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Image Report

Calvarial metastasis from malignant pheochromocytoma associated with multiple endocrine neoplasia

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ABSTRACT

Background: Malignant pheochromocytoma is a rare neuroendocrine tumor that may metastasize to the bones, liver, lungs, kidneys, and lymph nodes. Cerebral and skull metastases are even rarer, with only 17 cases reported in the literature. To the best of the authors' knowledge, this is the first reported case of a purely calvarial metastasis from malignant pheochromocytoma associated with multiple endocrine neoplasia type 2A (MEN2A).

Case Description: A 31-year-old Filipino man diagnosed with MEN2A was found to have elevated urine metanephrine on routine surveillance, and workup revealed right adrenal and hepatic masses and a focus of intense tracer accumulation on the right frontal bone on metaiodobenzylguanidine I-123 scan. All the newly discovered lesions were resected to achieve tumor control. Histopathology revealed a diagnosis of pheochromocytoma for the calvarial lesion.

Conclusion: Malignant pheochromocytoma may give rise to indolent metastatic foci that can easily be missed without a thorough examination. Misdiagnosis and delays in management of this disease can be detrimental, resulting in irreversible complications and death.

Keywords: Calvarial metastasis, Malignant pheochromocytoma, Multiple endocrine neoplasia type 2A, Pheochromocytoma

Pheochromocytoma is a rare neuroendocrine tumor arising from chromaffin cells in the adrenal medulla.[7] It occurs in 2–8 per million adults, and approximately 10% are malignant.[2,9] Distant metastasis to the liver, lungs, kidneys, and bones is even rarer and constitute one of the criteria for malignancy.[2,7,8] Metastatic work-up includes anatomic imaging studies such as abdominopelvic ultrasound and computed tomography (CT) scan, as well as functional molecular imaging modalities such as metaiodobenzylguanidine I-123 (MIBG) scan or 18F-flurorodeoxyglucose positron emission tomography CT scan.[1,4] Metanephrine assays (plasma or 24-h urine) also play a role in surveillance monitoring, in addition to establishing the diagnosis.[6,10,11] For patients with associated multiple endocrine neoplasia, additional testing such as serum calcium and parathyroid hormone levels, neck ultrasound, and sestamibi scan may also be warranted.[4,10,11] In this report, we present the first case of a purely calvarial metastasis from malignant pheochromocytoma associated with multiple endocrine neoplasia type 2A (MEN2A).

A 31-year-old Filipino man, previously diagnosed to have MEN 2A syndrome based on genetic testing and the presence of bilateral pheochromocytomas, medullary thyroid cancer, and parathyroid adenoma, was found to have elevated urine metanephrine on routine surveillance. He was clinically well, with an unremarkable physical and neurologic examination. Workup revealed right adrenal and hepatic masses, as well as a focus of intense tracer accumulation in the right frontal bone on MIBG-I-123 scan. Cranial CT scan showed a 2.3 × 2.3 × 0.7 cm well-defined, expansile, and lytic lesion with an enhancing soft-tissue component in the right frontal bone, with no apparent intracranial involvement [Figures 1a-e].

The patient underwent resection of the right adrenal and hepatic masses, followed by excision of the calvarial lesion. Intraoperatively, the outer and inner tables were found to be grossly intact. Histopathology revealed a diagnosis of pheochromocytoma for the right adrenal and calvarial lesions, and metastatic medullary thyroid carcinoma for the hepatic mass [Figure 2]. Urine metanephrine levels decreased to normal 1 month postoperatively.

Malignant pheochromocytomas may metastasize to nearby bony structures, liver, lungs, kidneys, and lymph nodes, but calvarial and intracranial metastases are less common.[2] Only 17 cases of intracerebral pheochromocytoma have been reported, and only two of these had calvarial involvement.[2] A purely calvarial lesion had only been reported once before, and similar to our case, was also an indolent skull metastasis that was detected on MIBG-I-123 scan.[5] However, it was not reported to be associated with MEN 2A, unlike our case.

It has been postulated that pheochromocytoma metastasizes only to tissues with the same cell of origin.[2] In general, the mammalian cranial vault is derived from two embryonic tissue origins, the neural crest, and mesoderm,[8] but the frontal bones, in particular, developed from neural crest cells.[2] Since the chromaffin cells of the adrenal medulla are also derived from the neural crest,[3] this may explain why the calvarial metastasis was located in the frontal bone.

A complete surgical resection of the calvarial lesion was performed on our patient despite the absence of symptoms. The treatment of malignant pheochromocytoma involves resection of the primary tumor and removal of all foci of metastases to control the overproduction of catecholamines.[2] This may prevent early mortality caused by persistent hypertension from high levels of catecholamines.[6]

This case demonstrated the importance of a thorough examination for patients with malignant pheochromocytoma. Unlike other foci, calvarial metastases may be indolent and asymptomatic, which may result in misdiagnosis and delay in management.

Statement of authorship

M.U.H: Conceptualization; resource; data curation; writing – original draft preparation; and writing – review and editing. K.O.K: Conceptualization; writing – original draft preparation; writing – review and editing; supervision; and project administration.

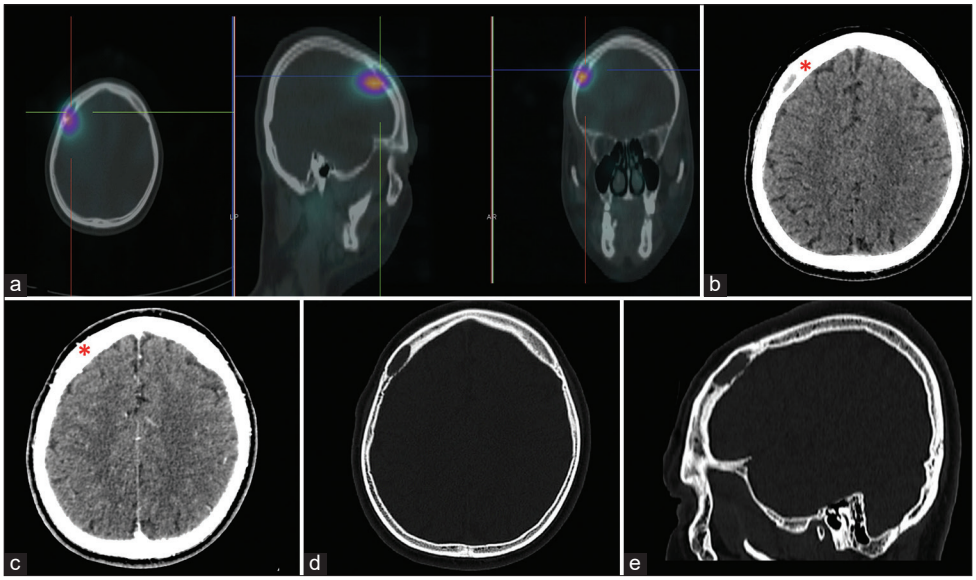

Figure 1: (a) Axial, sagittal, and coronal images showing the focus of intense tracer accumulation in the right frontal bone on metaiodobenzylguanidine I-123 scintigraphy, (b) axial image of plain cranial computed tomography (CT) showing the well-defined, expansile, and elongated lytic lesion in the right frontal bone (red asterisk) measuring 2.3 × 2.3 × 0.7 cm, with enhancement on contrast (c), (d and e) axial and sagittal view of the cranial CT bone window showing the lytic lesion in the right frontal bone.

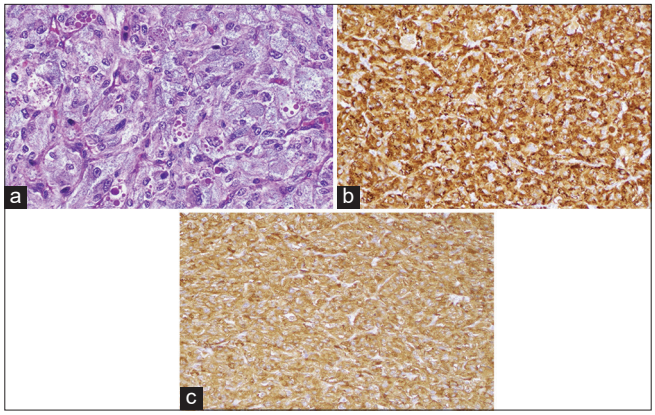

Figure 2: Photomicrographs of the calvarial lesion. (a) Hematoxylin and eosin staining, 400×, showing polygonal cells with round to oval nuclei and abundant granular cytoplasm, immunohistochemical staining with chromogranin (b), and synaptophysin (c) were strongly and diffusely positive, consistent with pheochromocytoma.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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