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By Mochamad Iskandarsyah Agung Ramadhan

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Calvarial metastasis with intracranial infiltration in patient with Hürthle cell carcinoma: A case report

Mochamad Iskandarsyah Agung Ramadhan[1], David Tandian[2], Eka Susanto[3], Reyhan Eddy Yunus[4], Irma Savitri[1], Henry Riyanto Sofyan[1], Tiara Aninditha[1]

[1] Department of Neurology, Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia
[2] Department of Neurosurgery, Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia
[3] Department of Anatomical Pathology, Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia
[4] Department of Radiology, Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia

Corresponding author:
Mochamad Iskandarsyah Agung Ramadhan
E-mail: mochamadiskandarsyah.ar@gmail.com

ABSTRACT

Background: Calvarial metastases from thyroid malignancy are rare and reported mostly in follicular types. Hürthle cell carcinoma is considered a rare variant of thyroid malignancy and is known for its aggressiveness. However majority of metastatic Hürthle cell carcinoma incorporates non-skull bones and lungs with almost no reports on skull metastasis letalone with intracranial involvement. This case report highlighted the unique course of metastatic Hürthle cell carcinoma manifested as an extensive calvarial mass infiltrating intracranial compartment.

Case Report: A 37-year-old man presented with a mass above his head that progressively enlarged and became painful within 2 years. The mass had grown from the size of a marble to that of a ball resembling a double head appearance. His medical history

was remarkable for growing neck mass since he was 12 years old. There were no abnormalities on vital and neurological examinations, including cognitive functions. Head contrast CT-Scan and Angiography revealed extensive calcifying and hemorrhagic solid mass fed by external carotid artery and destructing parietal bones bilaterally. This mass also appeared to infiltrate superior sagittal sinus and dura mater. Neck ultrasound was suggestive of solid bilateral thyroid nodules. Histopathological analysis of thyroid core biopsy and resected tissue from total thyroidectomy reported Hürthle cells neoplasm. A subtotal calvarial tumor resection followed by Orticochea flap was later performed sparing intracranial residual tumor along parasagittal location. Histopathology examination of resected tissue reported thyroid metastasis. After the resection, the patient developed self-resolving right hemiparesis and acute symptomatic seizure controlled by topiramate. Based on the multidisciplinary meeting held earlier, radioiodine therapy was planned for this patient thereafter with bevacizumab became an alternative when radioiodine therapy was either failed or non-feasible.

Conclusion: Calvarium is common distant metastasis site in patients with thyroid malignancy, including Hürthle cell carcinoma as its rare variant. This kind of metastasis could progress as a giant mass over the head with no neurological deficits. The tumor however was resectable with relatively good outcome observed.

Keywords: giant calvarial tumor, clinical manifestations, Hürthle cell carcinoma, intracranial infiltration, metastasis

Abbreviations:

CSF	Cerebrospinal Fluid
NRS	Numeric Rating Scale

INTRODUCTION

The calvarium is a potential site for malignancy to develop, either as a primary or secondary lesion. Among other musculoskeletal malignancies, it represents only 2% of cases, making it relatively uncommon [1]. A calvarial tumor typically begins as a painless lump on the head that gradually grows in size. The tumor can become extremely large due to the abundant blood supply in the calvarial region, which provides a suitable environment for the tumor cells to thrive. From an epidemiological standpoint, calvarial tumors with very large size are rare. The literature cites various underlying malignancies that are responsible for the tumors, ranging from benign conditions like lipoma to malignant conditions like Ewing sarcoma and metastasis [2-4]. Thyroid carcinoma is

hitherto the only type of carcinoma known to cause giant calvarial metastasis. The presence of giant calvarial metastasis has been reported in papillary, follicular, and oncocytic (Hürthle) thyroid carcinoma [4-6]. Hürthle cell carcinoma is one of the rare variants of thyroid carcinoma with a prevalence of 2%. cell carcinoma only report bone metastasis without specifying the specific bones affected.

The presence of giant calvarial metastasis in Hürthle cell carcinoma has two implications. Firstly, distant metastasis is a poor prognostic factor for disease-free survival in patients with Hürthle cell carcinoma [7]. Secondly, a giant calvarial tumor requires special attention because it can involve surrounding structures such as the dura mater, brain parenchyma, and superior sagittal sinus. It is known that in cases of intracranial tumors –regardless of their size, dural and parenchymal infiltration occurs in 61% and 34% respectively [1,8]. Massive tumors deposited in the calvarium might also cause osteolysis, fractures, and neurological deficits if the tumor infiltrates or damages the intracranial compartments [9-10]. This, along with the increased risk of intracranial pressure from the large mass effect and vasogenic edema, can significantly impact morbidity in patients. The presence of neurological deficits, either from direct tumor effects or iatrogenic causes, can greatly affect the patient's quality of life. This case report highlights the occurrence of Hürthle cell carcinoma metastasis in a rarely reported location.

CASE REPORT

An Indonesian man aged 37 years old, presented to our institution due to tumor on the top of his head, which had been growing larger over the past 2 years. Prior to the head tumor, he noticed a lump on the right side of the neck the size of a ping-pong ball since the age of 12 years old. The lump had been increased in size. However, the patient had never complained of difficulty swallowing, shortness of breath, palpitations, frequent thirst, fervency, or tremors in both hands. The patient had never sought medical treatment for the neck lump. His family medical history was unremarkable. On May 2021, the patient discovered a lump the size of a marble at the top of the head which was not painful and did not bleed. The patient sought treatment at local hospital and was advised to seek treatment at tertiary hospital, but due to financial limitations, the patient did not seek treatment.

Figure 1. Clinical picture taken on September 2022

The lump continued to grow and the patient started to experience pain, with an normal rating score (NRS) of 2, since early 2022. The pain was localized to the lump on the head and felt like being stabbed. In September 2022, the lump had reached the size of a soccer ball (figure 1) and the patient experienced pain throughout the head, especially in the lump and surrounding area, with an NRS of 4-5, described as intermittent stabbing pain. The patient also complained of fever and chills. The patient was hospitalized for 3 days and was given intravenous fluids, oral paracetamol, methylprednisolone 16 mg t.i.d, cefixime 200 mg b.i.d, and 500mg mefenamic acid t.i.d. The patient was discharged with no head pain and improved fever. However, the day after being discharged, there was brownish fluid draining from the head lump, thus the patient sought treatment at the Emergency Department of our institution.

Upon arrival, the patient underwent a CT scan and CT angiography of the head, which revealed a solid heterogeneous mass with calcification and hemorrhage components after contrast, measuring 14.7 x 16.9 x 11.1 cm, causing destruction of the bilateral parietal bones, infiltration of the superior sagittal sinus, and extensive involvement of the bilateral parietal subarachnoid space, with the tumor's blood supply originating from branches of the external carotid artery. A chest X-ray was also performed, showing multiple metastatic nodules in both lungs. The patient received wound care and was planned for elective embolization and consideration for tumor removal along with referral to the Endocrine and Oncology departments.

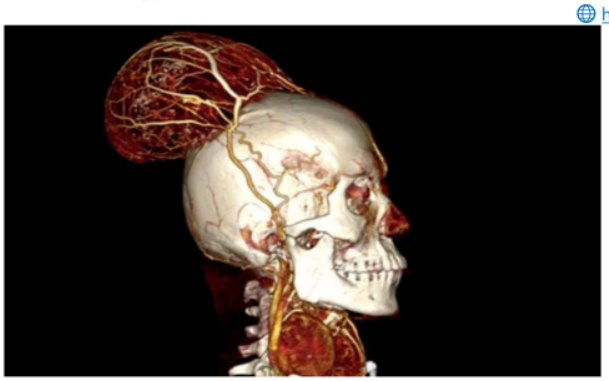

Figure 2. CT angiography of the head showing hypervascularized thyroid and mass on the vertex

In October 2022, the patient was referred to oncology surgery department for further thyroid mass workup. The ultrasound and nasopharyngeal CT scan (figure 3) confirmed bilateral thyroid mass with malignant characteristics. Histopathological analysis through needle biopsy demonstrated features consistent with Hürthle cell neoplasm corresponding to IVc degree based on the classification of the Korean Thyroid Association. He was later diagnosed with stage T4aN1M1 of Hürthle cell carcinoma with cranial and lung metastases. Subsequently, the patient underwent total thyroidectomy with radical neck dissection in January 2023. The histopathological examination of the removed thyroid tissue showed a mixed variant of Hürthle and follicular papillary thyroid carcinoma.

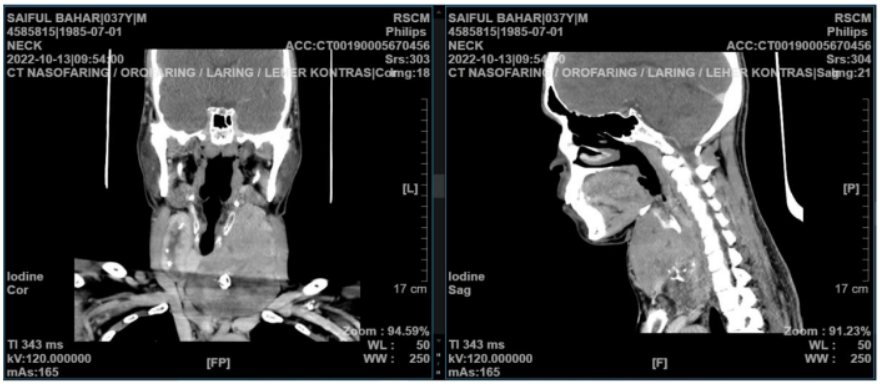

Figure 3. Nasopharyngeal CT scan showing asymmetric malignant mass on both lobes of thyroid

The patient underwent a contrast-enhanced MRI of the head on March 23, 2023 revealing a lobulated solid malignant mass with central necrosis in the bilateral

frontoparietal bones, growing exophytically into the extracalvarial space and extending intracranially, infiltrating the bilateral frontoparietal dura, superior sagittal sinus, and parietal lobe parenchyma. On June 21, the patient underwent DSA and embolization of the tumor feeder from the external carotid artery. According to the patient, the lump on the head did not grow larger, and the pain remained the same from September 2022 to June 2023.

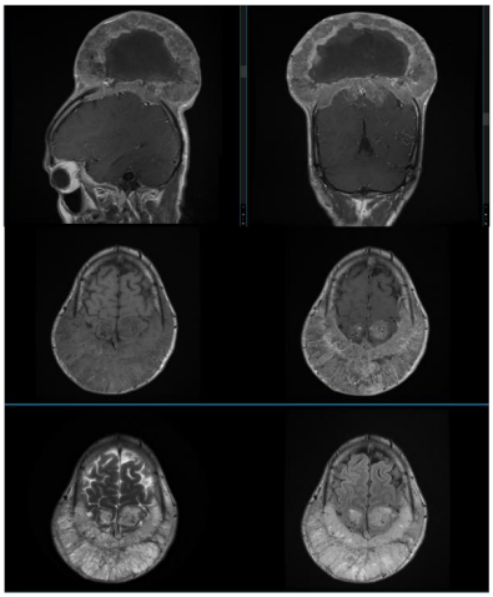

Figure 4. Contrast-enhanced MRI of the head infiltrating frontoparietal dura, superior sagittal sinus, and parietal lobe parenchyma

However, the day after the visit, the patient experienced worsening headache, with an NRS score of 7-8, described as a throbbing pain throughout the head, especially the vertex and forehead. The pain did not improve with over-the-counter medications. The patient also reported vomiting twice, but there was no projectile vomiting. The patient denied having seizures, decreased consciousness, or weakness on one side of the body. The patient was transferred to the Emergency Department and received treatment with intravenous paracetamol 1 g and ketorolac 30 mg. Eventually, the patient was scheduled for a craniotomy for tumor removal with Orticochea flap closure on June 27, 2023.

During the operation, necrotic tissue was found, some of which had spread to the bone, and there was tearing of the dura mater with relatively intact subcortical tissue. During the surgery, 90% of the tumor was removed, with the remaining 10% located intracranially, which was confirmed by a post-operative CT scan. More than 50% of the tissue showed necrosis, and there was a bleeding mass attached to the dura mater,

accompanied by dark brownish fluid. The histopathological examination of the tumor tissue confirmed that it was a metastasis of papillary thyroid carcinoma.

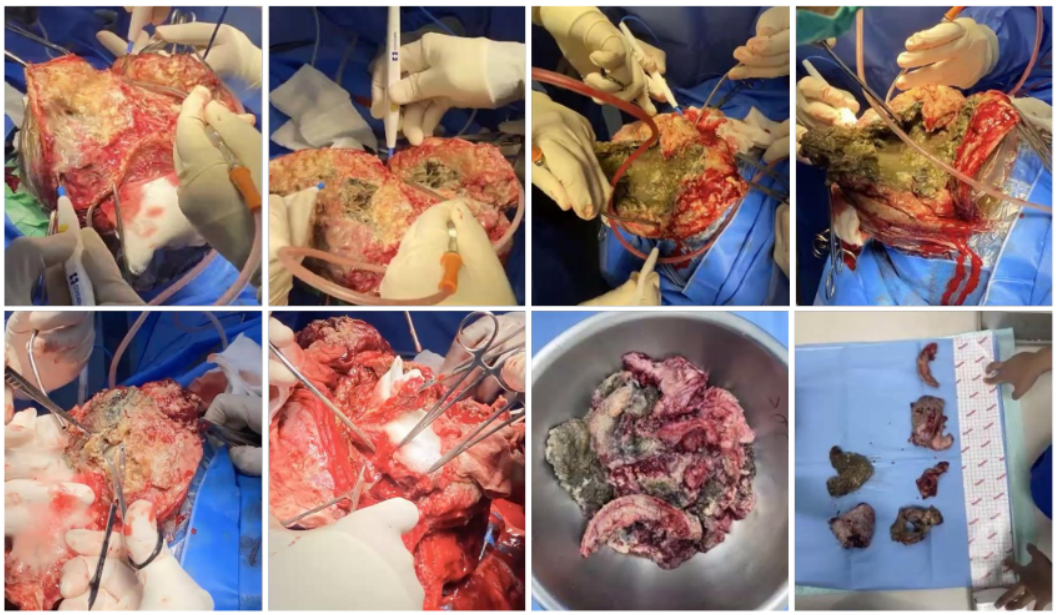

Figure 5. Tumor removal craniotomy with resected tissue appeared necrotic with muddish brown exudate

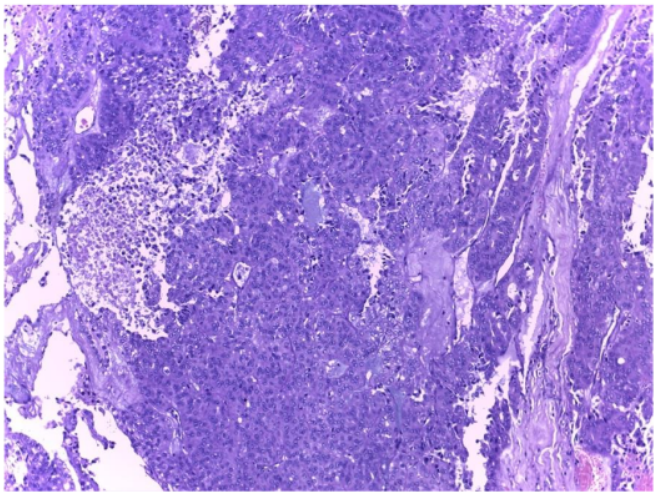

Figure 6. Histopathology analysis of resected tissue depicting tumor cells with necrotic foci. Several cells demonstrated Hürthle morphology

After the surgery, the patient was briefly hospitalized in ICU and then neurosurgical ward. There was no significant deficits but acute symptomatic focal clonic seizure and

self-resolving right-sided weakness. On July 1, 2023, a contrast-enhanced CT scan of the head revealed nodular lesions in the bilateral parasagittal regions in the vertex area, accompanied by perifocal edema and suspected residual lesion with hemorrhage and subarachnoid hemorrhage in the bilateral parietal lobes. The flap was found to be vital, with distal necrosis in the right parietal region and dark brownish exudate with an odor, as well as a vital flap in the left parietal region. The patient has been discussed in a multidisciplinary setting, and it is planned to perform iodine ablation followed by lenvatinib administration.

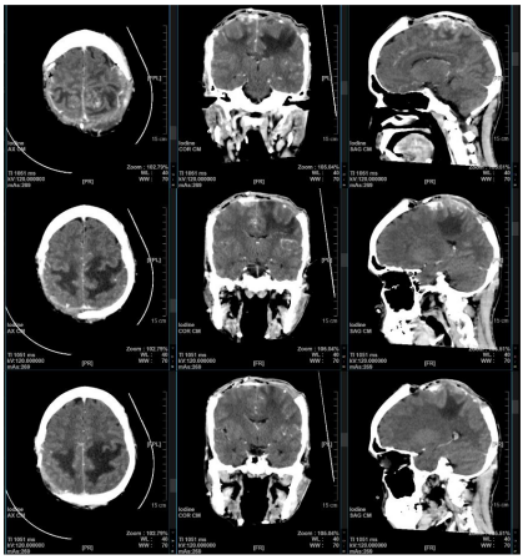

Figure 7. Post surgical CT-scan revealed nodular lesions in the vertex area, perifocal edema, and suspected hemorrhagic residual lesion in the bilateral parietal lobes

DISCUSSION

Giant calvarial tumors are extremely rare in epidemiology and there is no available data on their exact prevalence. Despite the large size, the tumors could exhibit a range of pathological processes from benign to malignant. The most commonly reported benign primary type is meningioma, while hamartoma, osteoma, and hemangioma were also reported [11-13]. There is even a report in the literature describing a benign, non-cancerous giant calvarial lipoma [2]. On the other hand, giant calvarial tumors might also be malignant as reported to unfold in osteosarcoma, chondrosarcoma, and Ewing sarcoma. Calvarial metastasis from various primaries could as well reach gigantic size, with metastasis in the calvarium region itself occurring in 15-25% of malignancies [9]. Only three cases of giant calvarial metastasis from thyroid carcinoma have been reported, each

associated with papillary, follicular, and Hürthle cell thyroid type –the latter was deemed as rare in occurrence [4-6].

Up to this point, there is no specific size limit for a tumor on the calvarium region to be considered giant. One literature stated that tumors larger than 3 cm are sufficient to be considered giant [14]. Another literature defined a giant lipoma as a lipoma with a minimum longest dimension of 10 cm [2]. From the case reports of various types of tumors mentioned earlier, there is a pattern that giant tumors have a largest dimension of at least 9.5 cm. Therefore, establishing 10 cm as the minimum threshold for a tumor to be considered giant seems rational. The patient in this case had a tumor size of 14.7 x 16.9 x 11.1 cm, thus the tumor in the patient is considered a giant tumor. Calvarial metastasis reported in various studies is extremely rare to reach such a large size.

Mendes et al reported a case of a 53-year-old woman with Hürthle variant of papillary thyroid carcinoma who presented with a progressively enlarged lump on the left parieto-occipital region alongside decreased consciousness and right-sided weakness [4]. A contrast-enhanced brain MRI revealed a giant mass that destroyed the skull in the corresponding region, invading the torcular herophili and intracranial compartment. However, unlike the patient in our case, no brain parenchymal infiltration was observed despite the demonstrated neurological deficits. It is believed that the epicranial mass exerted enough pressure on the eloquent area. In our case, on the other hand, parenchymal infiltration did occur in a non-eloquent area, resulting in non-specific headache. The mass in our case also obstructed the superior sagittal sinus, potentially disrupting cerebrospinal fluid (CSF) flow and indirectly increasing intracranial pressure.

There is no specific algorithm or management guideline for both primary and secondary calvarial tumors. The management of these tumors should be based on histopathology, involvement of surrounding tissues, and other comorbidities. However, various studies agree that surgery is the main treatment for calvarial tumors [1,15]. Surgical intervention is not only useful in removing solitary malignant or symptomatic benign lesions, but also in diagnostic settings [16]. In cases of small and asymptomatic tumors, expectant management is sometimes encouraged [17]. Nevertheless, given the low chance of complications, total tumor resection is not harmful in this scenario. If the calvarial tumor is known to involve the dura mater and brain parenchyma, resection of the infiltrated parts should also be performed. The decision for tumor resection should be determined through a multidisciplinary meeting [15].

In the context of Hürthle cell carcinoma, several modalities can be considered for treating bony metastasis, namely tumor resection with or without embolization, antiresorptive agents such as bisphosphonates and denosumab, and systemic therapy

such as lenvatinib and sorafenib. According to the guideline published by the National Comprehensive Cancer Network (NCCN) [18], thyroid mass resection followed by radioiodine ablation therapy is recommended for patients with large thyroid nodules ≥4 cm. Patient in our case had undergone thyroidectomy. However due to the imminent risk of increased intracranial pressure from both the direct and indirect effects of the mass, calvarium mass resection was performed after thyroidectomy. Radioiodine ablation therapy was reconsidered for the patient after the calvarial tumor resection, with the condition that the patient could mobilize actively, independently, and was not short of breath. As suggested by the NCCN guidelines, lenvatinib treatment could be considered if radiotherapy turned out to be ineffective or unable to do. Distant and extensively metastasized Hürthle cell carcinoma is associated with higher mortality, as high as 7.8 times [7].

CONCLUSION

This case reflects neurooncology case management in Indonesia. In middle-income countries, patients with any type of malignancy often seek medical help in the advanced stage of their disease. The lack of awareness about severity of in this patient was evident in the uncontrollable enlargement of the calvarial tumor [19]. This might be because even though the metastasis progressed as a giant mass over the head, there was no neurological defictis and therefore no medical complaints. Other factors attributed to this phenomenon including that one of patients, patient-healthcare provider relationship, treatment, and socioeconomic conditions that leads to a negative impact by discouraging timely medical treatment [20-21]. Consequently, treating this condition requires a more aggressive and comprehensive approach involving multiple disciplines such as neurooncology, neurosurgery, oncology surgery, plastic surgery, oncology, and endocrinology. By adopting this approach, the team was able to manage such a large tumor through resection procedure without causing significant damage to the patient.

Patient consent:

The patient consents to the use of their anonymized medical information in the case report and understands that their identity will remain confidential and that the case report will be submitted for publication.

Conflict of interest: There are no conflicts of interest.

Author's contributions: Data acquisition was done by MI. All authors analyzed and interpreted the data. The writing of the manuscript is mostly done by MI. All authors read and approved the final manuscript.

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