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Report 2013: Tumors of the pineal region

The management of pineal tumors as a model for a multidisciplinary approach in neuro-oncology

Prise en charge des tumeurs pinéales comme modèle de multidisciplinarité en neuro-oncologie

D. Frappaz[a,*], C. Faure Conter[b], A. Szathmari[c], A. Valsijevic[c], C. Mottolese[c]

[a] *Neuro-oncologie, centre Léon-Bérard, 28, rue Laennec, 69673 Lyon, France*
[b] *Institut d'hématologie et d'oncologie pédiatriques, 69673 Lyon, France*
[c] *Hôpital Wertheimer, 69677 Bron, France*

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ABSTRACT

The management of pineal tumors is a model for multidisciplinarity. Apart from an emergency situation that requires immediate shunting of cerebrospinal fluid (CSF), the initial discussion should involve at least a radiologist, a surgeon, a neurologist and an oncologist. The initial decision is whether obtaining a histological proof is obligatory. It depends on age and ethnicity, site (mono- or bifocality), presence of markers in serum as well as CSF, and/or of malignant cells in the CSF. In cases of marker elevation indicating a germ cell tumor, front line chemotherapy can avoid dangerous immediate surgery. When histological proof is required, the extent of surgery should be discussed, aiming either only at obtaining tissue or removal. If a germ cell tumor is detected, treatment will include a cisplatin-containing chemotherapy followed by focal or ventricular irradiation. Tumors of the pineal parenchyma will be treated according to grade, either by surgery alone (pinealocytoma) or chemo-radiotherapy (pinealoblastomas). Similarly, gliomas will be treated depending on their grade with several different possible lines in low grade, and usually radio-chemotherapy in high grade. A careful balance between improved survival rates and decreased long-term side effects will guide the decisions of all these specialists.

Mots clés :
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RÉSUMÉ

La prise en charge des tumeurs de la région pinéale est un modèle de prise en charge multidisciplinaire. En dehors des situations d'urgence qui imposent une dérivation immédiate du liquide céphalorachidien (LCR), chaque cas devrait faire l'objet d'une discussion collégiale entre un neuroradiologue, un neurochirurgien, un neurologue et un oncologue au moins. La première décision commune doit être de déterminer si l'obtention d'une preuve histologique est indispensable. Cette discussion doit tenir compte de l'âge et de l'ethnie du patient, du caractère mono- ou bifocal, de l'élévation éventuelle des marqueurs sériques et/ou du LCR, ainsi que de la présence possible de cellules malignes dans le LCR. En cas de marqueurs élevés, une chirurgie de première ligne doit être évitée. Si ce n'est pas le cas, le geste chirurgical doit être discuté : biopsie simple ou tentative d'exérèse à visée curative ? Si le diagnostic de tumeur germinale est porté, une association de chimio à base de dérivés du platine et de radiothérapie focale ou ventriculaire doit être proposée. Le grade d'une tumeur du parenchyme pinéal conduira soit à une chirurgie exclusive (pinéalocytome) soit à la réalisation d'une association chimio-radiothérapique (pinéaloblastome). De même, les tumeurs gliales seront traitées selon leur grade, utilisant une ou plusieurs lignes thérapeutiques pour les bas grades, et une association de chimio-radiothérapie pour les hauts grades. Dans tous les cas, la balance risque–bénéfice doit être pesée avec attention chez ces patients porteurs de tumeurs potentiellement curables à long terme.

* Corresponding author.
E-mail address: didier.frappaz@lyon.unicancer.fr (D. Frappaz).

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When a pineal swelling is detected in a patient, the decision tree should routinely explore the following questions:

- Is this a pineal tumor or a tumor from neighboring structures?
- Is it uni- or bifocal (i.e. also involving suprasellar region)?
- Is it localized or disseminated?
- What is the age and ethnic origin of the patient?
- Is it possible to reach a diagnosis without histological proof?
- Should there be a surgical approach, and if so, is it for biopsy or removal?
- What is the optimal treatment based on the final diagnosis?

In the following chapters, we shall describe the real life practice of a pineal tumor management.

Masses in the pineal region are found incidentally at MRI in 1 to 10% of cases and at autopsy in 20 to 40% of cases. The majority of these masses are benign and asymptomatic such as cysts that only require monitoring [1].

Tumors most often manifest initially as non-specific signs of cerebellar, corticospinal or sensory disturbance. When they grow, they compress or obstruct the aqueduct of Sylvius causing obstructive hydrocephalus and increased intracranial pressure. In some cases, compression of the superior colliculi results in a specific gaze palsy known as Parinaud's syndrome. In rare cases, patients may present with an endocrine disorder and precocious puberty may occur even if no mass is visible in the supraoptic region.

Once MR imaging has been performed, the pineal location is easily diagnosed if the volume of the tumor is small. However, the origin of larger tumors may be difficult to ascertain: i.e. the extension of a thalamic, tectal, occipital, cerebellar or meningeal tumor is open to debate.

Once the pineal region is considered as the site of origin, the cerebral imaging should be carefully reviewed, in particular ventricles, the parenchyma especially in supraoptic area, and meningeal sites. When hydrocephalus is present, urgent shunting should be discussed. If a second localization is detected in the supraoptic region, a germ cell tumor could be a potential diagnosis. If a second localization is detected elsewhere in the parenchyma, a lymphoma or a metastasis may be suspected. When meningeal enhancement is detected, a malignant tumor such as atypical teratoid rhabdoid tumor (ATRT), primitive neuroectodermal tumor (PNET) or pinealoblastoma may be suspected.

If the pineal mass is potentially a malignant tumor, a complete clinical examination and a staging may be required to discard the possibility of CNS metastases: spinal MRI (ideally performed preoperatively) and CSF cytology (performed during surgical shunting or by lumbar puncture when feasible) are obligatory. Evaluation of tumor markers (alpha-fetoprotein [AFP], total human chorionic gonadotropin [hCG], free beta-hCG test) in both serum and CSF is crucial to avoid unnecessary initial surgery. Ophthalmologic examination can be used to evaluate the consequences of increased intracranial pressure on visual acuity, and will eliminate any lymphomatous localization. When required, endocrinological investigations may be performed to eliminate the presence of diabetes insipidus, a perturbation of sexual hormones and/or growth hormone deficiency that may be present even if no supraoptic mass is detected on MRI.

Then, the multidisciplinary team should discuss on the necessity of pathological proof, as well as the optimal way to obtain it. Age also becomes an issue: although a pineal tumor may occur at any age, the incidence of pathologies varies according to age. In infants and babies, PNETS including pinealoblastomas, ATRT, and teratomas are the most likely diagnoses. In adolescents and young adults, germ cell tumors become the most likely diagnosis although gliomas and tumors of the pineal parenchyma (pinealocytoma or pinealoblastoma) remain possible. In adults, gliomas, lymphomas and metastasis become more prominent. At all ages, pineal cysts should be considered. Race is also an issue, as germ cell tumors are more frequent for instance in the Japanese population though this has recently been debated [2,3].

At this stage, positive markers in blood and/or CSF will suggest a germ cell tumor and initial surgery will be avoided. Specific alteration of fundi and/or lymphomatous cells in the CSF will argue for immediate chemotherapy. Malignant blue round cells may suggest PNET or pinealoblastoma: if the cytology is sufficiently reliable, and surgery is contraindicated, then medical treatment may be initiated. In all other cases, pathological proof should first be obtained by biopsy either during ventriculocisternostomy or an open biopsy or removal. This should be performed only by surgeons who have an extensive experience of pineal tumor management. This may minimize the risk of postoperative visual deficits and Parinaud's syndrome.

The treatment should then be tailored according to each case and may be summarized as follows.

1. Germ cell tumors [2,4,5]

Germinomas account for nearly 75% of cases, the rest being non-germinomatous germ cell tumors including yolk sac tumors, choriocarcinomas, embryonal carcinomas and more commonly mixed malignant germ cell tumors, that may contain a germinomatous or teratomatous component (mature or immature) mixed with malignant elements. The incidence of each component is however difficult to accurately assess in most series that do not perform either a biopsy or a complete removal front line: when surgery is performed after chemotherapy, only chemoresistant remnants may persist. Germinomas are more frequently observed in the suprasellar region or bifocal (both in the suprasellar and pineal regions) and in older children, adolescents and young adults. Non-germinomatous germ cell tumors have a predilection for the pineal region and a younger age group [6]. There is also a male preponderance. Germ cell tumors secrete proteins into the blood and CSF that can be measured and used for diagnostic purposes (see specific paper). In cases of positive secretion, a histological proof is not obligatory and chemotherapy may be initiated directly. Otherwise, a biopsy is indicated. Some protocols specify that in cases of a bifocal (only if pineal and suprasellar) tumor without secretion, a biopsy can be avoided because the frequency of a germinoma is so high.

Pure germinomas are very sensitive tumors with an excellent prognosis. The risk of relapse is primarily out of the focal radiation field (i.e. subependymal ventricular dissemination) [4]. The treatment of localized pure germinomas is still a matter of active debate. The treatment may either be a platinum-containing chemotherapy followed by focal and ventricular radiation, or exclusive craniospinal radiation, whole brain or whole ventricular irradiation [7]. As radiation therapy is developed elsewhere in this review, we will focus on the role of chemotherapy. Exclusive chemotherapy has now been abandoned by all groups [8], the results being inferior to chemo-radiotherapy. The French (Société française d'oncologie pédiatrique [SFOP]), the European SIOP CNS GCT-96 and the Japanese Cooperative Group studies have adopted a similar strategy with upfront chemotherapy (platinum based) followed by involved field irradiation to 40 Gy. All these papers reported relapses mostly in the ventricular field [4]. The current strategy is thus to use front line chemotherapy and extend the field of radiation therapy to include the ventricles. An overall survival (OS) of 100% with progression free survival (PFS) of 89% may be expected with this type of strategy in a cohort of properly staged patients [9]. Patients with a bifocal germinoma should be treated similarly [10]. Pure germinomas with CNS metastases are curable by craniospinal radiation and do not need any additional

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