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Case Series

Neoplastic Odyssey: Carcinoma's Leap to the Brain – A Series of Three Cases

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Abstract

Brain metastases represent the most common intracranial tumors, significantly outnumbering primary central nervous system (CNS) neoplasms. While the majority originate from lung, breast, melanoma, renal, and colorectal primaries, metastases from rare tumors such as Acinic Cell Carcinoma (ACC), Hepatocellular Carcinoma (HCC), and Alveolar Soft Part Sarcoma (ASPS) are exceptionally uncommon. Intracranial dissemination of ACC is exceedingly rare, and brain involvement in HCC occurs in less than 1% of cases. In contrast, ASPS, a TFE3-rearranged sarcoma, demonstrates a comparatively higher tendency for hematogenous spread, with brain metastases reported in 20–30% of advanced cases.

We present three rare cases of brain metastases arising from ACC, HCC, and ASPS, highlighting their clinicopathological features, radiological findings, histomorphology, and immunohistochemical profiles. Accurate diagnosis in such unusual presentations requires meticulous morphological evaluation, appropriate use of immunohistochemical markers, and correlation with current WHO CNS classification criteria. Reporting these rare metastatic entities contributes to improved diagnostic awareness, prevents misclassification as primary CNS tumors, and enhances understanding of their metastatic patterns and biological behavior.

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Introduction

Brain metastases are the most common intracranial tumors, far exceeding primary CNS neoplasms. They usually arise from lung, breast, melanoma, renal, and colorectal cancers, whereas metastases from Acinic Cell Carcinoma (ACC), Hepatocellular Carcinoma (HCC), and Alveolar Soft Part Sarcoma (ASPS) are extremely uncommon. [1, 5]

ACC rarely disseminates to the CNS and intracranial spread is exceptional.[1] HCC also shows a very low incidence of brain metastasis, reported in <1% of cases.[2] In contrast, ASPS, a TFE3-rearranged sarcoma, has a higher propensity for hematogenous spread, and brain metastases may occur in 20–30% of advanced cases.[3,5] Recognition of such rare metastatic tumors requires careful morphological assessment, appropriate immunohistochemistry, and correlation with WHO CNS diagnostic criteria.[6, 7] Reporting these rare occurrences enhances diagnostic accuracy and contributes to understanding metastatic behaviour.

Case 1

A 69-year-old male presented with complaints of decreased vision of right eye which is progressive for 1 month. Also complains of occasional headache & diplopia. CT orbit showed a well-defined lobulated extra-axial soft tissue density lesion seen along the anterolateral aspect of the right cavernous sinus, extending into the right orbital apex and superior orbital fissure. (Fig-1a) CT abdomen & thorax showed features suggestive of chronic hepatic parenchymal disease with multifocal LIRADS 5 lesions, small LIRADS 3 lesions in left lobe and small locoregional lymph nodes. (Fig-1b) Patient underwent Endoscopic endonasal trans spenoid trans ethmoid decompression of optic canal and biopsy under navigation and specimen was sent for

histopathological examination. We received multiple pale white to pale brown soft tissue bits aggregate m/s 0.3x0.2x0.2cm

Microscopy shows brain tissue infiltrated by a tumor composed of cells arranged in solid, trabecular and vague glandular pattern. Tumor cells are large polygonal with abundant eosinophilic granular cytoplasm, round to oval nucleus and prominent nucleoli. (Fig-1c) Microscopic features were favouring metastatic carcinoma possibly hepatocellular carcinoma. Immunohistochemistry was performed for confirmation. Hep Par 1 showed moderate to strong cytoplasmic positivity in more than 50% tumor cells. (Fig-1d) and Pan CK showed strong membranous positivity in tumor cells. (Fig-1e). Thus, confirming the diagnosis of metastasis from Hepatocellular Carcinoma.

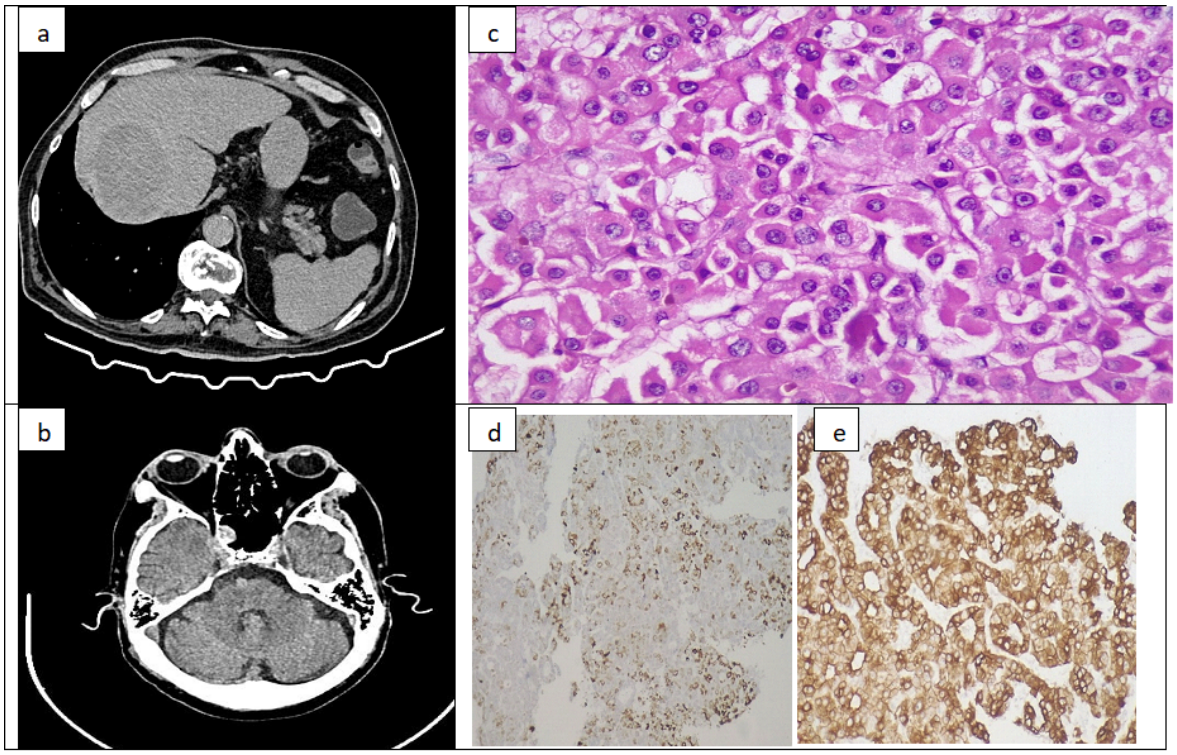

Figure 1: a) CT abdomen and thorax b) CT Orbitc) H&E section -large cells with prominent nucleoli d) IHC Hep Par1 >50% cytoplasmic positivity e) Pan CK-strong membranous positivity

Case 2

A 50-year-old male presented with complaints of swelling right side of the head and redness around right eye. There was no history of trauma or seizures. He was a known case of Acinic Cell Carcinoma of right Parotid who underwent Parotidectomy followed by Radiotherapy and canialmetastatectomy. CT brain showed post operative changes as air pocket and few haemorrhagic foci in deep scalp/epidural space in right temporo parietal region, heterogeneously hyperdense lesion in left corona radiata with surrounding edemaand old craniotomy defect with reconstruction was noted in left high parietal region.

(Fig-2a) Patient underwent right fronto temporal re-exploration. decompression and Tarsorrhaphy. Multiple dark brown soft tissue aggregate measuring 4.5x2.5x1cm was received in the Pathology department. Microscopy showed brain with an infiltrating neoplasm composed of lobules of tumor cells separated by fibrous bands. (Fig- 2b) Within the lobules cells are arranged in microcystic and vague follicular pattern.

Cells are large polygonal with finely vacuolated cytoplasm and round to oval eccentric nuclei. (Fig -2c) Immuno histochemistry showed strong & diffuse nuclear positivity with SOX10 (Fig -2e) and diffuse membranous positivity with DOG 1 (Fig-2f) confirming the diagnosis of metastasis from Acinic Cell Carcinoma.

Case 3

An18-year-old female presented with complaints of vomiting and headache of 3 days duration. She give a past history of Alveolar soft tissue sarcoma of left first web space for which excision was done .later she presented with brain metastasis and underwent right frontal craniotomy and excision of dural metastasis.

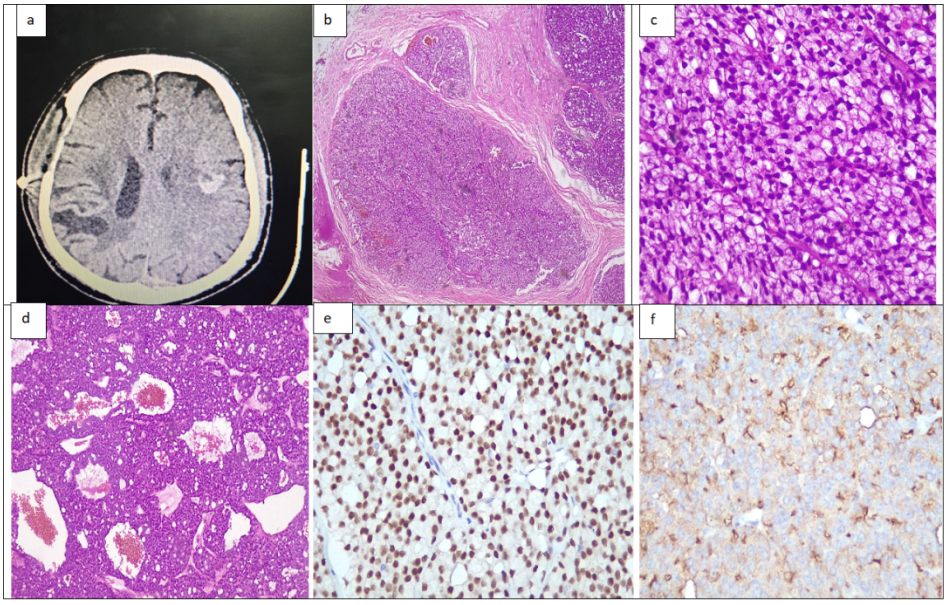

Figure 2: a) CT Brain b) lobules of tumor separated by fibrous bands c) cells have finely vacuolated cytoplasm and eccentric nuclei d) dilated vascular channels e) IHC SOX10 strong nuclear positivity f) DOG 1 diffuse membranous positivity

MRI brain showed two well defined extra axial lesions in the right parasagittal location were seen in the right high fronto-parietal location and right high parietal, parasagittal location likely dural metastases

Mild dural thickening in the right high parietal region up to the level of craniotomy defect also seen. (Fig-3a). Patient underwent left frontal craniotomy, excision biopsy and duroplasty. Multiple pale brown irregular tissue bits aggregate measuring 3.6 x3x2cm were received in the department of Pathology for histopathological examination. Microscopy showed brain tissue with an infiltrating tumor arranged in alveolar pattern composed of large polygonal cells with well-defined cytoplasmic borders and abundant eosinophilic granular cytoplasm, pleomorphic vesicular nucleus with prominent nucleoli. (Fig-3b, c) followed by immunohistochemical marker TFE3 which showed strong & diffuse nuclear positivity. (Fig-3d). Thus a diagnosis of metastasis from Alveolar soft part sarcoma was made.

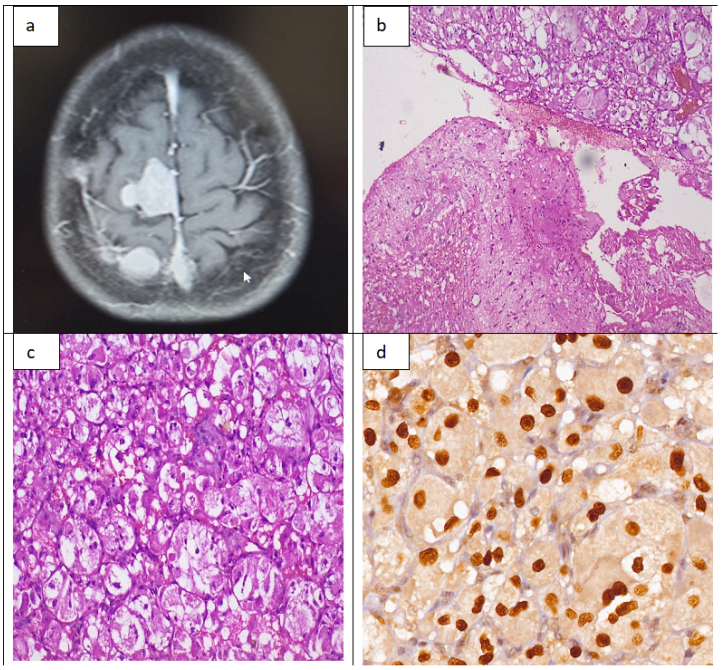

Figure 3: a) CT Brain b) Brain with infiltrating tumor c) Alveolar pattern of large polygonal cells d) IHC TFE3 showing strong diffuse nuclear positivity

Discussion & Conclusions

Brain metastases are the most common intracranial tumors, yet secondary involvement by Acinic Cell Carcinoma (ACC), Hepatocellular Carcinoma (HCC), and Alveolar Soft Part Sarcoma (ASPS) is exceedingly rare.[1, 5] Their uncommon presentation may mimic primary CNS neoplasms, making accurate identification essential.

ACC typically behaves as a low-grade salivary gland tumor characterized by slow growth and favorable prognosis, yet distant metastasis may occur following late recurrence or high-grade transformation, sometimes many years after the initial diagnosis. Intracranial metastasis from ACC is rarely reported but poses diagnostic and therapeutic challenges due to its delayed presentation and overlapping imaging features with primary brain tumors. Reported cases demonstrate favourable outcomes when treated with surgical resection and/or radiotherapy, emphasizing the importance of long-term surveillance. [1]Immunohistochemical studies have demonstrated that acinar cells stain positive for keratins CK7 and CAM5.2 and epithelial membrane antigen (EMA), and negative for p63, myeloid markers, and keratin CK20 Notably, the nuclear receptor 4A3 (NR4A3) and Discovered on Gastrointestinal Tumor Protein 1 (DOG1) have been shown to be highly expressed by ACC tumor cells and can be used to distinguish ACC from other forms of salivary gland tumors such as secretory carcinoma, mucoepidermoid carcinoma, and other oncocytictumors[8]

Brain metastasis from HCC is uncommon, accounting for only a very small proportion of all brain metastases, although its incidence appears to be increasing due to improved survival of patients receiving modern systemic therapies. These metastases frequently demonstrate intracerebral haemorrhage, attributed to the marked vascularity of HCC and associated coagulopathy or impaired liver function. Clinical outcomes remain poor, with reported median survival after diagnosis of brain metastasis being only a few months. Nevertheless, studies indicate that aggressive local management—including surgical resection combined with stereotactic radiosurgery or whole-brain radiotherapy—may significantly improve survival compared with radiotherapy alone. Early diagnosis may allow potentially curative intervention in selected patients. [2, 9]

ASPS, a rare TFE3-rearranged soft tissue sarcoma typically affecting young adults, exhibits a strong propensity for hematogenous dissemination, particularly to the lungs and brain. Brain metastases may occur in up to 20–30% of advanced cases and may even represent a presenting manifestation. Radiologically, lesions are often well-defined and highly vascular, while histologically they retain characteristic morphology and strong nuclear TFE3 immunoreactivity. Multimodal treatment strategies including surgical excision, radiotherapy, and systemic therapy are associated with prolonged disease control in selected patients. [3, 5]

Across all three tumors, the intracranial metastases generally appear as well-circumscribed lesions at the gray–white matter junction and retain the morphology and immunoprofile of their primary tumors—DOG1/SOX10 in ACC, HepPar-1/Arginase-1 in HCC, and nuclear TFE3 in ASPS.

In conclusion, although brain metastases from ACC, HCC, and ASPS are rare, recognition of their clinicopathologic features is crucial to avoid misdiagnosis as primary CNS tumors. Integrating histopathology, immunohistochemistry, radiology, and WHO CNS guidance is critical for correct classification. [6, 7] Recognizing and reporting such uncommon metastatic presentations expands current understanding of metastatic behavior, improves diagnostic accuracy, and guides optimal therapeutic decision-making improving patient outcomes in these rare but clinically significant entities.

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