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Report 2013: Tumors of the pineal region

# Histopathology of pineal germ cell tumors

## *Histopathologie des tumeurs germinales de la région pinéale*

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ABSTRACT

Germ cell tumors (GCTs) classically occur in gonads. However, they are the most frequent neoplasms in the pineal region. The pineal location of GCTs may be caused by the neoplastic transformation of a primordial germ cell that has mismigrated. The World Health Organization (WHO) recognizes 5 histological types of intracranial GCTs: germinoma and non-germinomatous tumors including embryonal carcinoma, yolk sac tumor, choriocarcinoma and mature or immature teratoma. Germinomas and teratomas are frequently encountered as pure tumors whereas the other types are mostly part of mixed GCTs. In this situation, the neuropathologist has to be able to identify each component of a GCT. When diagnosis is difficult, use of recent immunohistochemical markers such as OCT(octamer-binding transcription factor)3/4, Glypican 3, SALL(sal-like protein)4 may be required. OCT3/4 is helpful in the diagnosis of germinomas, Glypican 3 in the diagnosis of yolk sac tumors and SALL4 in the diagnosis of the germ cell nature of an intracranial tumor. When the germ cell nature of a pineal tumor is doubtful, the finding of an isochromosome 12p suggests the diagnosis of GCT. The final pathological report should always be confronted with the clinical data, especially the serum or cerebrospinal fluid levels of β-human chorionic gonadotropin (HCG) and alpha-fetoprotein.



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RÉSUMÉ

Les tumeurs germinales sont les plus fréquentes des tumeurs pinéales. Classiquement rencontrées dans les gonades, leur localisation en position intracrânienne peut être expliquée par la transformation néoplasique d'une cellule germinale primordiale ayant migré de façon anormale ou par celle d'une cellule souche neurale « résidente ». L'Organisation mondiale de la santé (OMS) reconnaît 5 types histologiques de tumeurs germinales intracrâniennes : le germinome et les tumeurs non germinomateuses incluant le carcinome embryonnaire, la tumeur vitelline, le choriocarcinome et le tératome mature ou immature. Les germinomes et les tératomes sont souvent purs alors que les autres types tumoraux entrent fréquemment dans la composition de tumeurs mixtes. Face à un prélèvement de tumeur germinale, le neuropathologiste doit donc pouvoir en caractériser toutes les composantes. Dans des situations de diagnostic différentiel difficile, des marqueurs immunohistochimiques récents tels qu'OCT(*octamer-binding transcription factor*)3/4, Glypican 3 et SALL(*sal-like protein*)4 peuvent être utiles. OCT3/4 est utile dans le diagnostic des germinomes, Glypican 3 dans celui des tumeurs vitellines et SALL4 dans celui de tumeur germinale. La présence d'un isochromosome 12p dans une tumeur pinéale est en faveur du diagnostic de tumeur germinale. Le compte-rendu anatomopathologique devra toujours être confronté aux données cliniques et notamment aux concentrations de la β-*human chorionic gonadotropin* (HCG) et de l'α-fœtoprotéine dans le sang et le liquide céphalorachidien.



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## 1. Introduction

Intracranial germ cell tumors (GCTs) mainly occur in the pineal region and the suprasellar compartment [1]. They are the most frequent tumors in the pineal region [2]. Intracranial GCTs account for approximately 0.5% of all central nervous system (CNS) tumors and 3% of pediatric intracranial tumors [3,4]. Intracranial GCTs most often occur before 20 years of age [4]. Pineal GCTs especially affect the young male [4]. Although incidence of intracranial GCTs in Japan and East Asian countries was classically considered higher than in Western countries, a recent analysis of four registries showed similar incidence in Japan and United States [5].

Histologically, pineal GCTs recapitulate various stages of embryonal and extraembryonal development as suggested by Teilum's scheme (Fig. 1) [6]. Accordingly, the 2007 World Health Organization classification distinguishes 5 main histological types of intracranial GCTs [7]. Germinoma, known as "seminoma" in the testis and "dysgerminoma" in the ovary, constitutes the neoplastic counterpart of the primordial germ cell (PGC), just as embryonal carcinoma is the neoplastic counterpart of totipotent embryonal stem cells and teratoma the neoplastic counterpart of the derivatives of the three embryonic germ layers. Finally, yolk sac tumor and choriocarcinoma are respectively the neoplastic counterparts of the yolk sac and trophoblast.

## 2. Histogenesis of intracranial GCTs

All histogenetic hypotheses of intracranial GCTs have in common the involvement of a totipotent cell, i.e. a cell that has the ability to generate the entire set of embryonal and extraembryonal tissues of the organism (Fig. 2).

The most reliable hypothesis involves the PGC as the cell of origin of all GCTs. During embryogenesis, PGCs appear in the yolk sac then migrate along the midline axis to reach the genital ridges where they become gonocytes. In the male, gonocytes will mature into spermatocytes, in the female into ovocytes. During their migration, PGCs are characterized by the erasement of the biparental imprinting of their genome. The result is a haploid uniparental imprinted gamete [8]. The extragonadal locations of a few GCTs are the likely results of an abnormal migration of some PGCs and their persistence in midline organs such as the anterior mediastinum, the pineal gland and the suprasellar region [9]. These ectopic PGCs may escape from physiological apoptosis as they benefit from a specific microenvironment [9].

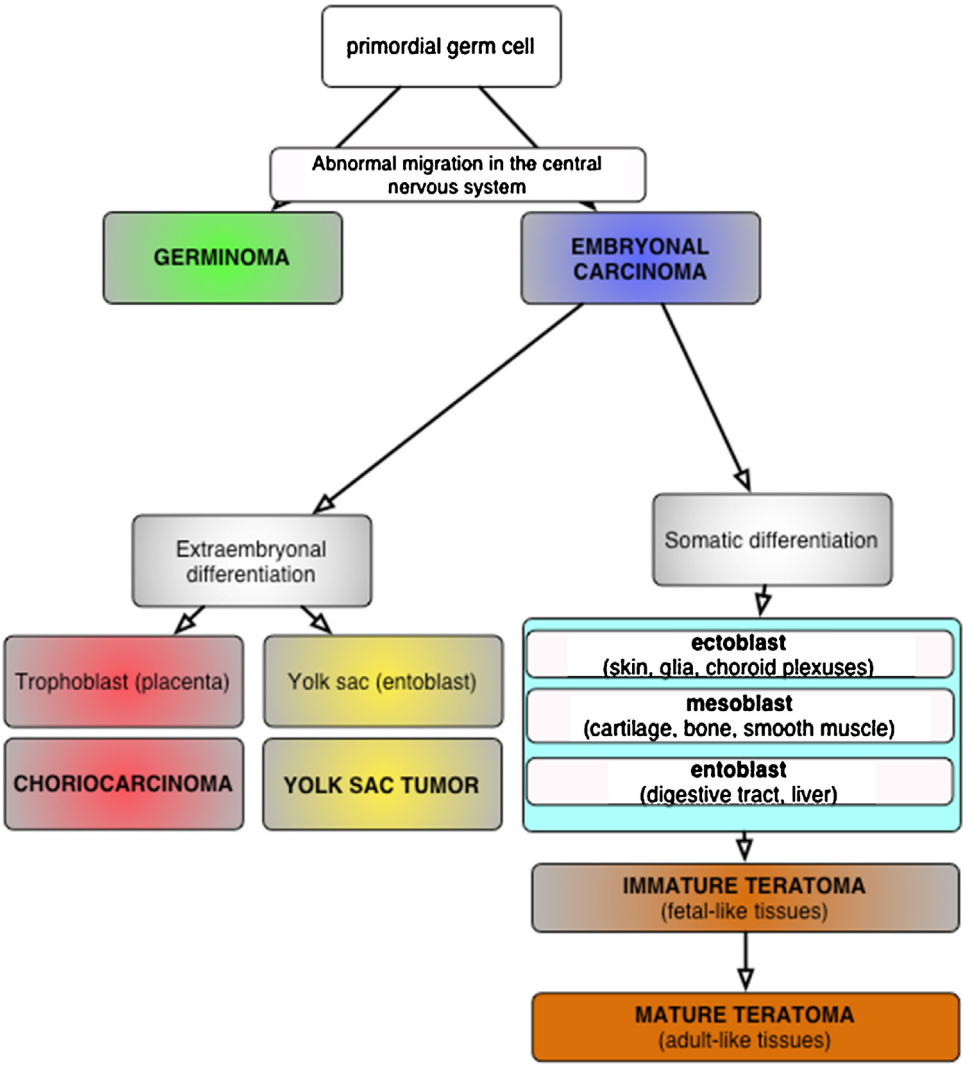


**Fig. 1.** Classical scheme of Teilum for extragonadal germ cell tumors. Primordial germ cell mismigrates in extragonadal sites and may give rise to germinomas and non-germinomatous tumors after neoplastic transformation.
*Schéma classique de Teilum pour les tumeurs germinales extragonadiques. La cellule germinale primordiale migre de façon aberrante dans des localisations extragonadiques et peut donner naissance par transformation néoplasique aux germinomes ou aux tumeurs non germinomateuses.*

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