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CASE REPORT

Glioblastoma with signet ring cell morphology: A diagnostic challenge

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ABSTRACT

Glioblastoma (WHO Grade IV), the most frequent malignant brain tumor, can have varied morphologic variations like epithelial/glandular structures, granular cells, and lipidized cells. Glioblastoma with signet ring cell morphology is very unusual and can mimic a metastatic carcinoma. These rare tumors may be just a morphological variant or may signify a different carcinogenic pathway.

Key words: Glioblastoma, signet ring morphology, mimic-metastatic carcinoma

Introduction

The prototype glioblastoma (WHO Grade IV), the most frequent and malignant primary brain tumor, generally does not pose a diagnostic difficulty to the pathologist. Occasionally variations in the tumor morphology like epithelial/glandular structures, granular cells, lipidized cells, and very rarely, signet ring cell morphology do challenge the pathologist. Herein, we report a rare case of glioblastoma with signet ring cell morphology and underlie its importance so as to prevent an erroneous diagnosis of metastatic carcinoma.

Case Report

A 29 year-old doctor came with complaints of persistent headache and occasional vomiting since 2 months. He had brief episodes of altered sensorium during this period. He was evaluated with a computed tomography (CT) scan [Figure 1] which showed a large 7 × 5 × 6 cm intraaxial space occupying lesion (SOL) in the right parietotemporal region with solid and cystic components and significant perilesional edema and midline shift. On magnetic resonance imaging (MRI) scan, the lesion was hyperintense on T2 with central area of T1 hypointensity. The lesion demonstrated diffusion restriction with apparent diffusion coefficient (ADC), showed intense enhancement on contrast administration, and MR spectroscopy revealed choline peak. Overall, radiological impression was of a high-grade glioma. Patient underwent craniotomy and excision of the lesion.

Histology [Figure 2] revealed a high-grade neoplasm composed of sheets and single scattered cells with majority of them having cytoplasmic inclusions pushing the nucleus to the periphery, thus displaying signet ring cell morphology. At places, the cells had a gemistocytic look, but processes from the cells or a fibrillary background were not conspicuous. Cells displayed moderate pleomorphism. Focal necrosis was noted. There was no microvascular proliferation. No other pattern or native brain tissue was identified. Stain for mucin was negative.

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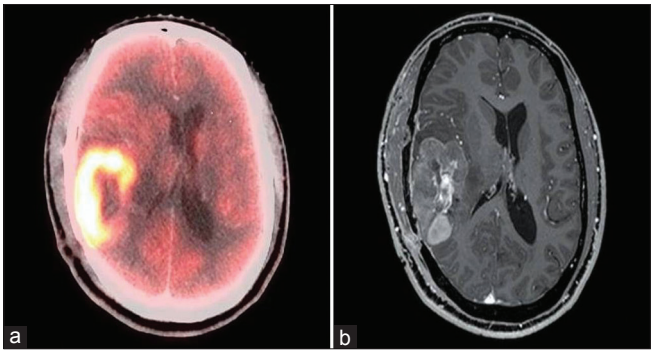

Figure 1: (a) Pet – CT scan and (b) T1-MRI showing right parieto-temporal lesion with solid and cystic components with significant perillesional edema and midline shift

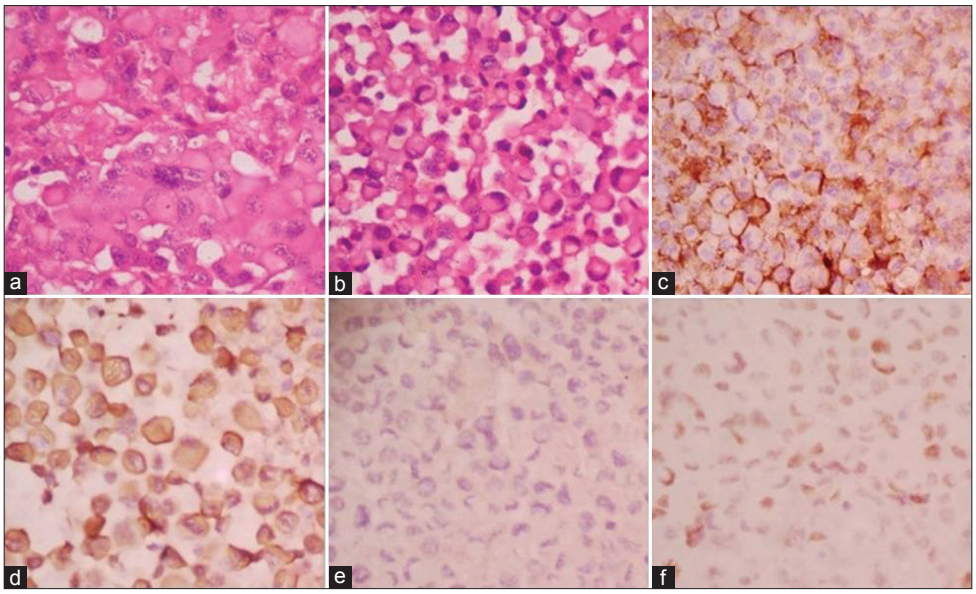

Figure 2: (a) Sheets of large cells exhibiting pleomorphism (b) individual cells exhibit signet ring cell morphology (H and E, ×200) tumor cells are positive for gfap (c), vimentin (d), negative for cytokeratin (e) and focaly positive for p53 (f)

On immunohistochemistry, the cells were positive for glial fibrillary acidic protein (GFAP), vimentin, and S-100 protein. They showed p53 positivity, suggesting astrocytic lineage. They were negative for cytokeratin, epithelial membrane antigen (EMA), synaptophysin, and HMB-45. Ki-67 proliferating index was around 10%. This confirmed a diagnosis of a glioblastoma with unusual signet ring cell morphology.

O6- methylguanine-DNA methyltransferase (MGMT) promoter methylation was demonstrated in this case by polymerase chain reaction (PCR).

There were no deletions of 1p19q chromosome on florescence *in situ* hybridization (FISH).

Discussion

Glioblastoma (WHO Grade IV) is the most malignant primary brain neoplasm and is of astrocytic lineage. The prototype histology comprises poorly differentiated pleomorphic astrocytes with nuclear atypia and mitotic activity. Microvascular proliferation and/or necrosis are necessary for its diagnosis.[1]

The presence of signet ring cells is very unusual in glioblastomas with only one previous case reported in literature till date.[2] However, signet ring cells have earlier been described in primary CNS tumors like oligodendroglioma,[3] ependymoma,[4] primary CNS lymphoma,[5] oligoastrocytoma,[6] and astroblastoma.[7]

This signet ring cell morphology can be confused with metastatic adenocarcinoma from the gastrointestinal tract. It is in these situations that immunohistochemistry is so useful to exactly delineate the cell of origin. Positivity for GFAP and negativity for cytokeratin confirmed glial origin of the signet ring cells. Furthermore, absence of 1p19q deletion and p53 positivity supported an astrocytic lineage of the tumor.

Rosenblum *et al*.[8] reported four cases of lipid-rich epithelioid glioblastoma, but those had cells with centrally placed nuclei and multiple cytoplasmic lipid droplets which expressed cytokeratin, unlike our case which had typical signet ring cell morphology and was cytokeratin negative.

Martin *et al*. described a glioblastoma very similar to our case, which had sheets of signet ring cells with nuclear atypia, mitoses, extensive necrosis, and vascular proliferation. On immunohistochemistry, the cells were positive for GFAP and S100, and negative to cytokeratin. Electron microscopy revealed stacks of intermediate filaments, and FISH for 1p19q did not show any deletions.[2]

Despite progress in surgery, radiotherapy, and chemotherapy of brain tumors, the overall survival of patients with glioblastoma remains extremely poor. Previous reports have shown a relative favorable prognosis for signet ring cell tumors of the CNS.[9,10] Our patient expired within 5 months of symptoms and 3 months of diagnosis as was the case reported by Martin *et al*.

Due to the very few cases in literature, it remains to be seen whether signet ring cell glioblastoma is just a morphological variant or signifies a different carcinogenic pathway.

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