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Title: Bifocal Germinoma of the Septum pellucidum and the sellar-supra-sellar region: an uncommon presentation for a rare tumor

Key Words: germ cell tumors; septum pellucidum; suprasellar; intracranial germinomas; bifocal germinomas.

Introduction

Intracranial germinomas (IGs) are rare malignant tumors which constitute only 0.5-2% of all primary intracranial tumors. They are a type of germ cell tumor (GCT) and account for approximately 60-70% of the brain GCT (2016 WHO classification, 1). They have a higher incidence in Asians. They usually occur in children and young adults (10-30 years old), with a male predominance. They affect in 90% of cases the pineal and sellar / suprasellar regions. In 10%-20% they are “bifocal”, synchronously involving both regions. Sometimes they involve the corpus callosum (CC), septum pellucidum (SP), basal ganglia (BG), thalamus, corona radiata, frontal and temporal lobe, cerebello -pontine angle, medulla oblongata, fourth ventricle. These IGs, also named “ectopic” IGs, represent approximately 5% of all IGs.

We report a very unusual presentation of an IG of the SP with synchronous involvement of the sellar-supra-sellar region. We discuss the MRI characteristics and review the literature (2- 6). This is the first documented report, to our knowledge, of a germinoma of the SP with a synchronous involvement of the sellar region.

Case:

A 28-year-old woman, without past medical history, presented with unsteady gait, mild left motor deficit, polydipsia and polyuria of two-month duration. Examination revealed a left hemiparesis. Non-contrast CT (NCCT) showed a cystic midline tumor consisting of solid areas slightly hyperdense extending to the CC and the frontal lobes (Fig 1-a). MRI revealed 2 lesions: one arising from the sella and extending in the pituitary stalk, and another one arising from the SP and extending in the fronto-callosal areas. The 60-mm-sized lesion of the SP had a butterfly aspect. The larger

cysts had 19 mm in maximum diameter. Both enhancing masses were slightly hyperintense on T1-weighted images (T1 WI), T2 WI, fluid attenuation inversion recovery (FLAIR) and diffusion-WI (DWI), with apparent diffusion coefficient (ADC) restriction and thick edema (Fig 1- b- e). Spine MRI and spinal tapering did not reveal any concomitant lesion. Serum α -foetoprotein and β -human chorionic gonadotrophin (β -hCG) were within normal limits. A whole-body CT did not reveal any lesions. Considering the radiological features, a presumptive diagnosis of IG was made. A biopsy of the frontal lesion was obtained by navigation-guided. The pathological result was pure germinoma. Immunohistochemical staining showed tumor cells positivity for Placenta alkaline phosphatase (PLAP) and c-kit (CD117) (Fig 1 -f-g). The patient received radiation therapy: 16 Gy focal boots to the 2 lesions, and 24 Gy to the whole ventricle. MRI at 12 months after the completion of the treatment showed complete resolution of the tumors and no intraspinal seeding (Fig 1 - h). The patient is fully working without disturbance 8 years after treatment.

Discussion

The WHO classification divided GCTs into benign (mature teratoma) and malignant (germinoma and non-germinoma) tumors (1). The SP represents an excessively rare location of GCT with only 6 reported cases to date including ours, making difficult to describe their radiological features (Table 1) (2-6).

Three of them were mixed GCTs, and 2/3 were metachronous (2, 5). However, they share a few common imaging features with ectopic IGs, different from those originating from sellar/suprasellar and pineal regions: well-defined margins, isointense on T1 WI, iso/hypointense on T2 WI, contain multiple cysts which tend to be large because of the minimal or nonspecific clinical signs and symptoms. The solid part presents moderate or strong enhancement of the lesion and cysts- walls enhancement and mild peritumoral edema are present (7-9). Ectopic IGs have a more marked male predominance than midline IGs and present predominantly as a single tumor (8). The reported cases of SP germinomas (SPG) present numerous and large (50-60 mm) cysts, marked enhancement, without associated hemorrhage or calcifications as demonstrated by NCCT and T2* sequence.

SPG share radiological features with CC germinomas, as shown in our literature review of 14 cases with enough radiological data. CC germinomas are often large

(9/14: ≥ 30 mm), with strong enhancement (12/14), well-defined margins (9/14), and present rarely with edema (2/14). They are hypo-isointense on T1WI and iso-hyperintense on T2WI. Calcifications and haemorrhage are absent and in 5/14 cases. However, none of the reported cases of CC germinomas presented with a synchronous lesion.

Nevertheless, our case presents many atypical features. First, the occurrence of synchronous lesions, a presentation not previously reported. Secondly the presence of a slight T1 WI hyperintensity of the solid parts which appear hyperdense on NCCT. These findings were not related to calcifications or hemorrhagic components. Slight restriction diffusion in our case was in concordance with the few reported cases (8,10).

Biological markers, such as serum and CSF α -foetoprotein and β -hCG may be useful, but they are rarely considered in the work-up of hemispheric tumors.

In the literature' cases the SP lesion was isolated. However, the presence of a synchronous lesion in SP IG, as in our case, and as in case of other ectopic IG, is a clue for the presumptive diagnosis.

The differential diagnosis includes mainly gliomas and lymphomas, as these lesions share the same MRI signal characteristics: hypo/ isointense on T1 WI, iso/hyperintense on T2 WI, with strong, homogeneous or heterogeneous enhancement (in case of cystic component) on post-contrast T1 WI. Furthermore the MRI appearance of our case mimics central neurocytoma (CN), as Park's case, making the preoperative diagnosis challenging in case of isolated IG of the SP (6). Our report adds one more case to such unusual presentation. Nevertheless, marked restricted diffusion in case of CN may help to differentiate them.

As ventricular seeding is common for IG, the radiotherapy field usually includes whole ventricles rather limited to tumoral mass. Craniospinal radiotherapy is usually underwent by patients with leptomeningeal seeding.

Conclusion

IG arising in the SP is rare but should be considered in the differential diagnosis, especially in young adult and particularly in male, presenting with multi-cystic lesion.

The presence of a synchronous mass is a clue for the presumptive diagnosis of germinoma.

These findings suggest that IG in SP may present as a large tumor with large cysts and may look as central neurocytoma. ADC value is helpful to differentiate them.

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Compliance with ethical standards

Conflict of interest All authors have no conflict of interest.

Informed consent

The reported patient was treated with standard of care therapy after informed consent was obtained.

Figures Legend:

Figure 1:

a -Non-contrast Brain CT shows a midline cystic lesion invading the frontal lobes. The solid parts are hyperdense.

b-c-d-e MRI realized 2 days later shows 2 lesions. First a 60-mm-sized cystic lesion of the septum pellucidum which invades the white matter of frontal lobes and has an asymmetric growth. The mass has a butterfly aspect and a honeycomb-like

appearance. Multiple cysts (7 to 19 mm in diameter) are present within and at the periphery of the tumor, well identified on coronal-T2-weighted image (T2-WI) (b). Secondly T1-weighted image (T1WI) in the 'sagittal plane shows a mass invading the sellae and the entire pituitary stalk. The bright spot of the posterior pituitary gland has disappeared on T1WI (c).

The solid parts of the two lesions are slightly hyperintense on T1-WI (c) and hyperintense on T2-WI and fluid attenuation inversion recovery (FLAIR) sequence (b-d). FLAIR image shows a thick peripheral edema (Fig 1 - d).

After contrast the solid components of the two masses enhance. The lesions have well-defined borders (Fig 1-e). The extension of the septum pellucidum lesion to the 2 frontal lobes and the linear enhancement of the cysts walls and cystic areas within the sellar mass are better visualized on post-contrast coronal T1-WI. (Fig 1- f).

g-h -Immunohistochemistry: The tumoral cells are positive for Placental Alkaline Phosphatase (PAP): objx16 (g), objx40 (h).

i – Post-operative MRI at 12 months:

Reformatted volumetric post-contrast 3D T1 acquisition shows that the lesions have completely disappeared. Cicatricial cysts are present in the body of the corpus callosum.

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