In patients with Down’s syndrome (DS), germinoma is the more common intracranial germ tumour, and two cases of intracranial yolk sac tumour (YST) have been documented in the English literature. In this report, we describe the appearance of YST with only a solid pattern identified on histology as a pineal neoplasm associated with DS. Unlike the previously reported cases, our case lacked the reticulated pattern typically present in YST. Although DS related intracranial germ cell tumours tend to occur in atypical sites—for example, basal ganglia—the tumour in our patient was midline.

CASE REPORT

A 22 year old Chinese man with DS and Hashimoto’s thyroiditis confirmed by positive serology for thyroid microsomal antibody, presented with headache of one month’s duration associated with nausea, vomiting, and some weakness in the lower limbs when walking. Physical examination showed characteristic Down’s syndrome, fair complexion, and coarse skin with increased buccal pigmentation. The testicles were not enlarged. Blood investigations revealed hypopituitarism and diabetes insipidus. Computer tomography of the brain showed a large pituitary–pineal axis mass, with homogeneous enhancement and focal calcification, compressing the back of the third ventricle and the aqueduct and causing hydrocephalus. A ventriculoperitoneal shunt was inserted and a subsequent magnetic resonance imaging scan delineated two solid enhancing masses. The larger mass, measuring 4 × 3.7 × 3.6 cm, was centred in the pineal region and the smaller mass, measuring 1.8 cm in maximum diameter, was present in the pituitary infundibular-suprasellar region. Biochemistry of the cerebrospinal fluid revealed a raised α fetoprotein (αFP) concentration of up to 995 µg/litre, whereas the human chorionic gonadotrophin (hCG) value was normal. A stereotactic biopsy was performed. He was scheduled for chemotherapy followed by radiotherapy; unfortunately, the patient developed fever of unknown origin postoperatively and died 1.5 months after the biopsy. Consent for necropsy could not be obtained from the next of kin.

PATHOLOGICAL FINDINGS

Grossly, the biopsy specimen received in small pieces was 1.3 cm in diameter when aggregated. On cytology, the crushed smears showed loose aggregates of medium sized hyperchromatic undifferentiated cells with ovoid nuclei, moderate anisonucleosis, discernible nucleoli, and scant to moderate amounts of cytoplasm (fig 1). Paraffin wax embedded sections showed a tumour composed of sheets of round to polygonal cells with apparently two populations of cells (fig 2). One population was composed of uniform cells resembling a germinoma, whereas another population was composed of larger cells disclosing eosinophilic polygonal cytoplasm and pale nuclei with prominent nucleoli. Occasional, more pleomorphic cells were noted but syncytiotrophoblastic cells were absent in the biopsy. Mitotic activity was readily apparent. Importantly, scattered periodic acid Schiff (PAS)-diastase positive hyaline globules were seen (fig 3). However, a typical reticulated pattern with Schiller-Duval bodies of YST was not identified and no fibrovascular septae associated with a lymphohytic infiltrate were present. No other germ cell components were featured in the biopsy. Immunohistochemistry showed the tumour cells to be positive for αFP (RB365A1; 1/60 dilution; Neomarkers, Fremont, California, USA) (fig 4) and α fetotransferrin or AAT (A012; 1/1200 dilution; Dako, Glostrup, Denmark). Staining for cytokeratin AE 1/3 (M3515; 1/200 dilution; Dako) was positive in the larger cells, sparing the areas resembling germinoma (fig 5). Staining for placenta-like alkaline phosphatase or PLAP (MS734-S1; 1/20 dilution; NeoMarkers), S100 protein (Z0311; 1/2000 dilution; Dako), leucocyte common antigen (250-2136; prediluted; Ventana, Freemont, California, USA) (fig 4) and placentin-like alkaline phosphatase or PLAP (MS734-S1; 1/20 dilution; NeoMarkers), S100 protein (Z0311; 1/2000 dilution; Dako), leucocyte common antigen (250-2136; prediluted; Ventana, Freemont, California, USA) revealed positive staining. Staining for placenta-like alkaline phosphatase or PLAP (MS734-S1; 1/20 dilution; NeoMarkers), S100 protein (Z0311; 1/2000 dilution; Dako), leucocyte common antigen (250-2136; prediluted; Ventana, Freemont, California, USA) showed positive staining. The case was considered positive for placenta-like alkaline phosphatase or PLAP (MS734-S1; 1/20 dilution; NeoMarkers), S100 protein (Z0311; 1/2000 dilution; Dako), leucocyte common antigen (250-2136; prediluted; Ventana, Freemont, California, USA) and positive for placenta-like alkaline phosphatase or PLAP (MS734-S1; 1/20 dilution; NeoMarkers), S100 protein (Z0311; 1/2000 dilution; Dako), leucocyte common antigen (250-2136; prediluted; Ventana, Freemont, California, USA) and was diagnosed as a pineal yolk sac tumour with a solid pattern: a case report in a Chinese adult man with Down’s syndrome. Histology revealed a pineal neoplasm associated with DS. Unlike the previously reported cases, our case lacked the reticulated pattern typically present in YST. Although DS related intracranial germ cell tumours tend to occur in atypical sites—for example, basal ganglia—the tumour in our patient was midline.

CASE REPORT

Pineal yolk sac tumour with a solid pattern: a case report in a Chinese adult man with Down’s syndrome

H W Tan, A Ty, S G N Goh, M C Wong, A Hong, K L Chuah

Abbreviations: αFP, α fetotransferrin; AAT, α1 antitrypsin; β hCG, β human chorionic gonadotrophin; DS, Down’s syndrome; PLAP, placenta-like alkaline phosphatase; YST, yolk sac tumour
Tucson, Arizona, USA), hCG (RB059-A1; 1/300 dilution; NeoMarkers), glial fibrillary acidic protein (Z0334; 1/1000 dilution; Dako), and CD30 (M0751; 1/60 dilution; Dako) was negative. MIB-1 (M7240; 1/70 dilution; Dako) staining was 90%. The light microscopy and immunohistochemical findings agreed with a diagnosis of YST with a solid pattern.

DISCUSSION

The histological classification of germ cell tumours arising in the brain follows those arising from the gonads and extragonadal sites.5 YST is known to exhibit a variety of microscopic patterns.6 Although the epithelial element may proliferate in solid sheets,5 the solid component often coexists with more typical patterns, having at least a focally reticular pattern with the characteristic Schiller-Duval bodies,6 thereby aiding the diagnosis. Although it is possible that the tumour in our report may contain other morphological patterns typical of YST, which were not biopsied, the presence of only the solid component of YST on biopsy makes the diagnosis challenging. Although the tumour in our case can be classified as pure using the criteria of Matsutani et al,7 the possibility of coexisting germ cell components apart from YST, which were not identified on biopsy, has to be entertained.

"The possibility of a purely coincidental manifestation of yolk sac tumour in the background of Down’s syndrome in our case cannot be excluded”

Although raised serum and cerebrospinal fluid αFP concentrations are helpful in the diagnosis and follow up treatment of intracranial YST,1,2 they are insufficient for a definitive diagnosis of YST in lieu of proper histological diagnosis because embryonal carcinomas and immature teratomas without YST can be associated with raised αFP values. Histologically, YST with a solid pattern in our case mimics germinoma or even embryonal carcinoma,5,6 by exhibiting non-overlapping, relatively uniform nuclei, clear cytoplasm, and well defined cell borders. However, fibrous septae with lymphocytic infiltrates characteristic of germinomas are absent. In contradistinction to YST, embryonal carcinoma displays a greater degree of nuclear pleomorphism. PAS-diastase resistant globules of YST are not featured in germinoma or embryonal carcinoma, underscoring the need of careful light microscopic examination with the PAS stain to identify this feature. In problematic situations, immunohistochmical studies are useful because YST is positive for cytokeratin, αFP, and AAT, whereas germinoma is PLAP positive. Cytokeratin expression alone cannot be used to differentiate YST from germinoma because germinomas can be cytokeratin positive.9 10 Embryonal carcinoma, although positive for cytokeratin and CD30, is negative for αFP. Interestingly, in our case, cytokeratin staining in some of the solid areas, especially those resembling germinoma, was negative, as seen in the solid variant of testicular YST.9 However, immunohistochemical staining for αFP should not be used alone in the diagnosis of YST because gastrointestinal epithelium and primitive neuroepithelial elements of immature teratoma may be positive for αFP.11 Rather, a constellation of light microscopy features in conjunction with a broad
We report a yolk sac tumour in the pineal region affecting a 22 year old Chinese man with Down’s syndrome—this is the third report of intracranial yolk sac tumour manifesting in a patient with trisomy 21. Histology revealed yolk sac tumour with only a solid pattern, potentially mimicking the more common germinoma in the pineal region. In cases of diagnostic difficulty a constellation of light microscopy features in conjunction with a broad panel of immunohistochemical stains and clinical findings is essential.

Take home messages

- We report a yolk sac tumour in the pineal region affecting a 22 year old Chinese man with Down’s syndrome—this is the third report of intracranial yolk sac tumour manifesting in a patient with trisomy 21.
- Histology revealed yolk sac tumour with only a solid pattern, potentially mimicking the more common germinoma in the pineal region.
- In cases of diagnostic difficulty a constellation of light microscopy features in conjunction with a broad panel of immunohistochemical stains and clinical findings is essential.

Although an association between DS and an increased occurrence of intracranial germ cell tumours has been noted,\(^1,3\)\(^12\) where trisomy 21 is proposed to cause tumour suppressor gene inactivation or direct activation of an oncogene,\(^7\) the possibility of a purely coincidental manifestation of YST in the background of DS in our case cannot be excluded. Whether trisomy 21 plays a significant role in the pathogenesis of YST or not, it is nonetheless apparent that intracranial YST has an extremely poor prognosis, with survival of more than three years being exceptional, regardless of therapeutic modalities.\(^7\)\(^8\)

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