosomes 1, 6, and 17 and numerical abnormalities of 7, 9, 12 and 20.

Monosomy 10 was reported in few cases of anaplastic ependymomas associated with LOH of 17p.

Monosomy 13 was observed in eight cases half of which occurred in paediatrics patients.

Rearrangements or deletions of chromosome 6 were reported in five tumors.

## Genes involved and proteins

### Note

Genes involved in ependymomas remain to be uncovered. Mutations or deletions of the tumor suppressor genes CDKN2 A et CDKN2 B and amplification of CDK4 or CCND1 have been reported. Mutations of TP53 were occasionally observed in ependymomas.

Increased incidence of ependymomas in neurofibromatosis type 2 has suggested that NF2 represents an obvious candidate gene. Some authors have presented evidence for mutations of NF2 suppressor gene at 22 q12. Whereas others have been unable to identify such mutations of the NF2.

Investigators show that the most frequently recurrent genomic loss in ependymomas does not involve the proximal 22 q11.2 chromosome region. They suggest

that another not-yet identified tumor suppressor gene located distally to the HSNF5/INT1 locus on the 22q and independent of NF2 locus may be involved in ependymomas.

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