Med. J. Cairo Univ., Vol. 90, No. 7, December: 2073-2082, 2022
www.medicaljournalofcairouniversity.net

Calvarial Mass as a Presenting Symptom of Metastatic Diseases

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Abstract

Background: Calvarial lesions can be the presenting lesion of a wide variety of malignancies. The lesions are usually palpable on the skin and cause local pain and/or paraesthesia and in some advanced cases large enough to be a reason for skin dehiscence. Depending on the lesion location and its aggressiveness, some may present with neurological deficits.

Aim of Study: This study aimed to present our experience with incidental calvarial mass as a possible manifestation of systemic metastasis.

Patients and Methods: This study retrospectively report 12 cases with presenting calvarial masses for a metastatic pathology. These lesions were proven to be metastatic lesions of a primary veiled lesion at time of first diagnosis of the calvarial mass. This was either proven by documented histopathological examination following excision or an incidental finding in pre-operative investigations. Our study only included such lesions, excluding any other calvarial primary neoplastic or non-neoplastic calvarial lesions.

Results: Of our 12 patients, most of the cases were females (58.3%). The patients' mean age was 50.5 years (range 31-70 years). Six lesions were mounting from the frontal bone, 5 in the parietal bone, and one in the occipital region. While all lesions did not invade the integrity of the brain parenchyma; hence in 2 cases, the lesion invaded the dural venous sinus (Superior sagittal sinus, SSS), and another invading the frontal dura. All cases presented with scalp swelling, to an extent of causing skin dehiscence in 3 and was the main reason of excision of the calvarial lesion. On the other hand, 3 cases had neurological deficits, with 1 case reporting to ER with uncontrolled convulsions. Nine of the 12 reported cases underwent surgery for excisionof calvarial mass which showed a metastatic pathology. In other cases, the primary pathology was diagnosed, yet surgery was not done as oncologist avowed any benefit from surgery. The most discovered primary tumor was lung carcinoma (4 cases). This was followed by hepatocellular carcinomas (HCC) (3 cases) and breast carcinoma in 2 cases. Renal cell carcinoma (RCC), multiple myeloma, and diffuse B-cell lymphoma each presented with one case.

Conclusion: The calvaria is a potential site for metastases. Not only that, but it might also be the primary presentation for metastasis. We suggestthat any calvarial mass should be alerting, puttingthe possibility of metastases when managing.Further workup is mandatory for suchpatients and integrated consultation with oncologist, when metastatic, to determine surgical decision.

Key Words: *Calvarial tumors – Calvarial swelling – Systemic metastasis – Calvarial surgery – Malignancy.*

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Introduction

METASTATIC lesion to the brain coverings, the calvarium, or the skull base is relatively uncommon, yet when present contemplates a diagnostic and management challenge in patients with malignancy **[1]**. Calvarial metastases were somewhat rarely reported asa part of clinically diagnosed malignancies.There is almost no complete publication discussing the topic from all perspectives. Nevertheless, most reporting suggested they were frequently found in autopsy or as a part of brain imaging for staging **[2,3]**. The true incidence of calvarial metastasis is unknown; hence, the literature lacks standardized management protocols for such calvarial lesions **[4]**. Several articles reported calvarial metastases from various malignancies, mostly seen from breast, lung, prostate, and thyroid primaries **[3,5]**. Secondaries from pelvis or liverhave been scarcely reported **[6-9]**.

Calvarial lesions are mostly an incidental finding, rendering themasymptomatic in most cases. However, metastatic calvarial lesions, when symptomatizing, were reported to present with various manifestations, from scalp swelling, mild pain, and headaches to the extent of neurological deficits. Dural sinus involvement or increased intracranial pressure (ICP) are the reasonfor deficits, sweeping patients' attention to seek medical advice **[9]**. Nowadays, advancements and the availability of modern imaging techniques have made diagnosing such lesions a more common finding than autopsy findings in the past. Magnetic resonance imaging (MRI) (before and after contrast administration) made a definitive test to detect calvarial metastases and reveal subsequent brain covering/sinus involve-

ment. Other variants for diagnosis include radioactive bone scans and CT scanning [10].

Calvarial metastases usually signify an advanced stage of malignancy [11]. Although there is no standardized management protocol forcalvarialmetastases, they are usually managed either by radiotherapy/chemotherapy with surgical options as almost alwaysa valid accepted option when offending [12]. This study aims to present our experience with calvarial masses as the primary presenting manifest to systemic metastases. We will highlight clinical scenarios and outcomes following surgery for our reported case series.

Material and Methods

We retrospectively studied and analyzed medical records of patients with calvarial lesions treated at our Neurosurgery Department between June 2018 to June 2022 after the Approval of the Research Ethics Committee. We were able to extract a series of 12 cases with a calvarial mass as a presenting lesion for a systemic metastasis clinical's scenario. Data were further analyzed, and subcategorized according to the timing and staging of malignancy when the calvarial mass was identified.

Patients' age, gender, tumor location and the integrity of the brain parenchyma, primary cancer, presenting symptoms and signs, preoperative and postoperative imaging studies and histopathological findings (when operated upon) were all analyzed and reported. Inclusion criteria included only calvarial masses that have proven to be metastatic, either histopathological following their excision or during investigational studies following diagnosis of the calvarial mass. Any other calvarial lesions were excluded.

Results

Of all 12 patients, there was a slight female predominance (58.3%) with a mean age of 50.5 years (range 31-70 years). Six cases (50%) were in the frontal bone, 5 cases (41.7%) arose from the parietal bone, and 1 case (8.3%) was from the occipital bone. We operated on 9 patients with calvarial lesions, while the remaining 3 were not for various reasons. Brain parenchyma integrity was preserved in all cases; nevertheless, 2 cases reported dural sinus invasion (superior sagittal sinus, SSS) and another irritating the high frontal dura. Although scalp swelling was a presenting manifestation in almost every case, hence there were 3 that presented with severe skin dehiscence. Additional signs of neurological deficits were also seen in 3 patients, in form of papilledema and signs of increased intracranial tension and nerve palsy in 2 cases, while the thirdwas admitted to the ER department with recurrent attacks of convulsions and calvarial lesion was discovered during convulsion workup.

According to the clinical scenario, we classified the patients into three groups. (Table 1) shows a complete breakdown of all patient data. Group (A) were 5 patients with a known history of prior malignancy, and the calvarial mass was the first site for metastasis. In this group, we operated on 4 cases, 3 to save scalp skin, as the mass was causing impeding skin dehiscence (this was done after consulting oncologist and confirming that the patient has 6 or more months of life expectancy and would benefit from surgery), and the remaining casewas operated after consulting his oncologist and recommended surgical excision of the mass to help confirming diagnosis of primary malignancy. The last patient was a candidate for surgery but refused surgery and continued management and follow-up with an oncologist. Group B included 6 patients whose primary malignancy was discovered during the preoperative assessment forthe calvarial swelling. A full metastatic workup was done for all cases. Surgical excision was done for 4 out of the 6 patients after the oncologist confirmation of possible benefit from surgery to confirm a diagnosis. The remaining 2 patients were not operated upon due to late-stage malignancy. The last group included a single patient and was included in a separate category (Group C). This patient's primary malignancy was discovered 3 months after the calvarial mass excised (hence the calvarial was the sole presenting manifestation for the primary malignancy), and the histopathology reported undifferentiated tumor cells. (Lung carcinoma was diagnosed 3 months following surgery).

The most common 1ry malignancy was lung malignancy (4 cases=33.3%). This was followed by liver malignancies, reported in 3 cases (25%). Breast andhematological malignancy werereported in2 cases each, while renal carcinoma was the primary malignancy in only 1 case. Accordingly, the commonest histopathological finding was metastatic lung adenocarcinoma. The cases with hepatic malignancies were all hepatocellular carcinomas (HCC). On the other hand, adenocarcinoma of the breast was found in the specimens from both cases with breast malignancies. Hematological malignancies were reported as one case of multiple myeloma; the other was diffuse large B cell Lymphoma. The case with renal malignancy was an Eosinophilic cytoplasmic RCC.

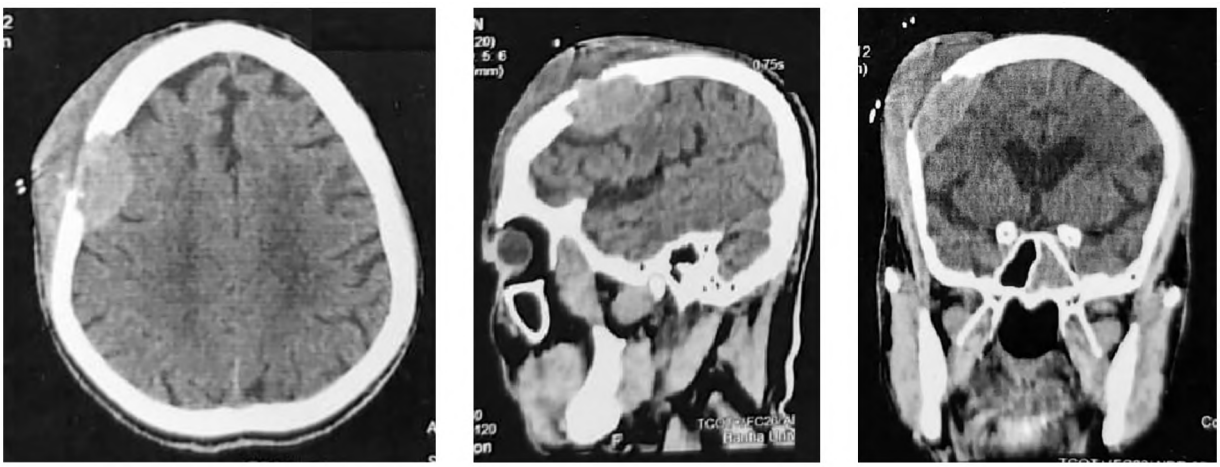
Table (1): Shows the complete breakdown of important patient data.

Patient	1ry site	Histopathology	Group	Mass size (cm)	Skin condition over mass	Neurological deficit	Invasion of neurological structure	Surgery
Case 1	Liver	Hepatocellular carcinoma	A	4x6 cm	Dehiscence	None	Dural irritation	Operated/Skin saving
Case 2	Renal	Eosinophilic cytoplasmic carcinoma	A	3x4 cm	Intact	None	None	Operated/confirm diagnosis
Case 3	Liver	Hepatocellular carcinoma	B	9x6 cm	Intact	Increased ICP	Sinus invasion	Operated/confirm diagnosis, relief manifestations
Case 4	Hematology	Lymphoma (germinal center B-cell type)	B	4x3 cm	Intact	Deficit, increased ICP	Sinus invasion	Operated/confirm diagnosis, relief manifestations
Case 5	Lung	Adenocarcinoma	C	6x9 cm	Intact	None	None	Operated/sole presenting mass
Case 6	Hematology	Multiple myeloma	B	4x5 cm	Intact	None	None	Operated/ confirm diagnosis
Case 7	Lung	Adenocarcinoma	A	5x5 cm	Dehiscence	None	None	Operated/Skin saving
Case 8	Liver	Hepatocellular carcinoma	B	4x5 cm	Intact	None	None	Operated/confirm diagnosis
Case 9	Lung	Adenocarcinoma	A	6x5 cm	Dehiscence	None	None	Operated/ Saving skin
Case 10	Lung	Undifferentiated carcinoma	B	3x4 cm	Intact	None	None	Not operated/End stage
Case 11	Breast	Invasive ductal carcinoma	A	2x3 cm	Intact	None	None	Not operated/refused surgery
Case 12	Breast	Metaplastic carcinoma	B	2x3 cm	Intact	Convulsion	None	Not operated/End stage

Illustrative Cases:

Case (1):

The patient, a 65-year-old male, is a known case of hepatocellular carcinoma (HCC). The patient presented with large scalp swelling in the right frontal area. Hisphysical exam and vital signs were within normal. Local examination revealed a hard and firm mass of about 6 x 4cm in diameter with distinct edges, fixed to the calvaria and invading the intracranial cavitywith overlying impeding skin dehiscence. Neurological examination revealed a conscious, alert, and intact motor power. CT brain was done (Fig. 1). Patient underwent craniectomy (replaced with rib graft) and removal of extradural mass with also excision of scalp mass. CT brain postoperative was done (Fig. 2). Histopathological examination of the bone and softtissue revealed necrotizing metastatic carcinoma, likely HCC, infiltrating softtissue and bone.



(A) (B) (C)

Fig. (1): Preoperative CT scan of the brain without contrast (soft and bone window) (A: Axial view, soft tissue), (B: Sagittal view, soft tissue) (C: Coronal view, soft tissue) showing right frontal bony lesion with intracranial extra axial component and subgaleal soft tissue mass.

Fig. (2): Post-operative axial CT brain without contrast (bone window) showing excision of right frontal mass with overlying bone (replaced with rib graft) and the soft tissue mass.

Case (2):

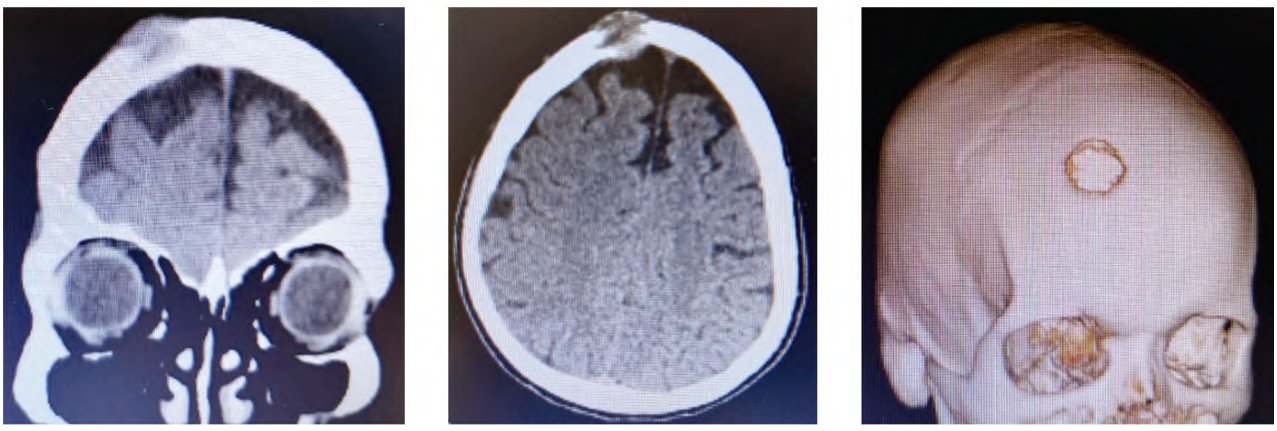
A 63-year-old male patient, with a known case of renal cell carcinoma (RCC) was operated onfor excision and the patient remained 4 years clear. Two months before the appearance of the calvarial mass the patient had a PET scan that was completely normal (Fig. 3). The lesion appeared in the right frontal region and was seen on a CT brain that was done to confirm the diagnosis (Fig. 4). Following excision, histopathology revealed Eosinophilic cytoplasmic carcinoma of renal origin (metastatic).

OPINION:

Status FU post-management for a known case of right RCC showing:

- Still negative study regarding the clear Rt. nephrectomy operative bed showing no glucose avid loco-regional residual/recurrent foci
- No metabolically active distant nodal/visceral metastatic lesions.
- Metabolically resolved isthmic thyroid nodule, for US correlation.
- Overall impression is of discase free body.
- PET CT follow-up; as clinically warranted is advisable.

Fig. (3): PET CT scan study is a negative study.



(A) (B) (C)

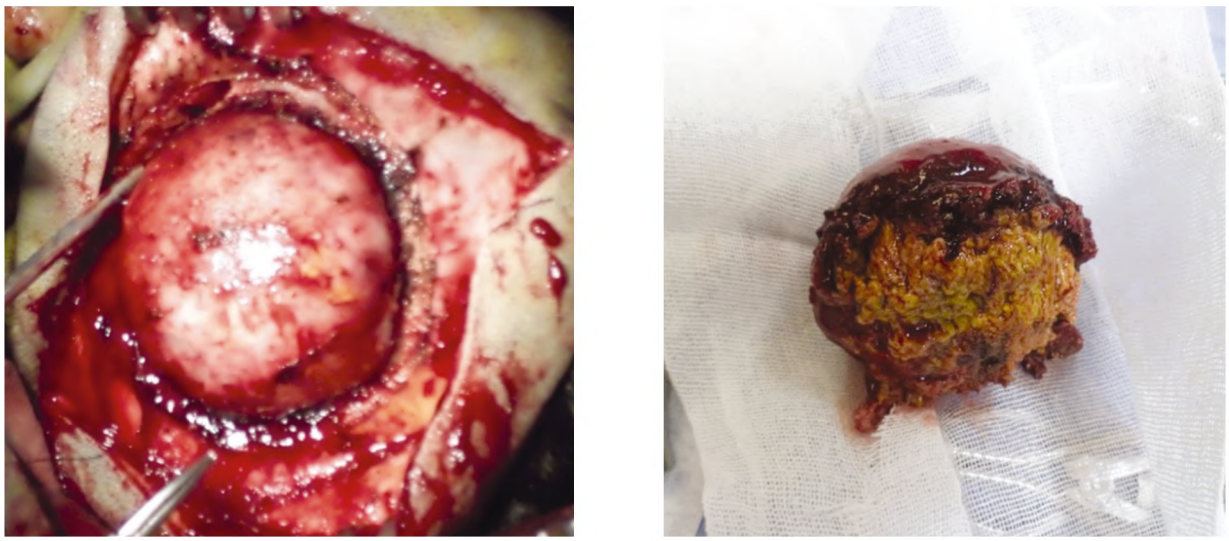
Fig. (4): Preoperative CT scan of the brain without contrast soft window) (A: Axial view) (B: Coronal view) showing right frontal bony lesion limited to the calvaria and extending to the subgaleal tissue. (C: Post-operative bone window 3D reconstruction) post-operative CT reconstruction showing reconstruction of bone following excision.

Case (3):

A 49-year-old female patient, not known to have any previous medical history. Thepatientpresented with scalp mass (9 x 6cm) at the high parietal region, headache, and blurredvision. CT brain, MRI brain with contrast, and CT angiography were done (Fig. 5). Fundus examination showed papilledema. During pre-operative preparation, liverenzymes and bilirubin were elevated. Pelvi-abdominal ultrasound was done and revealed ahepatic focal lesion. The patient was operatedon (Fig. 6: intraoperartive images), and excised mass was sent to histopathology, which revealed metastatic carcinoma, likely HCC.

(A) (B)

Fig. (5): Pre-operative (A: MRI brain with contrast, sagittal view) (B: CT brain angiography) showing high parietal bony lesion with extra-axial component compressing Superior sagittal sinus, (SSS).



(A) (B)

Fig. (6): Intraoperative images of the calvarial mass before excision (A) and after excision (B).

Case (4):

A 54-year-oldfemale patient with no previous medical history came with scalp swelling, headache and blurred vision. His physical exam and vital signs were within normal. Local examination revealed hard and firm mass of about 4 x 3cm in diameter withdistinct edges, fixed to the calvaria. Neurological examination revealed a conscious, alert, and oriented patient with 6 th nerve palsy (diplopia). MRI brain with contrast was done and revealed extradural SOL in the midline, high frontal, and infiltrating SSS andoverlying bone (Fig. 7). Fundus examination revealed papilledema. The patient underwent craniotomy, tumor excision, SSS was clipped and excised, calvarialbone excision, and gap reconstructed with titanium mesh. Post-

operative CT brain was done (Fig. 8). Histopathological examination of the bone and soft tissue revealed diffuse large B-cell lymphoma (germinal center B-cell type).

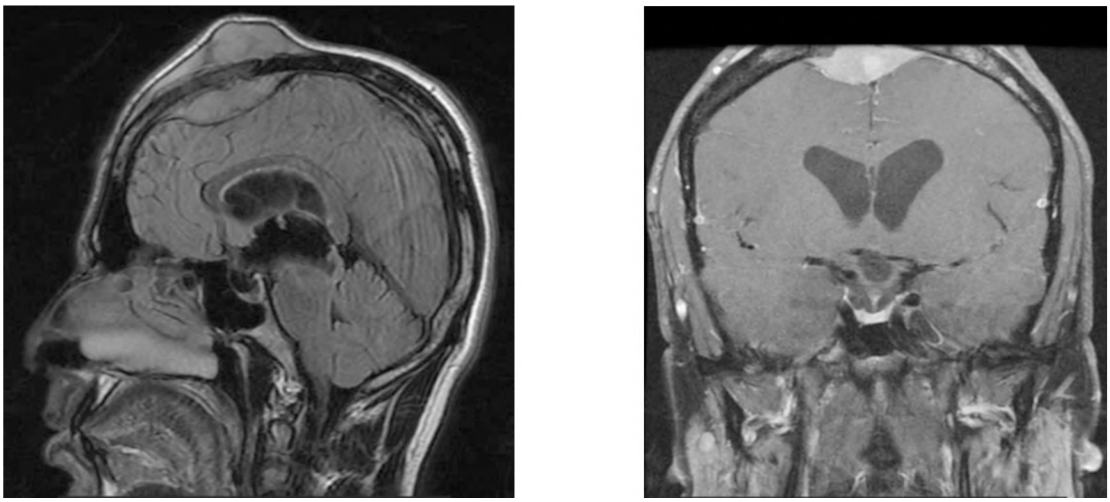


Fig. (7): Pre-operative MRI brain without contrast, (Right) pre-operative coronal view, (Left) pre-operative sagittal view MRI brain with contrast showing extra-dural high frontal extra-axial Space occupying lesion (SOL) in the midline (invading the superior sagittal sinus, SSS) with altered structure of the calvaria. Extracranial strong homogenous enhancement SOL.

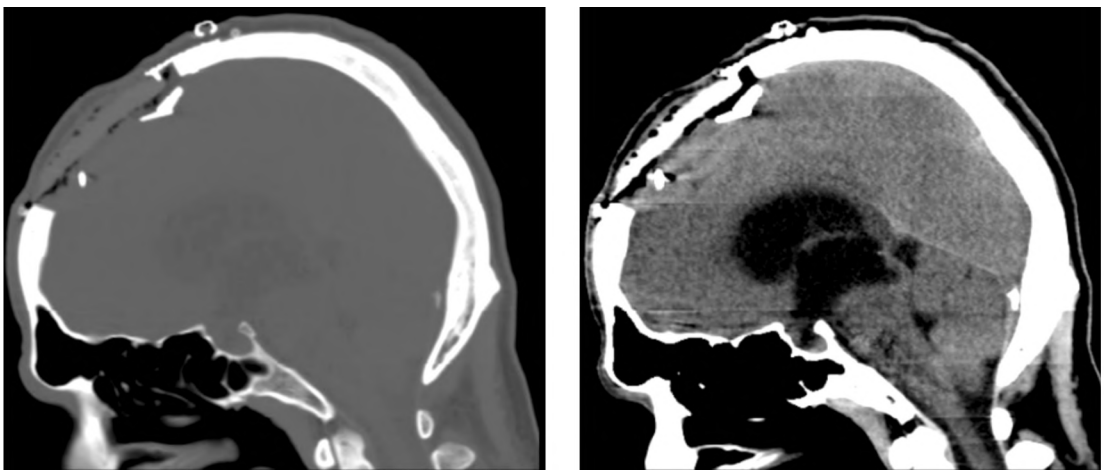
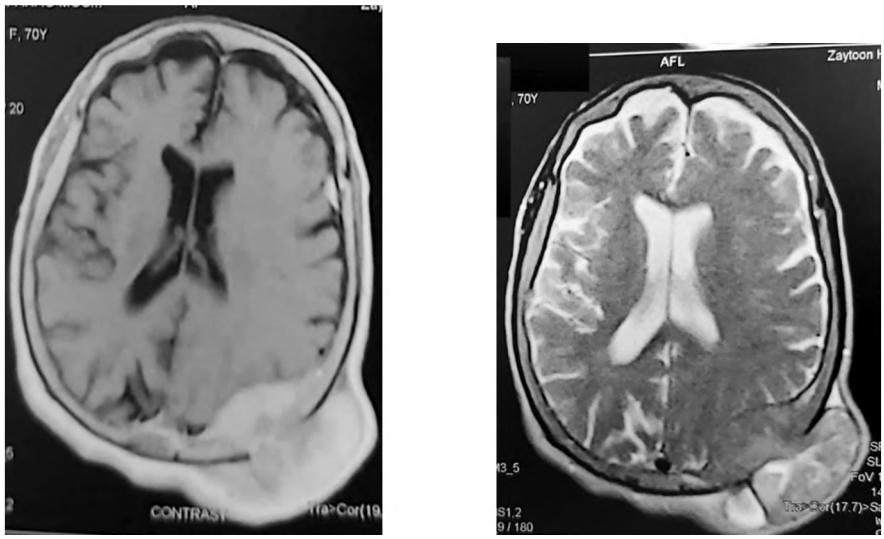


Fig. (8): Post-operative sagittal CT brain reconstruction without contrast (Right: Soft window, left bone window) showing bifrontal craniectomy with insertion of synthetic mesh, after excision of both extradural andextra-cranial SOL with clipping of SSS.

Case (5):

A 70-year-old female patient, not known to have any previous medical history. The patient presented with a scalp mass at the left parietal region. Her physical exam and vital signs were within normal. Local examination revealed hard and firm mass of about 6 x 9cm in diameter with distinct edges, fixed to the calvaria. Neurological examination revealed a conscious, alert, and oriented patient with no neurological deficits. MRI-brain with contrast was done (Fig. 9). The patient was operated on. Her histopathological examination revealed metastatic adenocarcinoma. CT chest and PET scan were done, and both were negative studies. Three months later, a follow-up PETscan was done andshowed lung carcinoma. Unfortunately, post-operative images were lost and could not be provided.

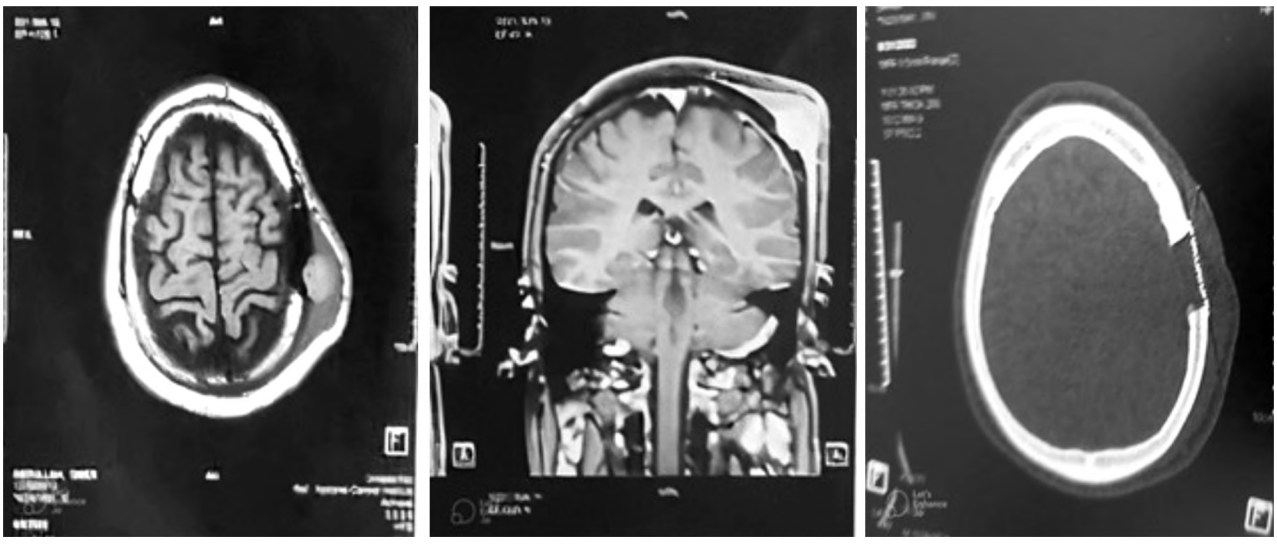


(A) (B)

Fig. (9): Pre-operative MRI brain with contrast axial view (a=T2WI) (b=T1WI with contrast) showing extra-dural left parietal extra-axial SOL with overlying bony destruction and subg aleal soft tissue mass.

Case (6):

A 31-year-old male patient, not known to have any previous medical history. The patient presented with a scalp mass at left parietal region. His physical exam and vital signs were within normal. Local examination revealed hard and firm mass of about 4 x 5cm in diameter with distinct edges, fixed to the calvaria. Neurological examination revealed a conscious, alert, and oriented patient with no neurological deficits. CT brain and MRI brain with contrast were done (Fig. 10), followed by a PET scan (Fig. 11). The patient was operatedon for the calvarial lesion excision and reconstructed with a mesh flap (Fig. 10). His histopathological examination revealed malignant round cell neoplasm, likely multiple myeloma. He was later sent to his oncologist that further investigated and confirmed the diagnosis.



(A) (B) (C)

Fig. (10): Preoperative MRI brain with contrast (A: Coronal view, B: Axial view) showing left parietal lesion with subgaleal soft tissue mass with erosion and sclerosis of underlying calvarial bone. (C: Axial view): Post-operative CT scan, bone window showing post excision with plate reconstruction.

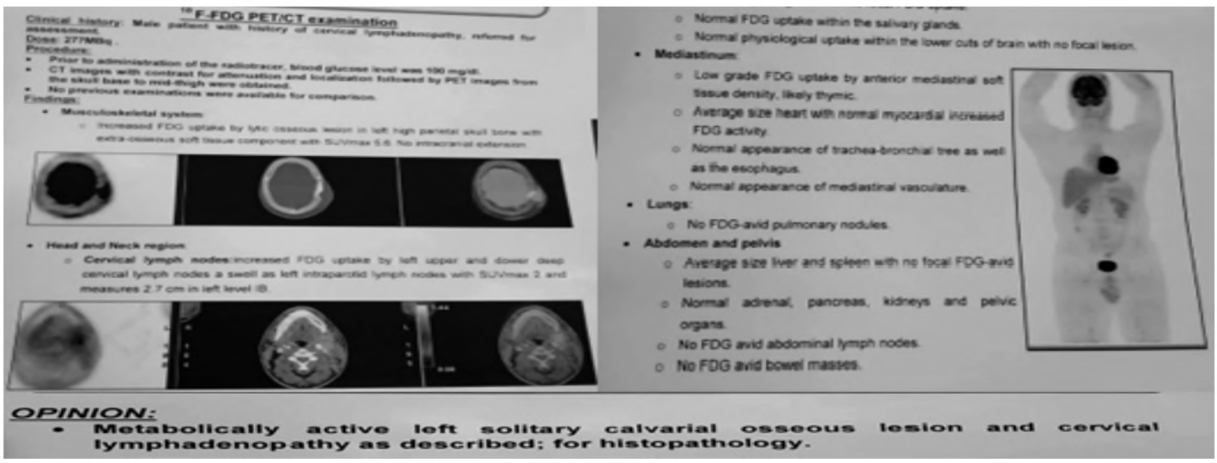


Fig. (11): PET scan study reveals metabolic active left solitary osseous lesion in calvarial bone.

Discussion

Like other bones, the calvaria is a potential site of metastases from systemic cancers **[10]**. It is believed that hematogenous spread is the leading route for calvarial metastases seen with all malignancies **[11]**. Certain cancers such as breast, lung, and kidney carcinoma, were commonly reported primaries for metastatic bone lesions **[3,13]**. Bone metastases from lung primaries account for around 36% of lung cancer patients **[13]**. Some advocate lung carcinoma with distant metastasis is identified as apoor predictor of survival **[11]**. Others have contradicted this and reported that patients that were operated upon for solitary lung calvarial metastases have shown to increased survival rates owing tototal excision of the metastatic lesion and aggressive adjuvant therapy and follow-up **[14,15]**. According to our results, 33.3% (4 cases) had lung primaries reported 3 of which were excised and had a good 3-5 years follow-up, yet one patient was not candidate for surgery due to late-stage malignancy.

Although hepatic malignancies were not reported in previous scholarly articles as a common primary for calvarial metastasis, never the less, in our series, we report it as the second most common (3 cases, 25%). We believe this is related to our region's high rates of liver malignancies consequently because of the higher incidence of viral hepatitis. Hepatocellular carcinoma (HCC), especially cholangiocarcinoma, is believed to initially present with solitary calvarial metastases **[16]**.

In our study, we analyzed data from 12 cases with calvarial masses that proved to be metastases either by histopathological examination or metastatic workup. Manifestations of calvarial metastases are believed to be different from other primary calvarial lesions. Other reports have even gone beyond that and suggested variant manifestations depending on the pathology **[11]**. Although commonly asymptomatic, it is usually discovered as an incidental finding, particularly those well-circumscribed **[17]**. Yet when symptomatic, they present as an isolated mass that may progressively become a visible swelling over the scalp while the mass erodes the outer table of the calvaria. Calvarial metastases extending into the cranial cavity tend to present as biconvex lens-shaped mass ponding the brain to the contralateral to the inner table(18). That is probably why more invasive and aggressive lesions may in turn elicits local pain, headache, and sometimes even nausea. Most of the cases in this study were either incidentally found or presented with a mass swelling in a scalp region. This is consistent with what Stark et al., concluded in their case series **[16]**.

More aggressive lesions in 3 patients also presented with skin dehiscence. Though less commonly seen, calvarial metastases may present with neurologic deficits. Such may occur when there is an extension to the eloquent structures as venous sinuses. Other neighboring structures may also be affected by calvarial metastases, such as dura. Ozgiray E. et al. **[19]** reported that most calvarial metastatic lesions in his studied skull lesions presented with neurologic deficits. In addition, when metastases occlude venous sinuses, cause raised intracranial pressure and papilledema **[1,9]**. In our study, we report 3 cases (25%) presented with neurological deficits. This is summarized in 1 case presented with symptoms of increased intracranial pressure, besides 1 case presented with recurrent attacks of fits and another with disturbed conscious level, both of which led patients to emergency medical services.

Contrast-enhanced MR of the brain and spine is the imaging modality of choice for detecting metastatic lesions, which is further integrated with metastatic workup. Radionuclide bone studies are also practical screening tests to detect bone metastases **[18]**. MRI aids in detecting the exact location, multiplicity, and relation of the lesion to surrounding structures, mainly dural sinuses **[5]**.

Dural sinus involvement in association with the calvarial mass must be further investigated with proper angiographic imaging. Chaudhuri et al., reported diagnosing with MRI 3 cases where the diagnosis of dural sinus involvement due to calvarial metastases was said to be missed by CT **[20]**.

Additionally, contrasted MR images are even more critical in detecting subtle intradiploic metastases **[21]**. We report the involvement of the dural sinuses in 1 case (superior sagittal sinus) of our 12 cases, which were all thoroughly investigated with variable imaging modalities for purposes of pre-operative diagnosis and metastatic workup.

The surgical option for calvarial lesions is somewhat controversial. Some scholars consider it a consider palliative surgical management of such lesions, rendering it is a usual safe option,especially when solitary and the patient's general condition and life expectancy **[8,11,22]**. Yet, several cases are considered not suitable for surgery rendering the stage of primary malignancy, large-sized lesions, and the patient's general condition **[13,17,18,23]**. However, our group advocatescalvarial mass surgical excision, with the reconstruction of the calvarial defect, no matter where they arise or its size as long as it is safe to excise after discussing the benefit of surgery with patient, and consulting oncologist's opinion on how it would influence patient outcome. Mass excision is considered a straight forward approach and is believed to help reach diagnosis in cases of solitary metastatic lesions and omitmanifestations when present, improving patient's quality of life.

Conclusion:

The calvaria is a potential site for metastases. Not only that, but it might also be the primary presentation for metastases. We suggest that any calvarial mass should be alerting, putting the possibility of metastases when managing. Further workup is mandatory for suchpatients and integrated consultation with an oncologist, when metastatic, to determine surgical decision and any further adjuvant treatment. Surgery for the calvarial mass is encouraged to save scalp skin, help diagnosis, and reverse neurological incapacity.

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تورمات الجمجمة كعرض تقديمى للأمراض النقيلية

يمكن أن تكون تور مات الجمجمة هى الآفة الحالية لمجموعة متنوعة من الأورام الخبيثة. عادة ما تكون التورمات محسوسة على الجلد وتسبب ألماً موضعياً أو تنميل وفى بعض الحالات المتقدمة تكون كبيرة بما يكفى لتكون سبباً لأنفتاح الجلد. اعتماداً على موقع الورم، قد يصاب البعض بعجز عصبى.

الغرض من الدراسة : تهدف هذه الدراسة إلى تقديم تجربتنا معتورمات الجمجمة العرضية كمظهر محتمل للأمراض النقيلية.

المرضى وطرق البحث : تضمنت الدراسة ١٢ حالة تعانى من تورمات الجمجمة كعرض تقديمى للأمراض النقيلية. تم إثبات ذلك إما من خلال الفحص النسيجى لعينة المريض أو من خلال فحوصات ما قبل الجراحة. وتم استبعاد تورمات الجمجمة الأولية.

النتائج : من أصل ١٢ مريضاً، كانت معظم الحالات من الإناث (٥٨.٣٪). كان متوسط عمر المرضى ٥٠.٥ سنة (من ٣١ إلى ٧٠ سنة). ستة تورمات تتصاعد من العظم الجبهى، ٥ فى العظم الجدارى وواحدة فى المنطقة القذالية فى حين أن جميع التورمات لم تغزو نسيج المخ لكن يوجد حالتين غزت الآفة الجيب الوريدى الجافوى (الجيب السهمى العلوى) وأخرى غزت الأم الجافية الأمامية. جميع الحالات ظهرت مع تورم فى فروة الرأس، لدرجة تسبب فى تفزر الجد فى ٣ وكان السبب الرئيسى لاستئصال تورم الجمجمة. من ناحية أخرى، كانت هناك ٣ حالات تعانى من عجز عصبى، مع حالة واحدة تعانى إلى من تشنجات غير منضبطة. وخضعت تسع حالات من أصل ١٢ حالة تم الإبلاغ عنها لعملية جراحية. كان الورم الأولى الأكثر إكتشافاً هو سرطان الرئة (٤ حالات). تبع ذلك سرطان الخلايا الكبدية حالات وسرطان الثدى فى حالتين. وظهر كلا من الورم النخاعى المتعدد وسرطان الغدد الليمفاوية (ب) وسرطان الخلايا الكلوية فى حالة واحدة لكل منهم.

الخلاصة : الجمجمة هى مو قع محتمل للأورام الثانوية. ليس ذلك فحسب، بل قد يكون أيضاً العرض التقديمى الأساسى لورم ثانوى خبيث. نقترح أن أى تورم بالجمجمة يجب أن تكون فى حالة تأهب، مع احتمالية وضع الأورام الثانوية فى الاعتبار. مزيد من العمل لمثل هؤلاء المرضى والتشاور المتكامل مع أطباء الأورام لتحديد القرار الجراحى.