

EPENDYMOMES DE L'ADULTE

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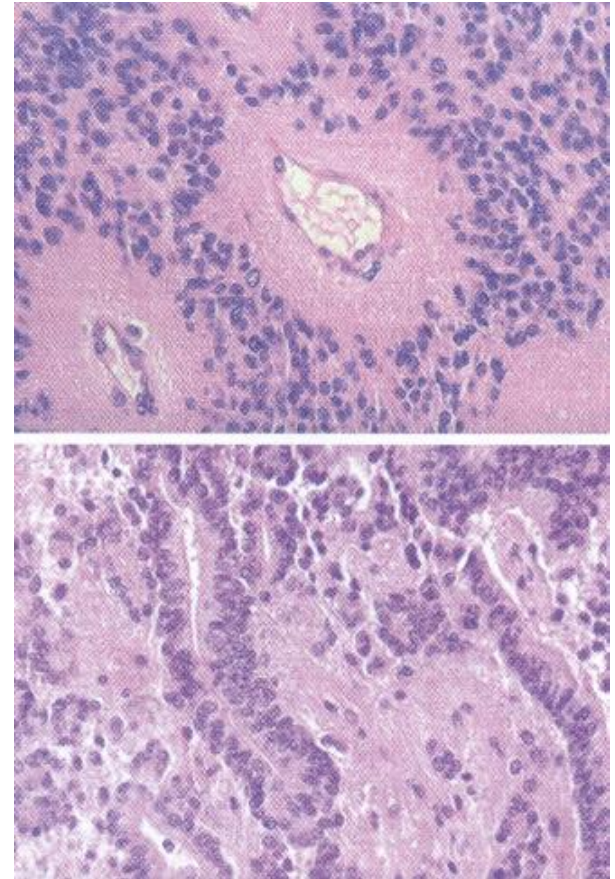
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Généralités

- Tumeur gliale rare (3% des tumeurs primitives SNC)
- Dérivé des cellules épendymaires
- Adulte jeune, <45ans
- Tumeur différente de celle de l'enfant
- Le plus souvent localisation médullaire
- Autre tumeur maligne associée dans 15% des cas
- NF II, LI Fraumeni, Turcot, MEN1

anatomie pathologique

- rosette périvasculaire
pseudo-rosette péri-épendymaire



Classification WHO

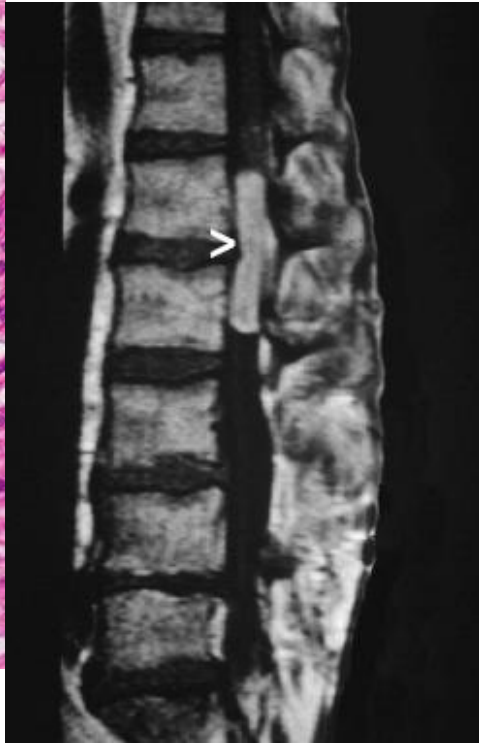
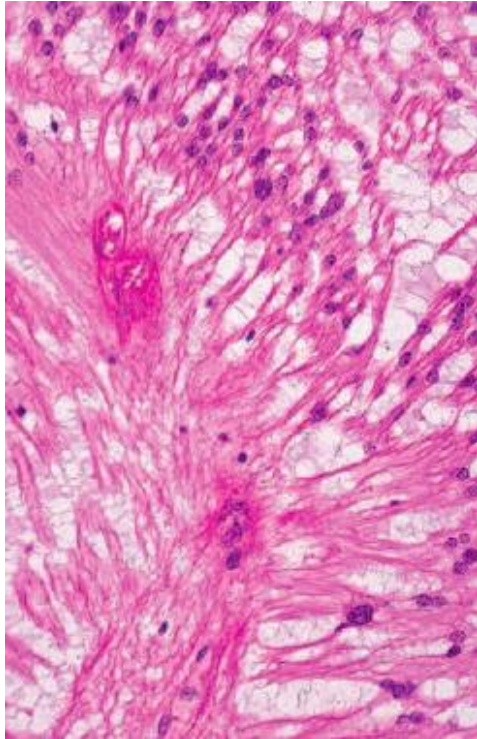
- Les épendymomes myxopapillaires
- Les subépendymomes
- Les épendymomes
- Les épendymomes anaplasiques

Gr 1

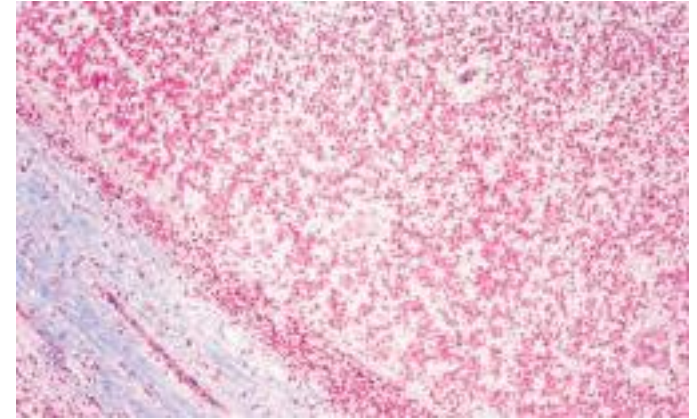
Gr 2

Gr 3

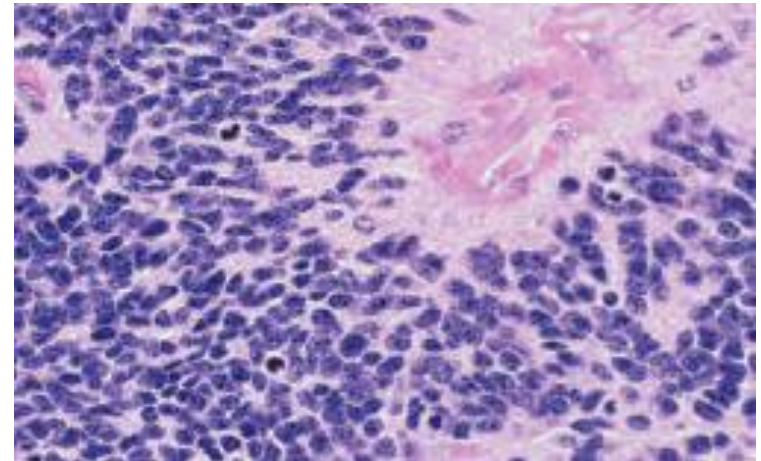
épendymome
myxopapillaire



épendymome



épendymome anaplasique



Pléomorphisme cellulaire, nombre de mitoses, densité cellulaire, invasion tumorale

Limites de l'examen histopathologique

- Souvent peu reproductible
- Intérêt des techniques complémentaires: IHC, CHG array, micro RNAs....
- Nombreuses études chez l'enfant, mais tumeurs différentes de celles de l'adulte (voie HOX)

Biologie moléculaire

VOLUME 28 • NUMBER 19 • JULY 1 2010

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Molecular Staging of Intracranial Ependymoma in Children and Adults

Andrey Korshunov, Hendrik Witt, Thomas Hielscher, Axel Benner, Marc Remke, Marina Ryzhova, Till Milde, Sebastian Bender, Andrea Wittmann, Anna Schöttler, Andreas E. Kulozik, Olaf Witt, Andreas von Deimling, Peter Lichter, and Stefan Pfister

In the screening cohort, **age at diagnosis, gain of 1q, and homozygous deletion of *CDKN2A*** comprised the most powerful independent indicators of unfavorable prognosis.

In contrast, **gains of chromosomes 9, 15q, and 18 and loss of chromosome 6** were associated with excellent survival.

	All	Brain	Spine
Total	123	40	80
Gender			
Male	63 (51%)	20 (50%)	42 (53%)
Female	60 (49%)	20 (50%)	38 (47%)
Age			
Range	18–72	19–72	18–69
Mean/median	40/39	40/38	42/40
Location			
Supratentorial		16 (40%)	
Infratentorial		23 (58%)	
Malignancy			
Grade II	112 (91%)	30 (75%)	79 (99%)
Grade III	11 (9%)	10 (25%)	1 (0.01%)
Grade III at recurrence	15	13	2

Clinique

- Variable selon la localisation tumorale
- Délai moyen entre 1ers signes et diagnostic:
 - 8 mois (2-38): si tumeur médullaire
 - 3,5 mois (1-18): si tumeur intracrânienne

Presenting symptoms	All	Brain	Spine
Range	0–13	1–7	1–13
Mean/median	4/4	4/4	4/3
Most common		Pain (70%) Mental status (50%) Coordination (45%) Nausea/vomiting (30%) Vision (30%)	Pain (85%) Sensory (70%) Weakness (30%) Bladder (25%) Bowel (11%)
		Seizures (15%) Weakness (13%) Sensory (12%) Emotional (13%)	Sexual (4%)
Mean time to diagnosis		3.5 months	8 months
Range		1–18 months	2–38 months

Dg Radiologique

- IRM cérébrale et médullaire

Séquences T1, T1 gado 3D, FLAIR (+ spectro? Perfusion? diffusion?)

Séquences T1 sans et après gado sag, T2 sag +/- axial

- Tumeur charnue parfois kystique, hypo T1, hyper T2 / FLAIR
- Prise de contraste
- Hydrocéphalie
- Calcifications (50% des cas), remaniements hémorragiques (10%)

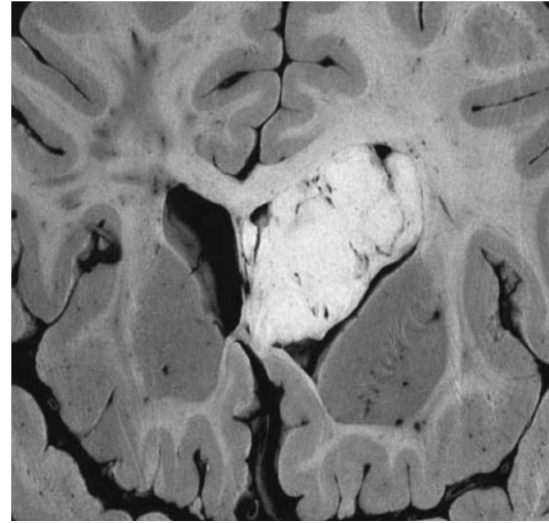
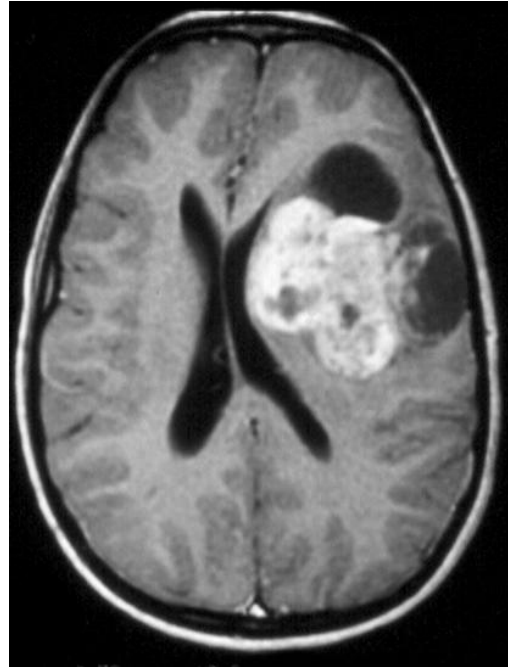
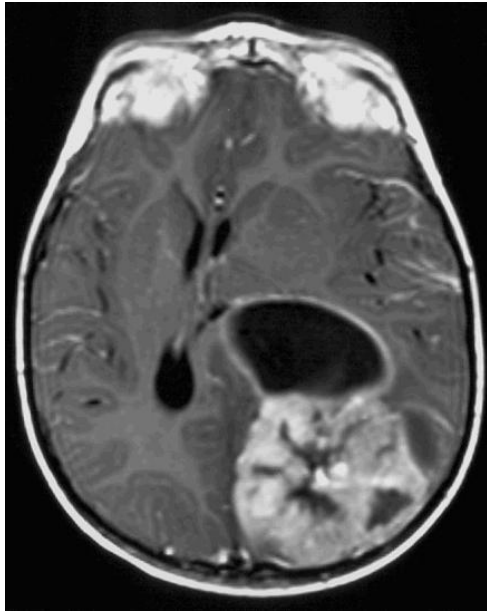
Médullaire

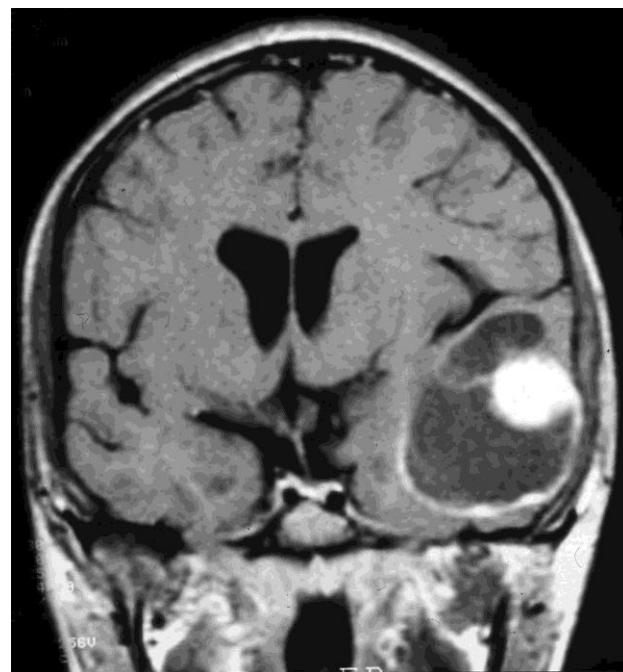
Supra-tentoriel: intraventriculaire, para-ventriculaire, lobaire

Fosse postérieure: implantation plancher, toit V4, récessus latéral, APCe

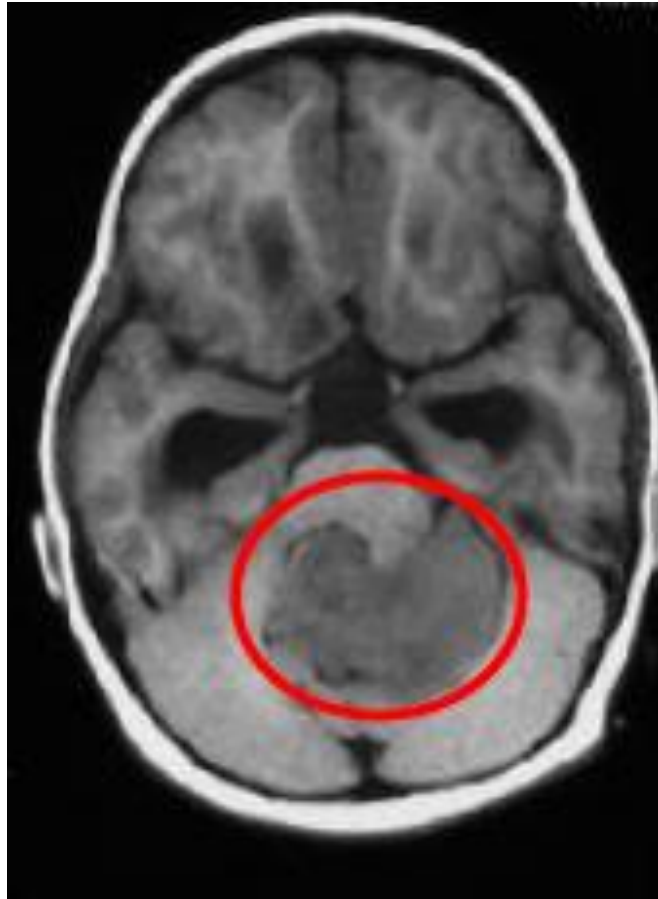
Métastases méningées

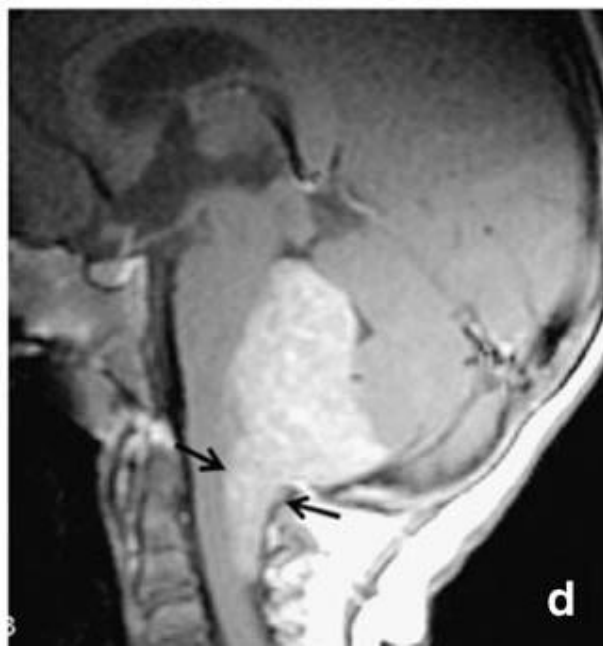
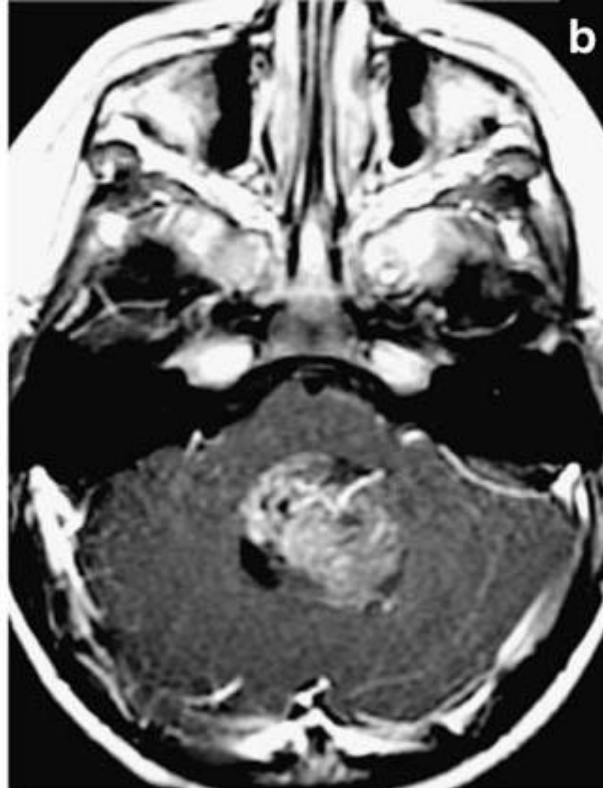
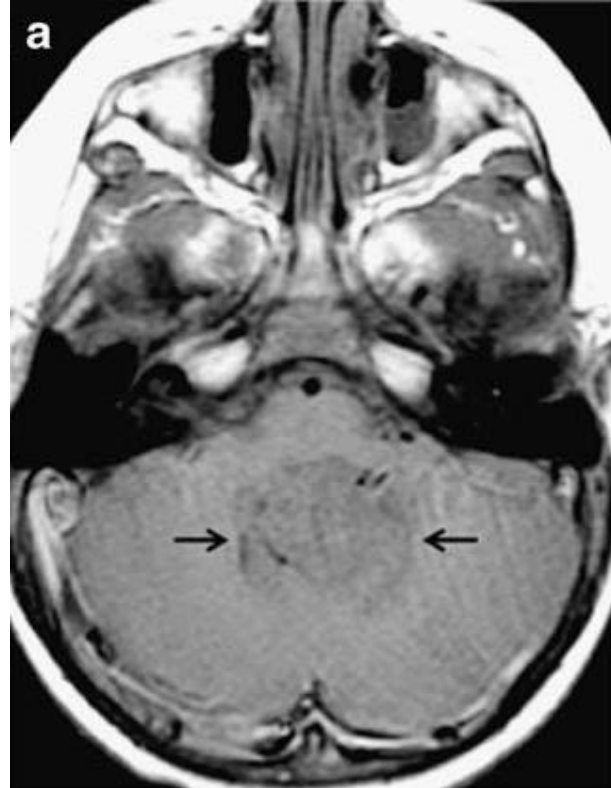
Sus tentoriei

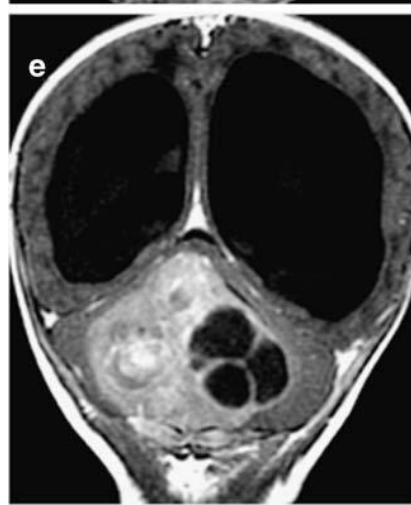
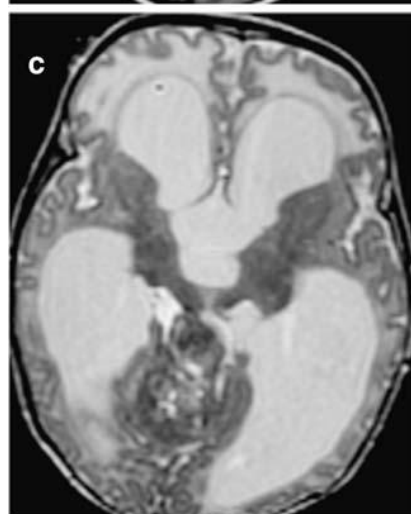




Sous tentoriel



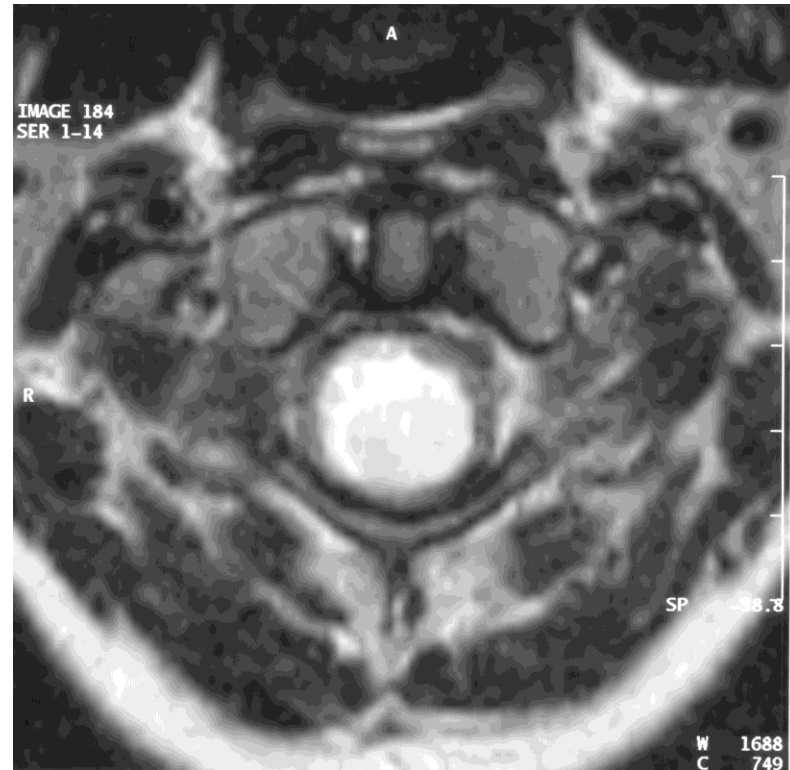




Médullaire



Ependymoma



Recherche d'une extension méningée

- Risque surtout si grade III
- IRM cérébrale et médullaire
- >>> Ponction lombaire (peu rentable)

Diagnostic différentiel

Métastases

Astrocytome

Médulloblastome

Hémangioblastome

Pronostic

Table 2. Treatment and outcome characteristics

	All	Brain	Spine
Range	0–20.75	0.25–20.75	0–18.5
Mean/median	5.5/5	5.5/4	5.5/5
Time to first/second recurrence			
Median			
First recurrence		21 months (Grade III: 18 months)	25 months
Second recurrence		16.5 months (Grade III: 12 months)	20 months
Overall survival		221 months (Grade III: 67 months)	
Died	16 (13%)	11 (28%)	5 (6%)

Pronostic

Table 5. Analysis of progression-free survival

Predictor	Variable	Hazard ratio (95% CI)	<i>P</i> value
Tumor grade	Grade III	1.000	<.0001
	Grade II	0.151 (0.064, 0.358)	
Ethnicity	Non-white	1.000	.8512
	White	1.110 (0.372, 3.310)	
Gender	Female	1.000	.4590
	Male	1.383 (0.586, 3.266)	
MIB ^a	MIB-1 < 10%	1.000	.0061
	MIB-1 ≥ 10%	4.694 (1.556, 14.163)	
Location of tumor	Spine	1.000	.0404
	Brain	2.522 (1.041, 6.110)	
Location in brain	Supratentorial	1.000	.3424
	Infratentorial	0.588 (0.197, 1.760)	
Resection extent	Incomplete resection	1.000	.2583
	Complete resection	0.593 (0.240, 1.467)	

^aMIB-1 data available on only 63 patients.
P values in bold are significant.

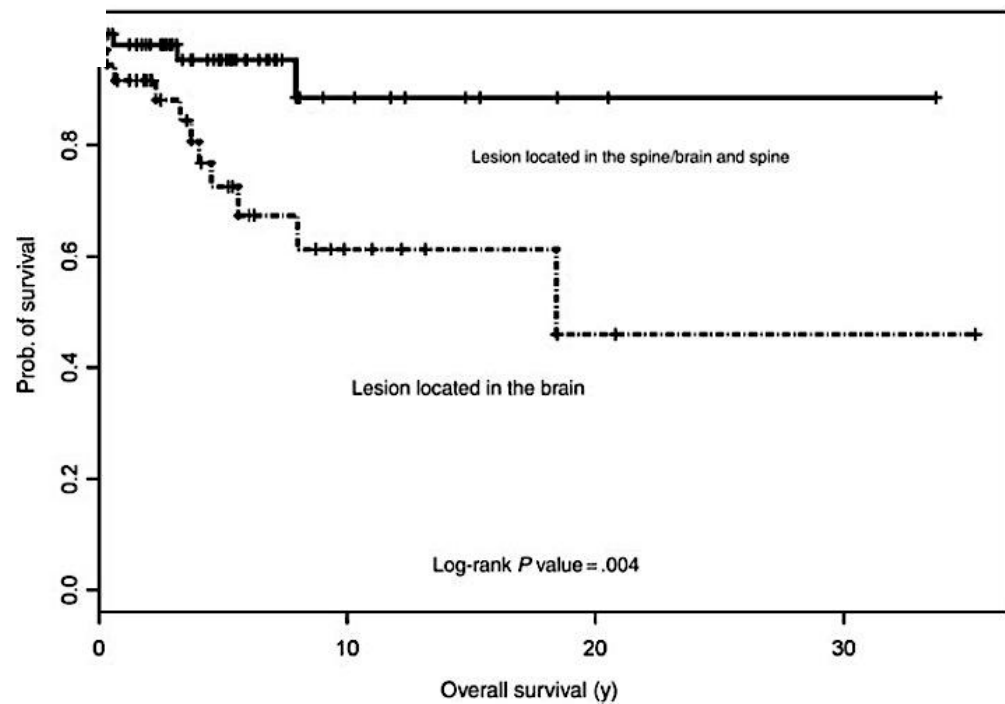
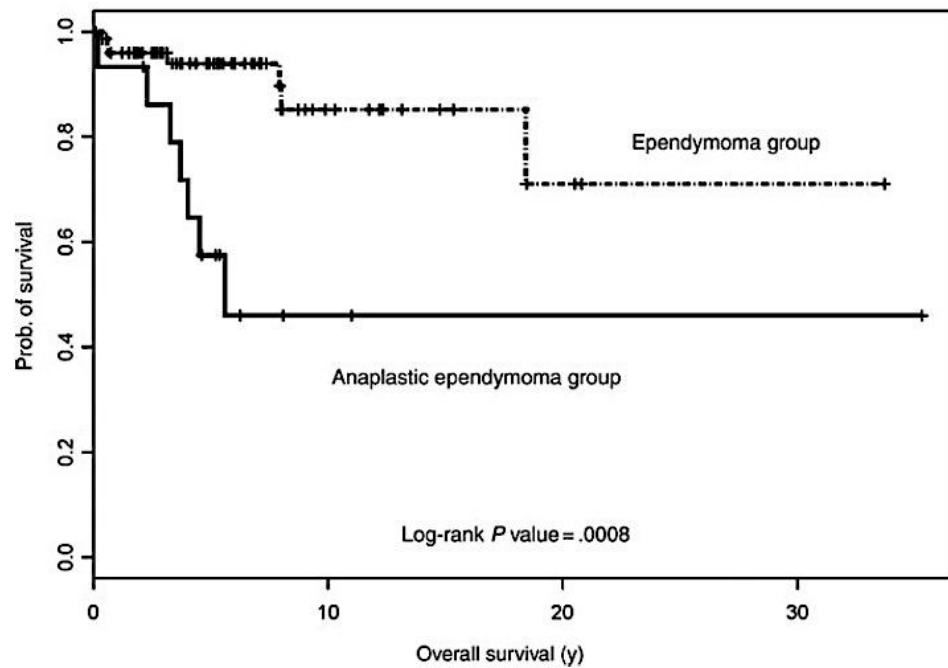
Table 4. Analysis of survival

Predictor	Variable	Hazard ratio (95% CI)	<i>P</i> value
Tumor grade	Grade III	1.000	.0025
	Grade II	0.197 (0.069, 0.565)	
Ethnicity	Non-white	1.000	.6600
	White	1.401 (0.312, 6.298)	
Gender	Female	1.000	.7527
	Male	0.843 (0.291, 2.443)	
MIB ^a	MIB-1 < 10%	1.000	.0278
	MIB-1 ≥ 10%	3.497 (1.145, 10.644)	
Location of tumor	Spine	1.000	.0107
	Brain	5.301 (1.473, 19.07)	
Location in brain	Supratentorial	1.000	.4452
	Infratentorial	0.627 (0.190, 2.076)	
Resection extent	Incomplete resection	1.000	.6624
	Complete resection	0.780 (0.255, 2.385)	

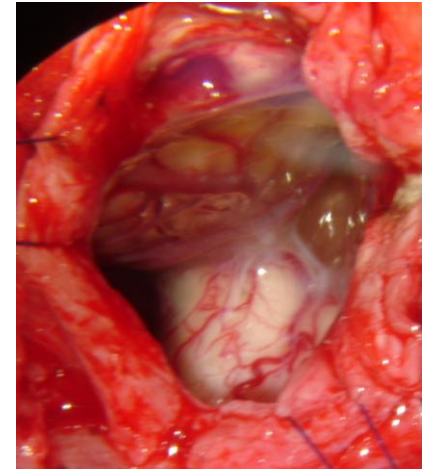
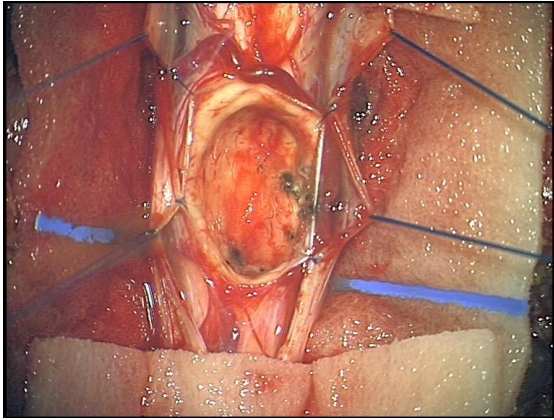
^aMIB-1 data available on only 63 patients.
P values in bold are significant.

Facteurs de bon pronostic

- Age
- PS
- Localisation tumorale médullaire
- Grade histologique II (>III)
- MIB-1 entre 1 et 10% (> supérieur à 10%)
- Qualité de l'exérèse chirurgicale

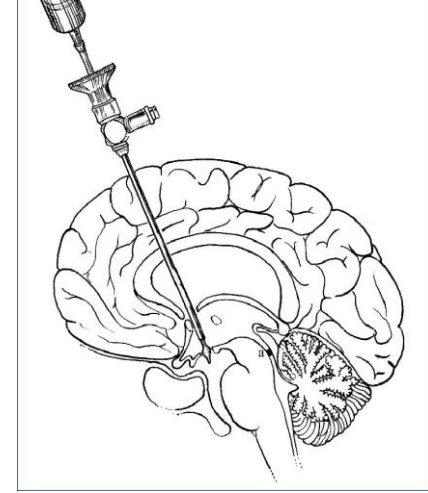


	All	Brain	Spine
<i>Treatment characteristics</i>			
Gross total resection	78 (63 %)	23 (58%)	53 (66%)
Radiation therapy	60 (49%)	29 (73 %)	30 (38%)
With Grade II	49 (82 %)	19 (66%)	29 (97%)
With Grade III	11 (18%)	10 (34%)	1 (3%)
At diagnosis	44 (73 %)	21 (72%)	22 (73%)
At recurrence	9 (15%)	5 (17%)	4 (13%)
With Grade II and at diagnosis	36 (60%)	13 (50%)	22 (84%)
With Grade II and at recurrence	6 (10%)	3 (12%)	3 (12%)
With Grade III and at diagnosis	8 (13%)	8 (31%)	0 (0%)
With Grade III and at recurrence	3 (5%)	2 (8%)	1 (4%)
Chemotherapy	16 (13%)	10 (25%)	6 (7.5%)
With Grade II	9 (56%)	4 (40%)	5 (83%)
With Grade III	7 (44%)	6 (60%)	1 (17%)
At diagnosis	6 (38%)	5 (50%)	1 (17%)
At recurrence	10 (62%)	5 (50%)	5 (83%)
With Grade II and at diagnosis	2 (13%)	1 (10%)	1 (17%)
With Grade II and at recurrence	7 (44%)	3 (30%)	4 (66%)
With Grade III and at diagnosis	4 (25%)	4 (40%)	0 (0%)
With Grade III and at recurrence	3 (18%)	2 (20%)	1 (17%)



Traitement
=
Exérèse chirurgicale
complète

Chirurgie



- Hydrocéphalie: contexte d'urgence
Ventriculocysternostomie
- Bilan, analyse et planification chirurgicale
- Moyens techniques
- IRM post op dans les 48 à 72h

TABLE. Clinical characteristics of 118 patients with ependymomas of the brain or spine. Modified, from *cancer* 28 Apr 2011 [Epub ahead of print].

Treatment	No. of Patient (%)			
	Overall	BT	ST	BT and ST
Initial surgery				
Biopsy	2 (2)	2 (4)		0 (0)
Partial resection	19 (16)	18 (35)		1 (17)
Gross total resection	35 (30)	32 (62)		3 (50)
Spine surgery for biopsy	5 (4)		5 (8)	0 (0)
Spine surgery with partial resection	13 (11)		13 (22)	0 (0)
Spine surgery with gross total resection	37 (31)		35 (58)	2 (33)
No surgery performed	2 (2)		2 (3)	0 (0)
NA	5 (4)	(0)	5 (8)	0 (0)
Condition after first surgery				
Better	61 (52)	34 (65)	24 (40)	3 (50)
Worse	38 (32)	12 (23)	25 (42)	1 (17)
Same	12 (10)	2 (4)	9 (15)	1 (17)
NA	7 (6)	4 (8)	2 (3)	1 (17)
Complications after first surgery				
Infection	12 (10)	6 (12)	4 (7)	2 (33)
Blood clot	6 (5)	4 (8)	2 (3)	0 (0)
Bleeding in brain	3 (3)	2 (4)	0 (0)	1 (17)
Seizure	7 (6)	6 (12)	0 (0)	1 (17)
Diabetes	5 (4)	2 (4)	2 (3)	1 (17)
Drug allergy	6 (5)	2 (4)	3 (5)	1 (17)
Weakness	45 (38)	17 (33)	24 (40)	4 (67)
Paralysis	23 (20)	6 (12)	16 (27)	1 (17)
Inability to urinate	10 (9)	2 (4)	7 (12)	1 (17)
Incontinence	14 (12)	1 (2)	11 (18)	2 (33)
Sexual dysfunction	22 (19)	5 (10)	17 (28)	0 (0)
Additional treatment after surgery				
Radiation therapy	30 (25)	19 (37)	10 (17)	1 (17)
Chemotherapy and radiation therapy	13 (11)	8 (15)	4 (7)	1 (17)
Chemotherapy, radiation therapy, and radiosurgery	2 (2)	2 (4)	0 (0)	0 (0)
None	64 (54)	22 (42)	38 (63)	4 (67)
NA	9 (8)	1 (2)	8 (13)	0 (0)

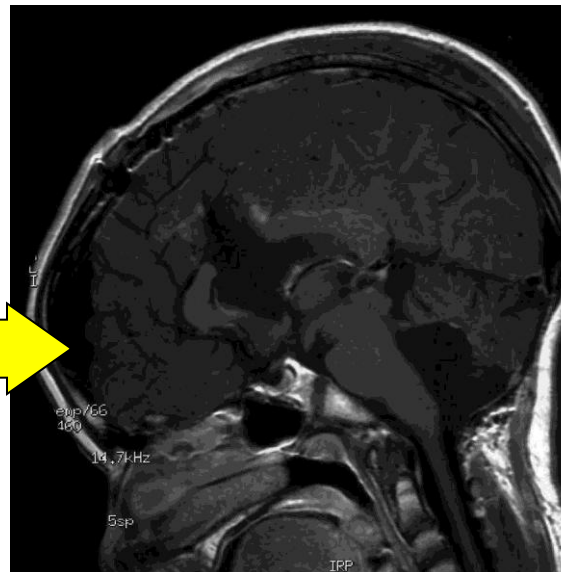
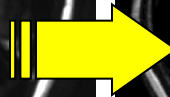
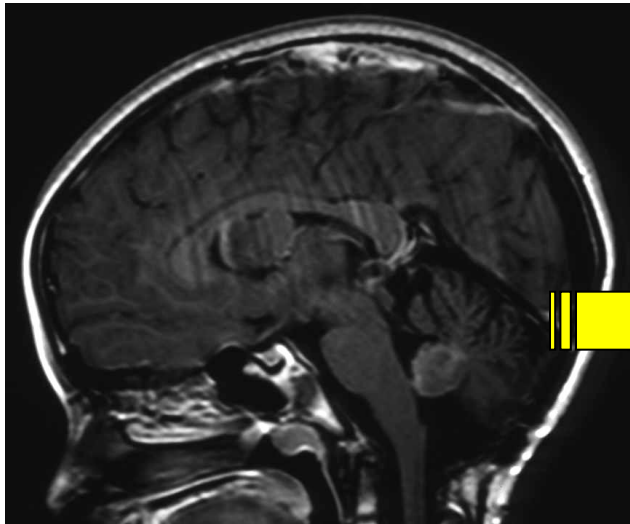
Abbreviations: BT, brain tumor; NA, not available; ST, spinal tumor.

Taux de morbidité variable selon:

- Localisation tumorale
- Histologie
- Expérience du neurochirurgien
- Comorbidités

Chirurgie des métastases

- décisions au cas par cas
- si métastase unique
 - ou deux ?
- si symptomatique



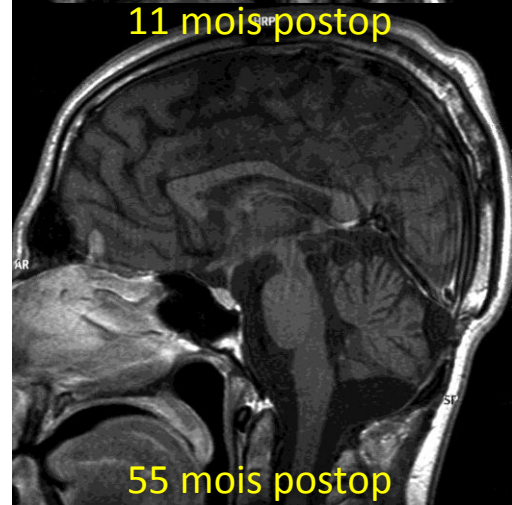
Radiothérapie

Indications:

- Grade III
- Reliquat après exérèse chirurgicale
- Maladie multifocale ou en dissémination méningée

Technique:

- Focale sur reliquat ou lit tumoral
(54 Gy en 30 f de 1,8 Gy avec complément de 5,4 à 6 Gy sur le volume résiduel post op)
- Cranio-spinale si métastases
(30 à 36 Gy en 15 à 18 f avec un complément de 54 GY sur le volume tumoral)



Chimiothérapie / Thérapie ciblée

- cyclophosphamide, cisplatine, étoposide, PCV, carbo/ VP16, Témozolomide

TMZ

25 patients, récurrence, tous traités par chirurgie, RT et platine

SSP médian: 2 mois (1 à 7), SG médiane: 3 mois (2 - 8)

(Chamberlain 2009)

- Bevacizumab?

8 patients, récurrence ou anaplasique

Tous traités par chirurgie et RT, et TMZ (5) ou carbo (4)

Bev seul ou associé à une chimio (3 irinotecan, 2 carbo, 1 TMZ)

SSP médiane: 6,4 mois, SG médiane: 9,4 mois

(Green 2009)

- Indications:

Le plus souvent en cas de récurrence non opérable et non accessible à la RT

Ependymome de grade II

Chirurgie complète?

NON

Chirurgie
Radiothérapie focale
Surveillance radio-clinique

OUI

Surveillance radio-clinique
tous les 6 mois

Ependymome de grade III

Chirurgie complète?

NON

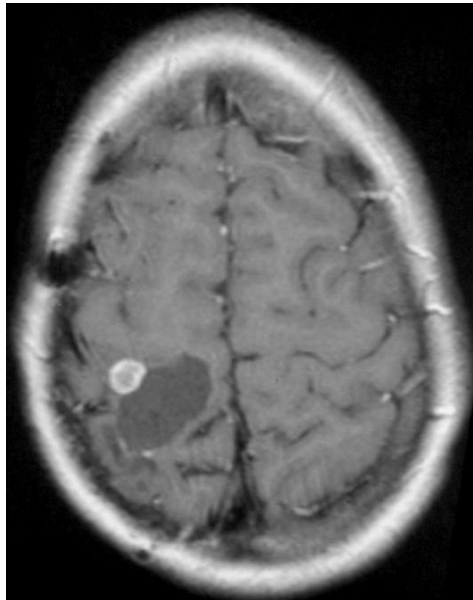
Chirurgie
Radiothérapie focale
Chimiothérapie

OUI

Radiothérapie focale
Surveillance radio-clinique
tous les 6 mois

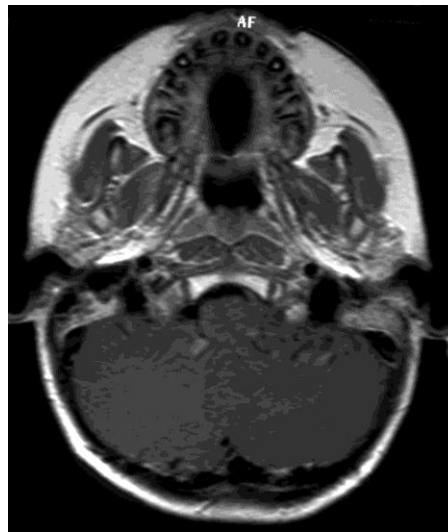
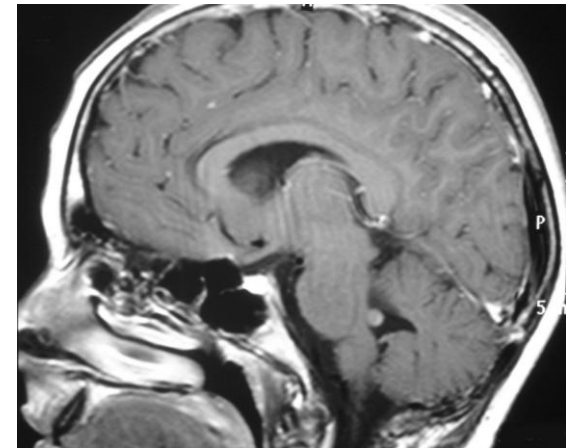
Récidive

- locale le plus souvent
 - liée à infiltration dans région inaccessible
- récidive locale + métastase névraxique
- métastases seules : exceptionnel
- \forall grade



diagnostic de récurrence

- IRM : interprétation souvent difficile
 - Fibrose avec effacement des plans
 - Pas ou peu de rehaussement
 - PdC non tumorales : cicatricielles, hypoPIC
 - Artéfacts mal placés
 - Intérêt de la spectro et de la perfusion



Traitement à la récurrence

- Pas de standard
- Reprise chirurgicale si possible
- Ré-irradiation (SRS)
- Chimiothérapie / thérapie ciblée

Neuro-Oncology 12(8):862–870, 2010.

doi:10.1093/neuonc/noq009

Advance Access publication February 5, 2010

NEURO-ONCOLOGY

Adult ependymal tumors: prognosis and the M. D. Anderson Cancer Center experience

Terri S. Armstrong, Elizabeth Vera-Bolanos, B. Nebiyu Bekele, Kenneth Aldape, and Mark R. Gilbert

conclusion

Classification histologique difficile, intérêt de nouveaux marqueurs

Efficacité de la radiothérapie : limitée

Efficacité de la chimiothérapie : discutée

"ependymoma is a surgical disease »

(E Bouffet)

Chirurgie totale chaque fois que possible