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PRIMARY YOLK SAC TUMOR OF THE CEREBELLUM: AN UNUSUAL OCCURRENCE

Pathology

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ABSTRACT

Primary pure yolk sac tumors (YST) arising in the central nervous system (CNS) are extremely rare and generally arise in pineal (62%) and suprasellar (31%) regions. To best of our knowledge, till date only 10 cases of Primary YST arising in cerebellum are reported in the literature. YSTs have very poor prognosis. Most of them occur in childhood, between 7 months to 3 years of age. Pathologist should be aware that the primary yolk sac tumors can present at unusual anatomical sites like cerebellum, which would aid its early diagnosis and appropriate treatment. Herein, we report a case of Primary YST involving cerebellar vermis and right cerebellar hemisphere in a 4-year-old female.

KEYWORDS

Cerebellum, Yolk sac tumor, Schiller Duval bodies, AFP

INTRODUCTION

Yolk sac tumor (YST) arising in the CNS are rare. It is also known as endodermal sinus tumor due to its similarity to rodent placental endodermal sinuses. [1] Extragonadal germ cell tumors (EGCTs) comprise 2-5% of all the germ cell tumors. Seminoma/ Dysgerminoma, Teratoma, YST and mixed germ cell tumors are few of them. Primary pure YST arising in the brain is extremely rare and usually involve pineal (62%) and suprasellar (31%) regions. [2] Other unusual sites described in CNS are fourth ventricle, frontal lobe, spinal cord with occasional cases in cerebellum.[3] Till date only 10 cases of Primary YST arising in cerebellum are reported in the literature.[4]

CASE HISTORY

A 4-year-old female child presented with headache since one month, vomiting, imbalance while walking, excessive crying and irritability since 15 days. CT Brain showed a 4.5x3.2 cm hyperdense lesion in the vermis extending to the right cerebellar hemisphere [Figure 1(a)]. MRI Brain showed a well defined lobulated round to oval lesion measuring 41x38x38 mm in the posterior fossa involving cerebellar vermis and right cerebellar hemisphere. It appeared iso to hyperintense to grey matter in T2W and FLAIR images and hypointense in T1W images with mild surrounding edema [Figure 1 (b, c)]. Few foci of blooming were seen within the lesion, suggesting the diagnosis of medulloblastoma.

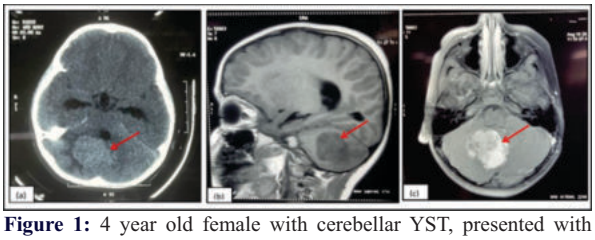

Figure 1: 4 year old female with cerebellar YST, presented with headache, vomiting and imbalance while walking (a): CT brain axial view showing hyperdense lesion in vermis (arrow) extending to right cerebellar hemisphere. (b): MRI brain T1W sagittal view showing hypointense lesion (arrow) in cerebellar hemisphere. (c): MRI brain T1W Post- contrast axial view showing hyperdense lesion involving cerebellar vermis and right cerebellar hemisphere (arrow).

Tumor was surgically resected by a midline suboccipital craniotomy. Intraoperatively tumor was firm, greyish pink, mildly vascular and was within the cerebellar parenchyma. Histopathology showed a tumor composed of cells arranged in papillae, tubules and reticulated pattern. [Figure 2(a)] Individual tumor cells had eosinophilic to clear cytoplasm, vesicular nucleus with few showing prominent nucleoli. Nuclear pleomorphism, hyperchromatism and multinucleation were seen. Schiller Duval bodies (columnar neoplastic cells surrounding the blood vessels) were seen. [Figure 2(b)] Hyaline droplets and foci of necrosis noted. Atypical mitoses noted. No other germ cell component was identified.

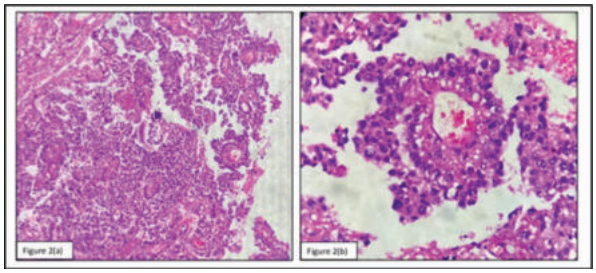

Figure 2: 4 year old female with cerebellar YST, presented with headache, vomiting and imbalance while walking (a): H&E 10x, showing tumor cells arranged in papillae and tubules. (b): H&E 40x, Schiller duval body.

Tumour cells showed diffuse immunoreactivity for alfa-feto protein (AFP) [Figure 3(a)], Glypican-3 [Figure 3(b)] and Cytokeratin(CK). Tumor cells were immunonegative for CD30 and Epithelial membrane antigen (EMA). IHC thus confirmed the diagnosis of YST. Preoperative Serological Human chorionic gonadotropin-β and α-fetoprotein (AFP) were not measured, since YST was not suspected clinically or radiologically. After a month of tumor resection, serum AFP levels measured 74.52ng/ml and human chorionic gonadotropin-β was less than 0.13mIU/ml.

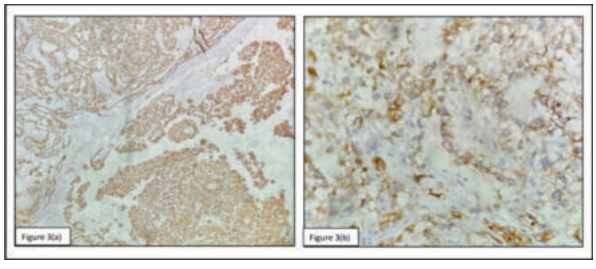

Figure 3 : 4 year old female with cerebellar YST, presented with headache, vomiting and imbalance while walking (a): H&E 10x, Immunohistochemical staining showing diffuse and strong positivity of AFP (b): H&E 40x, Immunohistochemical staining showing positivity of Glypican-3.

Patient was completely screened to identify the primary lesion. However, no lesion was identified in the ovaries or elsewhere on ultrasound examination of the abdomen and pelvis. Hence, the diagnosis of primary pure YST was rendered.

Patient presented with hypertension and bradycardia after a month of tumor resection. MRI done therein suggested residual/recurrent tumor

with tonsillar herniation and spinal metastasis. Patient was prescribed Carboplatin and Etoposide, but succumbed to the disease within three days of starting this medication.

DISCUSSION

Extragonadal germ cell tumors (EGCTs) are extremely rare. Seminoma/ dysgerminoma, teratoma, YST and mixed germ cell tumor are few EGCTs arising in the brain.[2]

EGCTs have an interesting pathogenesis. One of the proposed theories is related to the aberrant migration of primordial germ cells. These cells normally migrate to primitive gonadal folds during embryogenesis, misplacement from midline may occur, giving rise to extragonadal germ cell tumors. Another theory suggests the mechanism of metastases developed from undiagnosed or regressed ("burned out") primary germ cell tumor in the gonads. Third theory involves genetic alterations like aneuploidy and chromosome 12 abnormalities.[5]

YST usually originates from the gonads. Approximately 10% YSTs arise in extragonadal sites in females which have midline distribution like in sacrococcygeal region, retroperitoneum, mediastinum, stomach, liver, omentum, pelvis, genital system and central nervous system(CNS).[6] Within CNS, primary YST occurs in pineal(62%) and suprasellar(31%) regions. Other unusual sites described in CNS are fourth ventricle, frontal lobe, spinal cord with occasional cases in cerebellum.[3] Till date, only 10 cases of pure primary YST of cerebellum have been reported in the literature excluding our case. Most cases of YST are children aged between 7 months to 3 years,[2] although few cases are reported in adults,[7] post- pubertal[8] and post-menopausal females.[2] 9 Out of 10 cases of Primary cerebellar yolk sac tumors reported in literature, were males[Table 1].[4] However our case is of 4-year-old female child.

Table 1: Brief Review Of Yolk Sac Tumor Cases Of The Yst In Cerebellum In The Literature.

Case No.	Authors and year	Age (Yrs.)	Sex	Tumor location
1	Takeda et al. 1985	4	M	Left cerebellar hemisphere
2	Tajika et al. 1988	2.5	Un	Cerebellar hemisphere
3	Tsukamoto et al. 1992	2	M	Cerebellar vermis
4	Fujiwara et al. 1994	4	M	Right cerebellar hemisphere
5	Nakase et al. 1994	5	M	Cerebellar vermis
6	Yang et al. 2003	2.5	M	Right cerebellar hemisphere
7	Cheon et al. 2006	3	M	Left cerebellar hemisphere
8	Kuang et al. 2014	3	M	Left cerebellar hemisphere
9	Shenoy et al. 2014	2	M	Cerebellar vermis
10	Wu N et al. 2021	6	M	Left cerebellar hemisphere
11	Present case	4	F	Cerebellar vermis and right cerebellar hemisphere

F: Female, M: Male, Un: Unknown.

No definite risk factors or neurological syndromes are known to be associated with the occurrence of YST in CNS. Primary YST of CNS generally present with gait disturbances, headache, vomiting, limb ataxia and visual disturbances.[4] Our patient complained of headache, vomiting, imbalance while walking and excessive crying which may be attributed to the tumor distorting the cerebellar structure, causing intracranial hypertension.

There are no definite radiological criteria to diagnose YST. Most case reports of YSTs showed typically a well-defined round or oval tumor which was isointense on T1-weighted images and slightly hyperintense on T2-weighted images.[9]

Histopathology is essential for exact diagnosis. Typical morphological feature of YST is the presence of the Schiller Duval body, which is composed of monolayer of cuboidal or columnar neoplastic cells surrounding the capillaries/thin walled blood sinus/ small venous blood vessels; was seen in our case.[10]

Studies have reported that AFP, Sal-like protein 4 (SALL-4) and glypican-3 are sensitive diagnostic markers for YST[10]. AFP is a useful marker not only for immunohistochemical staining and pathological diagnosis but also for evaluating the treatment response and for detecting recurrence.[9] Our case showed diffuse immunostaining for AFP, Glypican-3 and CK and negative staining for CD30 and EMA which confirmed the diagnosis.

While 5-year survival in cases of intracranial germ cell tumor is over 90%, the prognosis in case of yolk sac tumor is relatively poorer. YST has shown strong tendency for spread via cerebrospinal fluid (CSF). Many studies have recommended combination of surgical resection (gross total resection favored over Subtotal resection) along with adjuvant chemotherapy and radiotherapy.[3] In our case, there was recurrence of tumor with spinal cord metastases due to the dissemination via CSF, within a month of resection. Cerebellar mass would have caused pressure on the vital areas in the brainstem resulting in bradycardia and asystole, to which the patient succumbed.

Thus, to conclude, Primary Intracranial Yolk sac tumor is a rare tumor and is associated with poorer prognosis. Pathologist should be aware that primary yolk sac tumors can be present at unusual anatomical sites like cerebellum, which would aid early diagnosis and appropriate treatment.

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