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Intradiploic epidermoid cysts – a series of three cases and our experience with literature data

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Abstract

Intracranial epidermoid cysts are rare, representing almost 1% of all primary tumors and when are located in the diploe result from entrapped ectodermal embryonic remnants. Because of frequent complications, imaging studies are mandatory for highlighting erosions of both outer and inner table of the calvaria and treatment preparation. We enlisted three female patients within our study, comparing imaging with histopathology aspects. Even though the bone destruction was evident, no atypia or malignant signs were highlighted in serial sections. The interesting fact that we present is that our patients are all females, opposed to what is written in literature. Although the positive diagnosis can be made by imaging, histopathological examination of these cysts is mandatory for identifying malignant behavior.

Keywords: intradiploic epidermoid cysts, ectodermal embryonic remnants, bone reconstruction, malignant behavior.

Introduction

Keratinous cyst is encountered frequently on the scalp and face, with a peak incidence in fourth decade of life and most common cutaneous cyst are diagnosed as epidermoid cyst (EC) [1].

Intracranial ECs represent approximately 1% of primary lesions, being benign, with a slow grow rate (due to repetitive desquamation): most frequent are found in cerebellopontine angle (40–60% of cases) and it can adhere intimately to the surrounding neurovascular structures [2–5].

Intradiploic epidermoid cysts (IDECs), although rare, result mainly from entrapped ectodermic embryonal remnants (ectodermic cell rests between third and fifth gestational weeks) because of incomplete cleavage of neural crest and a sequestration of skin elements within skull bones; some authors imply an acquired state due to trauma and implantation of epidermal cells in the connective tissue of the diploe [6–9].

IDEC was first described by Müller, in 1838, and by 1990 a total of 223 cases of this type of cyst were cited in the literature. This type of cyst was described as a "pearly tumor" or "ectodermal inclusion cysts". Similar to EC in the skin, IDECs are more commonly seen in male patients [10].

In the past, these cysts were erroneously described as "neuroenteric cysts", but this theory was quickly disbanded because IDEC has ectodermal origin and enteric cysts had endodermal features [11].

Clinical manifestation in majority of IDECs includes tenderness, headache (due to calvaria erosions), with small subcutaneous lumps of the scalp represented by bone swelling. Major neurological signs (seizures, meningeal reaction, intracranial hypertension) can occur due to large size, perforation of internal diploe and dura mater, involvement of brain convexities. As mentioned in the literature, trigeminal neuralgia can be caused additionally by rupture or excessive bleeding of intradiploic cyst [6, 9, 10].

Except temporal bone, IDECs are more often located in the rest of calvaria bones (frontal, parietal, and occipital). IDECs account for approximately 5% off all intracranial ECs and the natural evolution of these cysts is mainly benign, with a very slowly development. Occurrence of atypia is relatively rare in IDEC [1, 10, 12].

The clinical findings often are subject to rely on the overlying skin thickness and its laxity; however, this limits the ability to detect cortical change in the peripheral area of IDEC [1].

Using computed tomography (CT) scan, IDEC has shown in many cases simultaneous erosion of inner table and outer table of the calvaria; the radiological appearance depends mainly on the ratio between keratin lamellae and cholesterol clefts inside the cyst. Dural infiltration appears

in only 10% of IDEC patients and produces a chronic granulomatous meningitis (aseptic) because of keratin release, cholesterol, and cellular debris into the subarachnoid space. Having a capsule that has growing cells in it, the correct treatment for these cysts is total surgical removal with capsule dissection [7, 12].

When performing histological examination, the inner lining of the cyst is represented by keratinized squamous epithelium, with an outline of a collagen capsule. The cyst contains keratin, debris, and cholesterol clefts; the wall is devoid of skin appendages [4, 10].

Complete surgical resection of subdural ECs may have an unacceptable rate of morbidity and even mortality, due to neurosurgical intraoperative and postoperative complications [3].

Aim

In order to prevent intracerebral complication, a swiftly imaging diagnosis of intradiploic cyst is mandatory. We present a series of three cases of IDEC occurred, interestingly, in female patients.

Patients, Materials and Methods

We enlisted in our study three female patients with IDEC, with presentation in the Emergency Department of Emergency County Hospital, Oradea, Romania, from rural background. All patients were hospitalized in the Clinic of Neurosurgery and their ages at admission were 12, 71 and 78 years old.

Imaging studies were made on three females using craniocerebral CT (native, or with intravenous contrast) followed by multiplanar reconstructions (MPRs – coronal, sagittal and virtual reality sections by volume rendering). We used a 16-slice Optima CT scan from General Electric.

Only two patients from our group gave consent for surgery (while the older patient refuse it), and a surgical treatment was performed for the removal of the cysts. Both surgical interventions were performed in Emergency County Hospital, Oradea, and the lesions (intradiploic cysts) were sent in a fixative solution (10% neutral buffered formalin) to Department of Pathology for microscopical examination. After 24 hours, we examined the specimens grossly, trim them and softer areas were harvested. For examination and trimming of bony fragments, we placed them, for a few days, in decalcifying solution (5% nitric acid), so we could section the bone and examine the extend of the cyst.

All the specimens were histologically processed using paraffin-embedding technique. Sections with a thickness of 4 μm were cut from tissue blocks with a manual rotary microtome, displayed on regular slides, and manually stained with Hematoxylin–Eosin (HE). Microscopy was performed with Leica DM 1000 LED optical microscope and photos were made with the Leica integrated camera.

At admission, all patients signed the informed consent and agreed with publication of their data in scientific purposes. All clinical data and the scientific reports were performed in accordance with Declaration of Helsinki from 1975. We have the accept of the Hospital management to search for clinical data from these patients and we have the approval of the Ethics Council and the Ethics Committee from Emergency County Hospital, Oradea.

Results

The youngest patient had an acute clinical onset, with a lump in the frontal area behind the hair line that develop quickly followed with headache. Clinical examination showed an elastic, unpainful tumor, with a clear demarcation from pericranial tissues, but adherent to the calvaria. Imaging techniques revealed a frontal cystic bone tumor with dural distortion (Figure 1, A and B). Surgical resection was performed in general anesthesia, with total excision of the cyst tumor and followed by cranioplasty with dynamic mesh and acrylic cement. Surgical follow-up was simple, without complications, clean wound, and no neurological signs. No residual tumor was found on post-operatory magnetic resonance imaging (MRI).

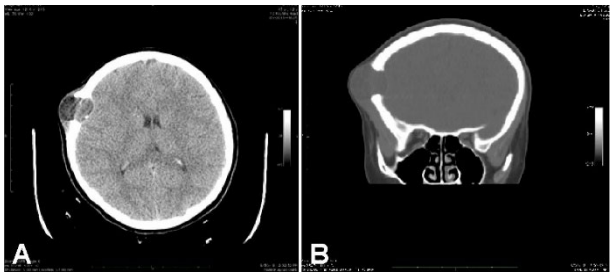

Figure 1 – ***Native CT scan (parenchymal section) reveals and expansive lesion in frontoparietal region lined by a capsule with microcalcification; the bone shows osteolysis (A) and MPR in coronal view shows a nodule associated with osteolysis of calvaria and skin's surface deformation; a fine capsule can be observed (B). CT: Computed tomography; MPR: Multiplanar reconstruction.***

According to surgical procedures made with a limited operation field, the brain surgeon sent to Department of Pathology multiple tissue fragments from the tumor and the excised cyst wall. All specimens had cumulative dimensions of 4 cm.

Microscopic examination points out the cyst layer, having a stratified keratinizing squamous cells with a nonspecific chronic inflammation in the pericranial tissue. No malignant behavior of the squamous cells in the examined slides. The cyst was heavily keratinized, with orthokeratosis and lamellar keratin production (Figures 2 and 3). The epithelium has an attenuated basal layer, squamous cells arranged in 3–4 levels, a thin granular *stratum lucidum* coating (Figure 4) and overlapped lamellar keratin.

The second patient presented in the emergency room with severe headache, dizziness, balance disorder and fatigue. Clinical examination and imaging technique (Figure 5, A and B) revealed a 5 cm cystic bone tumor located in right parietal and occipital diploe. In general anesthesia, entire bone lesion was resected in one piece and cranioplasty was performed with titan mesh. No intra-operatory or post-operatory complication occurred. The surgical follow-up of this patient was simple. No residual tumor was found on CT scan.

The resected specimen measured 7 cm in the greatest dimension with an intradiploic cyst that deforms bone cortical, but without infiltrative margins, or extension in the dural space. In the center of the cyst, necrotic debris was found.

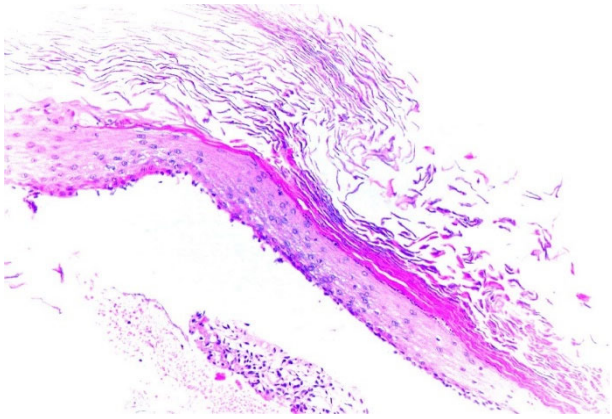

Figure 2 – ***Inner layer of the keratinous cyst (HE staining, ×100). HE: Hematoxylin–Eosin.***

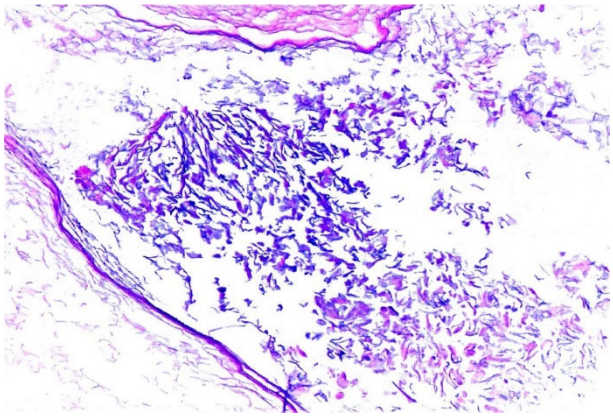

Figure 3 – ***Multiple layers of lamellar keratin filled the cyst (HE staining, ×100).***

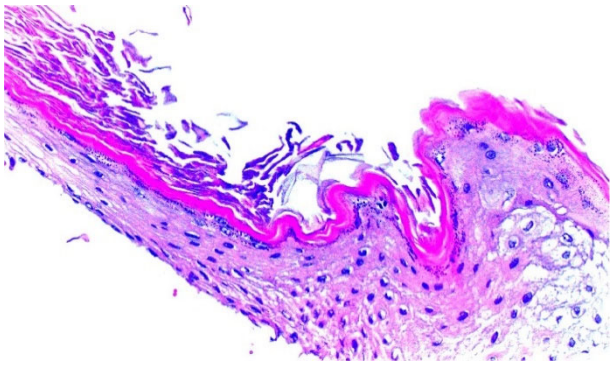

Figure 4 – ***Intradiploic epidermoid cyst with ortho-keratosis (HE staining, ×200).***

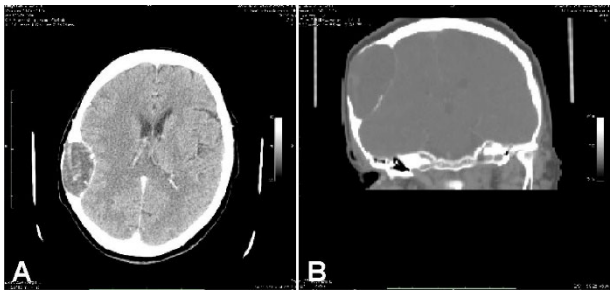

Figure 5 – ***An osteolytic and expansive tumor is shown in CT scan with intravenous contrast (parenchymal view); this lesion is located in parietal bone, well delineated by a capsule (with moderate enhancement after contrast) with microcalcifications (A) and CT bone reconstruction, coronal view highlights internal bone osteolysis (B). CT: Computed tomography.***

The inner ling of the cyst is made entirely of squamous stratified epithelium, with granular layer and lamellar keratinization (Figure 6). The base of the epithelium is almost flat with typical mitotic figures. Focally, we can appreciate a different pattern in maturation of the epithelium, with indistinct cellular borders, less granulation and without lamellar keratin, although these areas lack parakeratosis (Figures 7 and 8).

In the analysis of bone structure, the Haversian architecture (Figure 9) is not altered and there is present an osteoblastic rim at the periphery of the tissue. In some areas (Figure 10), bony tracts of the diploe were destroyed by activated osteoclasts and intraosseous hemorrhage occurred. This aspect was quite patchy, and we did not find any dysplastic features in the cyst wall near these areas. Also, in all HE slides harvested from the specimens, no nuclear atypia or malignant signs were revealed.

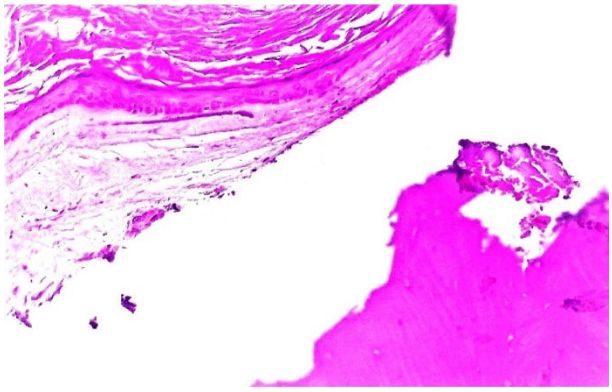

Figure 6 – ***Stratified squamous epithelium with inner keratinization (HE staining, ×200).***

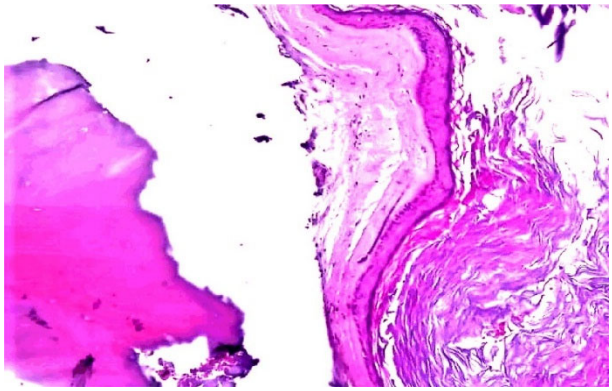

Figure 7 – ***Intradiploic cyst wall with overt lamellar keratinization of the epithelial lining (HE staining, ×100).***

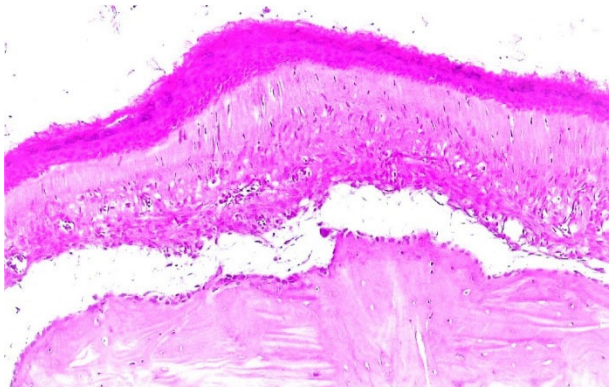

Figure 8 – ***Intradiploic cyst wall lined with squamous epithelium; bone tissue has a Haversian architecture with an osteoblastic rim (HE staining, ×100).***

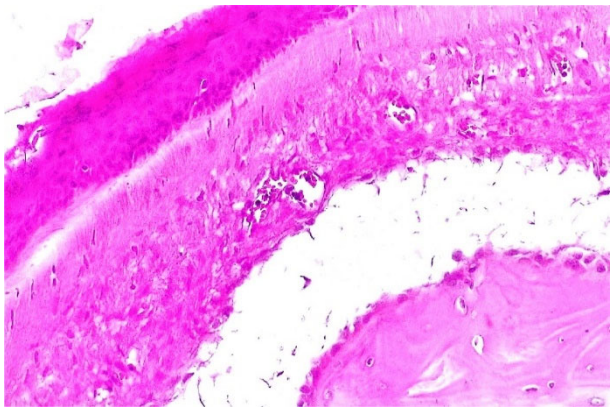

Figure 9 – ***Cyst wall fibrosis and blood vessel proliferation beneath the epithelium, osteoblasts from the diploe are more visible (HE staining, ×400).***

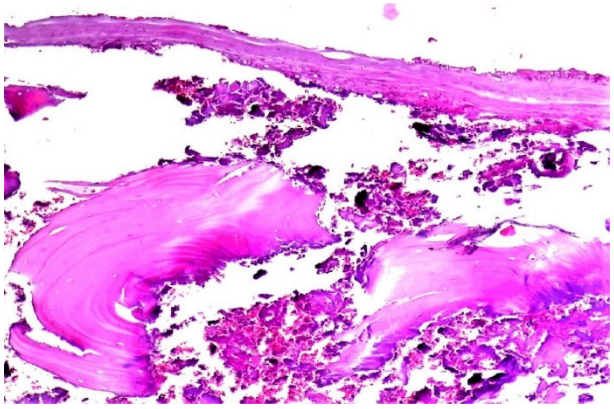

Figure 10 – ***In the upper part of the image, we can highlight the cyst wall and the destruction of diploe (HE staining, ×100).***

We also included in our paper a case of a 78-year-old female patient, with an expansive intradiploic tumor associated, with massive osteolysis and we present the imaging acquisition (Figure 11, A and B). This patient refused surgical removal of the tumor and died in 2018, not because of cyst rupture or neurological complications but from cardiovascular comorbidities.

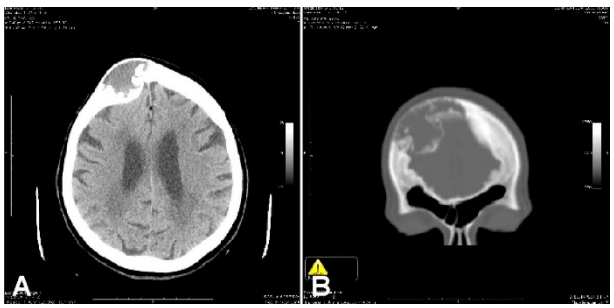

Figure 11 – ***(A and B) Cranial native CT scan reveals an expansive cystic tumor in right frontal bone which deforms calvaria and right frontal intradiploic osteolysis in MPR of bone in coronal view. CT: Computed tomography; MPR: Multiplanar reconstruction.***

Discussions

IDECs commonly affects males with ages between 15 and 50 years old and in CT scan, these cysts appear typically as low-density lesions, hypodense without enhancing effect, similar to fat density [4]. Moreover, in MRI examination, IDEC has a high signal intensity in T1 and a variable signal intensity in T2 fluid-attenuated inversion recovery (FLAIR), making it inhomogeneous and at the periphery, we can highlight enhancement after contrast intake. These type of cysts shows restricted diffusion, with higher signal intensity on diffusion-weighted imaging (DWI) sequences than cerebrospinal fluid and if we appreciate a hyperdense signal in MRI examination, we can assume that intra-cystic hemorrhage occurred [7, 10].

In differentials of IDEC, we can include dermoid cyst, cystic tumors (acoustic schwannoma and craniopharyngioma), *calvaria cavernous* hemangioma (with honeycomb aspect), calcified cephalohematomas, cholesterol granuloma, eosinophilic granuloma (when present in young adults or children, are tender, less heterogeneous and have beveled edges), arachnoid cyst, occult meningocele, aneurysmal bone cyst, giant cell reparative granuloma (without lateral sclerosis but with signal enhancing after gadolinium intake), fibrous dysplasia, neurocysticercosis (multiple small inflammatory cysts), plasmacytoma, osteolytic intradiploic metastasis (from breast, lung, thyroid, renal cell carcinoma) [10].

MRI has a great value in the diagnosis because it can provide essential features, such as dermoid cysts are hyperintense (in T1 images, due to fat content), typically associated with sutures, arises more often in childhood, in orbital region or midline. In some studies, IDECs are four to nine times more frequent than intracranial dermoid cysts at the latter have a mesodermal origin, containing skin annexes [11, 13].

Arachnoid cysts are less lobulated, have connection with *cisterna magna*, being isointense signal in MRI T1-weighted including FLAIR sequences [7].

While cystic tumors have vascular signature at the periphery, skull metastasis can present with irregular margins and hyperintense appearance in CT scan [6].

Comparing to IDECs, subdural ECs have a restricted signal on DWI, with an irregular shape, non-enhanced, with spreading along cerebrospinal fluid cistern [4].

An accurate imaging diagnosis followed by a complete resection of the cyst and its capsule are essential for a very good prognosis on long term [12].

Even if IDEC vary in size, skull location and grow rate, rare presentation sites of skull involvement include *torcular Herophili* (this location in the occipital bone is a surgical challenge) or venous sinuses confluence (superior sagittal, straight, and occipital sinuses) [9].

Malignant transformation is quite rare but has been reported mainly in cerebellopontine intracranial ECs with posterior fossa tumor mass compressing fourth ventricle, associated with hydrocephalus, altered sensorium and severe neurological signs [6, 14].

MacMahon *et al.* (2018) [2] suggest that malignant transformation of intracranial EC is depicted secondary to chronic inflammation or cyst rupture, fact confirmed by a review from Nagasawa *et al.* (2012) [15] (having an analysis on a cohort of 58 reported cases of malignant

transformation). The average interval from initial diagnosis to epidermoid carcinogenesis [into squamous cell carcinoma (SCC)] was depicted to be between six to 15 years. The overall survival in these patients was less than one year, regardless of any adjuvant therapies performed [2, 15].

Malignant transformation should be suspected if IDECs show exponential growth rate or sudden development of neurological symptoms [3].

Conversely of IDEC, intracerebral EC, with the same odontogenic origin, involves Sylvian fissure, frontal lobe, and temporal lobe. Cerebellum is currently not interested in primary intraparenchymal EC, but it can occur in brainstem and even epiphysis [10, 11].

Local complications of IDECs are important to be identified before surgery for a successful neurosurgical treatment. Some authors showed the benefit of ultrasonography as additional imaging technique mainly in scalp ECs associated with calvarias defect [1].

It is challenging to determine if IDEC in our patients was a long-term clinical manifestation of a congenital ectodermic remnants or it was acquired, or maybe both. Although, in our patients, trauma or iatrogenic etiology were excluded from the personal medical history [16].

Even if clinical examination is very useful for diagnosis of IDEC, the important message is that we have to complete our diagnosis with imaging technique for a better neurosurgical resection plan and for a complete excision of the cyst capsule [17, 18].

After resection, follow-up in IDEC is based solely on MRI sequences. Some authors suggest that we can use in post-surgery period some tumor biomarkers, such as carbohydrate antigen (CA) 19-9, CA125, carcinoembryonic antigen (CEA) and SCC, because these can be secreted by inner epithelium lining of the cyst [4, 19].

Probably, these markers can be correlate with their value before cyst resection and nonetheless, in our opinion, we consider that imaging studies are more sensitive for detecting cyst remnants [20].

Conclusions

Intradiploic locations of ECs are very rare in female patients and findings of these unusual cases in our group are due to intensive imaging studies. CT scan with bone reconstruction is the most useful tool in assessing the bone defect and possible complications occurred in intradiploic cysts. The crucial assignment in the pathological examination, in these types of cysts, is to find one with malignant behavior.

Conflict of interest

The authors declare that they have no conflict of interests.

Authors' contribution

Ovidiu Ţica and Alina Cristiana Venter have equal contributions to the study.

All authors of this original paper have directly participated in the planning, execution, and all authors of this paper have read and approved the final version submitted.

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