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Report 2013: Tumors of the pineal region

Pineal parenchymal tumours and pineal cysts

Tumeurs du parenchyme pinéal et kystes de la glande pinéale

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ABSTRACT

Background and purpose. – Pineal parenchymal tumours (PPTs) and pineal cysts represent one third of the pineal region lesions. PPTs are subdivided into pineocytoma (PC), pineoblastoma (PB) and PPT with intermediate differentiation (PPTID). We report morphological and immunochemical features which permit to grade these tumours.
Methods. – The description of histopathological features and grading is based on a large cooperative series and on the WHO 2007 classification.
Results. – PCs occur in adults between the third and the sixth decade of life. PBs typically occur in children. PPTIDs have a peak incidence in young adults between 20 and 40 years of age. There is no sex preference. PC is characterized by a uniform cell proliferation with large fibrillary pineocytomatous rosettes. PB is a high-density tumour composed of small blue cells with hyper-chromatic, round or carrot shaped nuclei. PPTIDs have lobulated or diffuse patterns. Grading is based on morphological features, count of mitoses and neurofilament protein (NFP) expression. PCs (grade I) have no mitosis and NFP is highly expressed in pineocytomatous rosettes. PBs (grade IV) are high mitotic tumours and present low or no expression of NFPs. PPTIDs are grade II when mitoses are fewer than 6 for 10 high-power fields and NFPs are expressed, and are grade III when mitoses are greater or equal to 6 or are fewer than 6 with NFPs lowly expressed. Pineal cysts may be differentiated from PPTs by the high expression of NFPs and no expression of Ki-67.

Mots clés :
Tumeur du parenchyme pinéal
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RÉSUMÉ

Contexte et objectifs. – Les tumeurs du parenchyme pinéal (TPP) et les kystes de la glande pinéale représentent 30 % des processus expansifs de la région pinéale. Les TPP comprennent les pinéalocytomes (PC), les pinéaloblastomes (PB) et les TPP à différenciation intermédiaire (TPPDI). À partir d'une série multicentrique, nous avons établi un classement en quatre grades reconnu par l'OMS en 2007 : grade I (PC), grades II et III (TPPDI) et grade IV (PB).
Méthodes. – La description histopathologique, les données des immunomarquages et le grading sont basés sur la classification de l'OMS.
Résultats. – Les PC sont des tumeurs de l'adulte. Les PB s'observent le plus souvent chez l'enfant. Les TPPDI sont des tumeurs de l'adulte jeune. Il n'y a pas de prévalence de sexe. Les PC présentent de larges pseudorosettes fibrillaires au sein d'une prolifération de cellules pinéalocytaires, n'ont pas de mitoses et expriment les neurofilaments (NF). Les PB correspondent à une prolifération de petites cellules bleues indifférenciées aux noyaux hyperchromatiques ronds ou en forme de carottes, aux index mitotique et de prolifération élevés. L'architecture des TPPDI est lobulée endocrinoïde ou diffuse sans pseudorosette. Les TPPDI grade II ont moins de six mitoses pour dix champs × 400 et une forte expression de NF. Les TPPDI grade III ont soit six ou plus de six mitoses pour dix champs soit moins de six mitoses mais une faible expression de NF. Les kystes de la glande pinéale expriment très fortement les NF.

Tumours of the pineal region (TPRs) are rare, accounting for 2 to 3% of all intracranial tumours. Neuroepithelial tumours, such as pineal parenchymal tumours (PPTs), glial tumours and papillary tumours of the pineal region (PTPRs) represent approximately 50% of tumours in the pineal region. Germ cells tumours account

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for 30% of the TPR. Miscellaneous tumoural lesions (meningiomas, metastases) and non-neoplastic lesions (pineal cysts, arachnoidal cysts, vascular malformations) correspond to the last 20% of TPR. All histopathological and clinical data of TPRs are collected in a National Registry in Lyon (Hôpital Neurologique, Groupement Hospitalier Est) that contains more than 500 cases.

This report is focused on the pathological classification of PPTs and on glial cysts that need to be distinguished from pineal tumours, particularly pineocytoma.

PTPRs, described as a novel neoplasm in pineal region, are presented in another section.

1. Pineal parenchymal tumours

1.1. Introduction and historical considerations

The study of PPT in our institution began in the 1990s with an ultrastructural study of 20 cases [1]. A prognosis classification was proposed in 2000 on a multicentric series of 66 cases [2]. This classification in four grades of PPTs is based on morphological patterns, on mitotic count and immunohistochemical staining for neurofilament proteins (NFPs). The 2007 WHO classification subdivides this continuum into three distinct tumour categories: pineocytoma (PC) (Grade I), pineal parenchymal tumour of intermediate differentiation (PPTID) (Grades II and III) and pineoblastoma (PB) (Grade IV) [3].

1.2. Incidence, age and sex distribution

PPTs account for approximately 30% of tumours in the pineal region [4]. Our registry of TPRs includes 173 cases of PPTs in 2012 from 19 French centers, 53 were cases from Lyon (Neurosurgical Hospital). Histopathologically, they constitute a morphologic continuum from slowly growing well-differentiated lesions to highly proliferative tumours.

In a literature review of 16 papers covering 326 PPTs, 145 (44%) were found to be PCs [4]. This percentage might be overestimate, as some PPTIDs were classified as PCs before the 2007 WHO classification.

PCs account for 14% to 30% of all PPTs [5] and may present at any age, but mostly occur in adults, with a peak incidence between the third and sixth decades of life [3]. There is no gender preference.

PBs typically occur in children, with a mean age of 12.6 years, but adults may also be affected [4,6], with reports of individual patients older than 60 years [7–8]. There is no gender predilection.

The relative frequency of PPTIDs varies in the literature because, in some reports, this intermediate group of tumours was considered as PCs or PBs, reflecting the difficulties in establishing reproducible definitional criteria. If only studies with a true intermediate group are considered, PPTIDs represent 20 to 62% of PPTs [4,9–10]. These studies clearly indicate that tumours with mixed or intermediate features are not uncommon among pineal parenchymal neoplasms. These neoplasms occur mostly in adults, with a peak incidence in young adults between 20 and 40 years of age. Most present as localized disease. Dissemination via the cerebrospinal fluid (CSF) is less common than for PBs [4,7,11].

1.3. Macroscopic examination

PCs are circumscribed, grey or grey-brown tumours, with a cut surface that is homogeneous and often finely granular. Some show degenerative changes, such as small cysts. Necrosis is rare.

PBs are poorly demarcated, soft or gelatinous, grey-pink tumours. Haemorrhagic and necrotic areas may be present. The tumours often destroy the pineal gland, bulge into the posterior third ventricle and compress the colliculi and the aqueduct.

The gross appearance of PPTIDs is similar to that of PCs. The tumours are circumscribed, soft in texture and lacking gross evidence of necrosis.

1.4. Microscopy

Typical PCs are composed of well-differentiated tumour cells that resemble pineocytes and grow in a sheet-like pattern. The tumour cells are remarkably uniform, with a sparse, eosinophilic cytoplasm, short processes and round-to-oval nuclei with finely dispersed chromatin and inconspicuous nucleoli. Silver impregnation techniques highlight short cytoplasmic processes, often with bulbous or club-shaped terminations. Micro-calcifications may be seen. Mitotic figures are absent or exceedingly rare. Necrosis is very rare. The most characteristic feature of the PC is the formation of relatively large, sometimes confluent “pineocytomatous” rosettes (Fig. 1A). These structures appear as ovoid eosinophilic areas composed of a delicate meshwork of tumour cell processes. Pineocytomatous rosettes are similar to neuroblastic rosettes of the Homer Wright type, but considerably larger. A subset of PCs is characterized by the presence of large ganglionic cells and/or pleomorphic multinucleated giant cells [2,12–13]. They show no evidence of significant proliferative activity and have an indolent biological behaviour.

PBs are composed of densely packed small cells with a scant cytoplasm, hyper-chromatic, round or oval nuclei and high nuclear/cytoplasmic ratios. They resemble other small cells or PNETs of the CNS (Fig. 1B). The tumour cells grow in patternless sheets, usually without any obvious lobular architecture. Pineocytomatous rosettes are absent. However, PBs often contain neuroblastic rosettes of the Homer Wright type or retinoblastic rosettes of the Flexner–Wintersteiner type. Large cell/anaplastic features, as seen in medulloblastomas, can be present. PBs occasionally show evidence of advanced photoreceptor differentiation, with the formation of “fleurettes”. Rare tumours contain cells with melanin pigment. Mitotic figures are frequent. Apoptotic bodies and areas of necrosis may be prominent, the latter sometimes being associated with micro-calcifications. Vessels are usually thin-walled, but focal endothelial proliferation may be seen.

Histologically, PPTIDs present variable features [2]. These include an endocrine-like lobular architecture (Fig. 1C) or a more diffuse growth of isomorphic tumour cells with round nuclei and a clear cytoplasm (Fig. 1D). Such neoplasms should not be mistaken for neurocytoma or oligodendroglioma. Another phenotype, reported as a “transitional variant”, has mixed lobular/diffuse areas, in addition to regions with a PC-like morphology. Finally, some rare tumours may present with a biphasic pattern combining the typical features of PCs and PBs. These mixed PC/PB may correspond to pineoblastoma with residual pineal gland. Neoplastic cells have less cytoplasm than in PCs, but it is still visible on standard staining. Nuclear atypia is moderate. Mitotic activity is usually present in intermediate tumours, but may vary considerably. Foci of necrosis or vascular proliferation have been reported in subsets of PPTIDs, although they lack the primitive “small blue cell” appearance of PBs [2]. A pleomorphic variant may be encountered in low-grade PPTIDs [13].

1.5. Immunohistochemistry

PCs are immunopositive for neuron specific enolase (NSE), synaptophysin (SYN) (Fig. 2A) and NFPs (Fig. 2B), with strong reactivity in pineocytomatous rosettes. Immunoreactivity for several other neuronal or neuroendocrine antigens, including class III beta-tubulin, microtubule-associated protein 2 (MAP2), tau protein and chromogranin A, is also common [2,14–15]. In pleomorphic PCs, the pleomorphic cells show strong expression of SYN and NFPs

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