Germ cell tumor

A germ cell tumor (GCT) is a neoplasm derived from germ cells. Germ cell tumors can be cancerous or non-cancerous tumors. Germ cells normally occur inside the gonads (ovary and testis). Germ cell tumors that originate outside the gonads may be birth defects resulting from errors during the development of the embryo.

General information

When they arise in the CNS, they are homologs of germ cell tumors of the gonads and other sites. GCTs occur in the midline in the suprasellar and/or pineal region (simultaneous suprasellar and pineal region lesions are diagnostic of a GCT; so-called synchronous germ cell tumors comprise 13% of GCTs and are highly sensitive to XRT). In the pineal region, these tumors occur predominantly in males. In females, GCTs are more common in the suprasellar region. Aside from benign teratomas, all intracranial GCTs are malignant and may metastasize via CSF and systemically.

Epidemiology

Primary germ cell tumors (PGCT) of the central nervous system usually develop in the third ventricle area, and most frequently in the pineal region. The suprasellar region is the second preferential site for development of these tumors which are rarely simultaneously present in these two sites.

Germ cell malignancies are common and increasing in males. However, a handful of cases have reported the rare occurrence of testicular germ cell tumours some years after initial extragonadal presentation [1) 2) 3) 4)].

Of all anterior mediastinal tumors, 15-20% are germ cell tumors of which approximately 50% are benign teratomas.

Classification

Intracranial germ cell tumor

Extragonadal germ cell tumor.

The WHO classification of CNS tumours divides intracranial germ cell tumours into:

Germinoma (account for 60-80% of all cases)

embryonal carcinoma

yolk sac tumor

choriocarcinoma

Teratoma

immature

mature

teratoma with malignant transformation

mixed germ cell

Germ cell tumors are broadly divided in two classes:

The germinomatous or seminomatous germ cell tumors (GGCT, SGCT) include only germinoma and its synonyms dysgerminoma and seminoma.

Nongerminomatous

see nongerminomatous germ cell tumor.

Types

1. germinomas: malignant tumors of primitive germ cells that occur in the gonads (called testicular seminomas in males, dysgerminomas in females) or in the CNS. Survival with these is much better than with nongerminomatous tumors

● variant: syncytiotrophoblastic giant cell variant

2. nongerminomatous germ cell tumors (NGGCT) include:

a) embryonal carcinoma:

b) choriocarcinoma

c) endodermal sinus tumor (EST) AKA yolk sac carcinoma: usually malignant

d) teratoma.A germ cell tumor composed of at least two of the three germ cell layers: ectoderm, endoderm, & mesoderm.

Subclassifications:

● mature: composed of mature skin, skin appendage organs (sweat glands, hair follicles…) adipose tissue cartilage, bone…

● immature: contain immature embryonic or fetal tissue alone or in combination with mature tissues

● exhibiting malignant transformation: teratomas that contain a component resulting from malignant transformation of a somatic tissue (usually a carcinoma or sarcoma)

3. mixed germ cell tumor.

Etiology

It is generally thought that the germ cell tumour represents a second primary tumour, as opposed to metastases. Previous reports have suggested that genetic mutations contribute to their development [5) 6) 7)].

A genetic basis has been proposed for these tumours. Mutations in the KIT gene at codon 816 are associated with gonadal and extragonadal germ cell tumours. Furthermore, it is thought such mutations occur very early during embryogenesis, prior to the migration of germ cells to gonadal and extragonadal locations. Coffey et al. found a KIT mutation in a patient who suffered from a pineal germinoma and a testicular seminoma [8)]

Some investigators suggest that this distribution arises as a consequence of abnormal migration of germ cells during embryogenesis. Others hypothesize a widespread distribution of germ cells to multiple sites during normal embryogenesis, with these cells conveying genetic information or providing regulatory functions at somatic sites.

Extragonadal germ cell tumors were thought initially to be isolated metastases from an undetected primary tumor in a gonad, but it is now known that many germ cell tumors are congenital and originate outside the gonads. The most notable of these is sacrococcygeal teratoma, the single most common tumor diagnosed in babies at birth.

Diagnosis

Germ cell tumor diagnosis

Treatment

The management of intracranial germ-cell tumours is complex because of varied clinical presentations, tumour sites, treatments and outcomes, and the need for multidisciplinary input. Participants of the 2013 Third International CNS Germ Cell Tumour Symposium (Cambridge, UK) agreed to undertake a multidisciplinary Delphi process to identify consensus in the clinical management of intracranial germ-cell tumours. 77 delegates from the symposium were selected as suitable experts in the field and were invited to participate in the Delphi survey, of which 64 (83%) responded to the invitation. Invited participants represented multiple disciplines from Asia, Australasia, Europe, and the Americas. 38 consensus statements encompassing aspects of intracranial germ-cell tumour work-up, staging, treatment, and follow-up were prepared. To achieve consensus, statements required at least 70% agreement from at least 60% of respondents. Overall, 34 (89%) of 38 statements met consensus criteria. This international Delphi approach has defined key areas of consensus that will help guide and streamline clinical management of patients with intracranial germ-cell tumours. Additionally, the Delphi approach identified areas of different understanding and clinical practice internationally in the management of these tumours, areas which should be the focus of future collaborative studies. Such efforts should translate into improved patient outcomes [9)].

Case reports

Combination of Germinoma with Teratoma is very rare. A case of Mixed Malignant Germ cell tumor of third ventricle with recurrence with emphasis on histopathological and radiological findings [10].

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