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Case report ■

Mature Intracranial Teratoma

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SUMMARY

Teratomas constitute a group of nongerminomatous germ cell tumors that are composed of an admixture of different tissue types representative of ectoderm, endoderm and mesoderm. Intracranial teratomas are rare, comprising approximately 0.5% of all intracranial tumors. They preferentially involve the midline structures, and occur primarily in children.

We presented an unusual case of mature intracranial teratoma with extracranial extension in a 24-year-old man who complained of headache, nausea and vomiting. The intracranial expansive lesion was localized in the left frontotemporobasal region extending into the ipsilateral orbit. The patient underwent total resection of the tumor. No adjuvant treatment was given. On gross examination, the resected tumor was lobulated, containing heterogeneous solid and cystic components. Histologic investigation revealed the presence of various fully differentiated tissues representative of the three germ cell layers, including adipose tissue, cartilage, bone, striated muscle bundles, brain tissue, respiratory epithelium and glandular structures. The diagnosis of mature teratoma was established. Follow-up at four years did not show any evidence of recurrence.

The presented case is an unusual example of mature teratoma with regards to the age of the patient and, especially, to the location of the tumor, both intra- and extracranially. It is critical to recognize this rare entity by extensive sampling to rule out the presence of immature elements which may constitute only a minor part of the tumor.

***Key words*: germ cell tumor, mature teratoma, intracranial, orbit, diagnosis, diagnostic techniques and procedures**

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INTRODUCTION

Teratomas constitute a group of nongerminomatous germ cell tumors that are composed of an admixture of different tissue types representative of ectoderm, endoderm and mesoderm. They recapitulate somatic development from the three embryonic germ layers (1). Teratomas account for 3% of all childhood tumors (2), with the majority occurring in the sacrococcygeal regions and in the gonads. The histologic picture of these tumors is strikingly similar, regardless of location. Intracranial teratomas are rare, comprising approximately 0.5% of all intracranial tumors (3), but the incidence is substantially higher in the paediatric series (3-6).

Like their extragonadal counterparts, intracranial teratomas preferentially involve the midline structures. Teratomas are classified into three groups: mature teratomas, immature teratomas and teratomas with malignant transformation (1). Among them, the immature variant predominates (4, 6, 7). The mature teratomas arising within the central neuraxis in adulthood are uncommon.

We reported an unusual case of mature intracranial teratoma with extracranial extension into the orbit in an adult patient.

CASE REPORT

A 24-year-old man was admitted at the Clinic of Neurosurgery, Clinical Center Niš, with strong headache, nausea, vomiting and fatigue. The physical and neurological examination revealed a subtle right side weakness and proptosis of the left eye. Laboratory data were unremarkable. Magnetic resonance imaging (MRI) demonstrated an expansive intracranial mass in the left sphenoid ridge region, with a greatest dimension of 45 mm. The lesion was localized in the left frontotemporobasal region extending into the ipsilateral orbit. The neigh boring intracranial and orbital structures were displaced and compressed, but apparently not invaded. The patient underwent craniotomy and the intracranial tumor with orbital extension was completely excised. The postoperative clinical course was uneventful and preoperative symptoms improved gradually. No adjuvant treatment was given.

On gross examination, the tumor was lobulated containing heterogeneous solid and cystic components. The cut surface was variegated, with white, yellowish and reddish areas. The samples from excised tumor were fixed in 10% formalin, routinely processed and paraffin-embedded. The sections 5 μm thick were stained with hematoxylin and eosin (HE) and by periodic acid-Schiff (PAS) method. Tissue sections with representative histological features were selected for immunohistochemistry and this was performed using the labeled streptavidin-biotin (LSAB) method with a panel of antibodies. These included: vimentin (clone Vim 3B4), smooth muscle actin (clone 1A4), desmin (clone DE-R-11), glial fibrillary acidic protein (GFAP, clone 6 F2), S-100 protein (polyclonal), cytokeratin (clone AE1/ AE3) and alpha-1-fetoprotein (AFP, polyclonal). All antibodies (from Dako Cytomation) were prediluted except pancytokeratin antibody whose working dilution was 1:50. The reaction product was detected with 3.3-diaminobenzidine as the chromogen. Counterstaining was done with Mayers' hematoxylin.

The entire specimen was submitted for histologic examination, which revealed the presence of various fully differentiated tissue elements. Mesodermal derivatives (Figure 1a-b) including adipose and fibrous connective tissues, cartilage, bone and striated muscle were abundant.

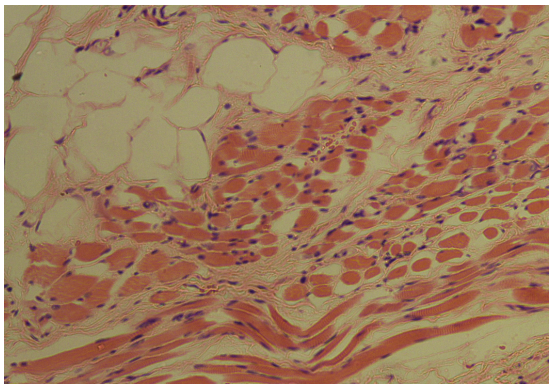

Figure 1a. *Striated muscle bundles surrounded by connective fibrous and adipose tissues (HE, X100)*

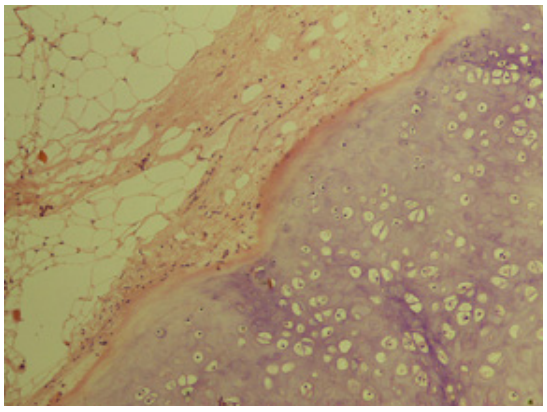

Figure 1b. *Nodule of moderately cellular cartilage, connective fibrous tissue and mature fat cells (HE, X100).*

The muscle cells were mostly arranged in bundles of variable size surrounded by fibrous septa. Neuroectodermal component was represented by delicate fibrillar tissue, in which mature glial elements (mainly astroglia) predominated (Figure 2), but mature neuronal elements were also present.

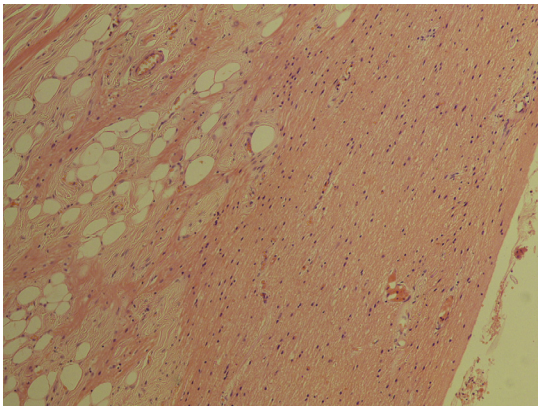

Figure 2. *Neuroectodermal component of mature teratoma, hypocellular fibrillar tissue in which glial cells predominate (HE, X100).*

The respiratory epithelium and glandular structures were observed, surrounded by fibrous connective tissue and mature fat (Figure 3a). The cysts with fluid-filled cavities of varying size were intermingled with solid areas. The wall of the cysts was composed of a connective tissue with an inner lining of columnar epithelium (Figure 3b).

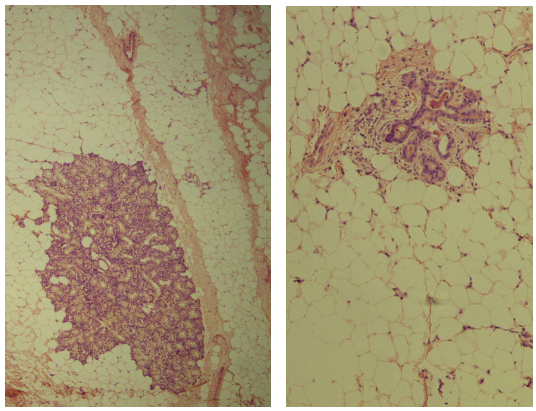

Figure 3a. *Differentiated glandular structures in fibro-fatty background (HE, X100).*

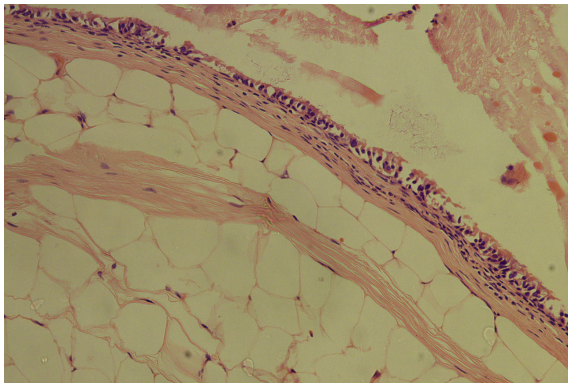

Figure 3b. *The cyst lined by columnar epithelium with connective tissue in the wall (HE, X200).*

The tumor was moderately vascular, with predominantly smaller vessels and small foci of recent hemorrhage were suggestive for operative origin. Mitotic figures were not present.

The immunohistochemical analysis revealed positive staining for GFAP in the glial cells (asrocytes) of the neuroectodermal component (Figure 4). In addition,

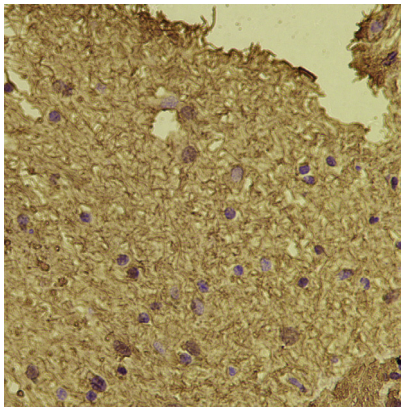

Figure 4. *GFAP-positive glial cells (astrocytes) with intensive immunostaining of the cellular processes (fibrillary matrix) (LSAB, X200).*

immunoreactivity for vimentin and S-100 protein could be detected. The epithelial elements of the tumor were cytokeratin (AE1/AE3) - positive, while immunoreactivity for AFP was negative, confirming their mature appearance. Immunoreactivities of the mesodermal elements were those corresponding to normal tissues.

Extensive analysis of multiple sections of the tumor did not reveal any primitive neuroepithelial or other immature tissue elements. The diagnosis of mature teratoma was established. At the 4-year follow-up examination the patient was asymptomatic, with no evidence of recurrence.

DISCUSSION

Intracranial teratomas are rare nongerminomatous germ cell tumors. They occur primarily in children, and congenital examples are well-recognized (1, 8, 9). Teratomas account for 2% of intracranial tumors in patients younger than 15 years of age (3, 10). The frequency is higher in Japan**,** Taiwan and Korea, which is in agreement with that of germ cell tumors in general (4-6). These tumors preferentially arise in the midline, and males are more often affected than females (1, 3-5). The pineal and suprasellar regions are their favourable sites of origin (3, 5, 7). Other tumor locations include the region of the third ventricle, the pituitary fossa, the fourth ventricle, lateral ventricles and posterior fossa (3-5, 10).

The World Health Organization classification of intracranial teratoma delineates three histological variants: mature, immature and teratoma with malignant transformation (1). Mature teratomas are composed of fully differentiated tissue elements of the three germ cell

layers. If the lesion is completely excised, patients with mature teratomas have a good prognosis with a reported 10-year survival rate greater than 90% (5, 11). The prognosis for patients with immature teratoma is less favorable, with a 5-year survival rate up to 70% (6, 11). The hallmark of immature teratomas is the presence of undifferentiated components exhibiting embryonal or fetal appearances (7). The immature component is frequently composed of neuroepithelial elements that can give rise to more malignant tumors (12). Mature tissues identical to those encountered in mature teratomas are usually present. These tumors tend to recur frequently. Teratomas with malignant transformation, containing a conventional malignant tumor of somatic type (i.e. sarcoma or carcinoma), are associated with poor prognosis (5, 6).

It is interesting to note that the potential for phenotypic differentiation and cellular maturation within immature teratomas arising in the gonads (13, 14) has also been documented in their intracranial counterparts (10, 15). Intracranial immature teratoma was reported to differentiate to fully mature tissues spontaneously (10) or after radio- and/or chemotherapy (10, 15). The distinct clinicopathologic entity with paradoxical response to treatment, termed "growing teratoma syndrome" has been recognized in the intracranial tumors as well (1, 15). The enlargement of residual, differentiated lesions presumably reflects the selective radio- or chemoablation of immature components.

On the other hand, there are several single case reports describing a second intracranial germ cell tumor developing usually at a different site and showing a different histological type after total resection of primary intracranial tumor that was in all cases a mature teratoma (16-19). Moreover, the second tumor was a germinoma. Mature teratomas are considered to have a good prognosis and an extremely low recurrence rate after gross total resection (17). The longest latency between the manifestation of a mature teratoma and a later germinoma was found to be 22 years (19). These data indicate that close follow-up is necessary even after a total removal of mature teratoma.

Although the vast majority of teratoma cases are diagnosed in children, there have been single case reports in adults. Kim et al. (18) reported the case of a 29-year-old man who developed germinoma 30 months after the resection of mature teratoma in the third ventricle. Park et al. (20) reported the case of intracranial mature teratoma in a 47-year-old women. The present case is unusual with regards to the age of the patient (24y 8m) and, especially, to the location of the tumor, both intra- and extracranialy. Excluding congenital supratentorial teratomas (9), only a childhood case of teratoma in this location showed extension into the orbit, and was immature at initial presentation (10). To our knowledge, the present case may represent the first example of mature intracranial teratoma extending into the orbit in an adult patient. Extensive study of multiple sections from the entire tumor specimen did not detect any evidence of immature components. The presence of fully differentiated tissue elements may be related to the relatively late onset of clinical manifestation.

The histogenesis of the intracranial germ cell tumors including teratoma remains poorly understood, but they are thought to arise from ectopic primordial germ cells, which failed to undergo apoptosis and are retained in the midline of the central nervous system (CNS) (21). At present, a disturbance in the mechanisms that control germ cell migration appears to be the most probable cause of these tumors (22). The mechanisms are unknown, and may include a mutation in one of the genes involved in anti-apoptotic or pro-survival pathways (21, 22). Epigenetic changes that lead to aberrant gene expression and consequent protein dysfunction may also be involved (22). Alternatively, it was suggested that each type of germ cell tumor represents the neoplastic correlate of an embryonic stage of development, so that the germinoma would derive from the misrouted primordial germ cells, while teratomas derive from the embryonic differentiated cells (23). Another hypothesis implicates toti- or pluri-potential stem cells in the histogenesis of CNS germ cell tumors (1).

The correct histological diagnosis is of high priority in intracranial teratomas as that determine the choice of treatment. Total surgical resection of the tumor is thought to be the gold standard for treatment of mature teratoma and generally shows no recurrence (3, 5, 6, 17). The follow-up period after the resection of a mature teratoma is seldom longer than 10 years (19). Having in mind metachronous occurrence of the germ cell tumors after 10 or more years suggests that longer follow-up period may be recommended. The patient in the present case underwent a total resection of the tumor in October, 2008. During the follow-up period of four years, there was no evidence of tumor both intracranialy and in the orbit.

CONCLUSION

The presented case is an unusual example of mature teratoma with regards to the age of the patient and, especially, to the location of the tumor, both intra- and extracranialy. It is critical to recognize this entity by extensive sampling (that is mandatory) to rule out the presence of immature elements which may constitute a minor part of the tumor. Total surgical resection is the treatment of choice for mature teratoma. A long-term follow-up period is recommended.

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ZRELI INTRAKRANIJALNI TERATOM

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Sažetak

Teratomi predstavljaju grupu negerminomskih tumora germinativnih ćelija, koji su građeni od mešavine različitih tipova tkiva ektoderma, endoderma i mezoderma. Intrakranijalni teratomi su retki i čine oko 0.5% svih intrakranijalnih tumora. Pretežno zahvataju strukture srednje linije i javljaju se primarno kod dece.

U radu je prikazan bolesnik star 24 godine sa zrelim intrakranijalnim teratomom uz ekstrakranijalno širenje, što je praćeno glavoboljom, mukom i povraćanjem. Intrakranijalna ekspanzivna lezija bila je lokalizovana frontotemporobazalno levo sa širenjem u istostranu orbitu. Tumor je odstranjen u celini. Adjuvantna terapija nije primenjena. Makroskopskim pregledom, odstranjeni tumor bio je lobuliran sa heterogenom solidnom i cističnom komponentom. Histološkom analizom utvrđeno je prisustvo različitih diferentovanih tkiva sva tri germinativna ćelijska sloja, uključujući masno tkivo, hrskavicu, kost, snopove poprečno-prugastih mišićnih ćelija, moždano tkivo, respiratorni epitel i žlezdane strukture. Postavljena je dijagnoza zrelog teratoma. Nakon četiri godine praćenja nije otkrivena pojava recidiva.

Prikazani slučaj zrelog teratoma je neuobičajen primer u pogledu godina starosti bolesnika i, posebno, lokalizacije tumora, intra- i ekstrakranijalno. Prepoznavanje ovog retkog entiteta ispitivanjem brojnih preseka tkiva je od presudnog značaja, budući da nezreli elementi mogu da čine samo minorni deo tumora.

Ključne reči: **tumor germinativnih ćelija, zreli teratom, intrakranijum, orbita, dijagnoza, dijagnostičke tehnike i procedure**