

C A S E R E P O R T

FNA cytology in pediatric small cell glioblastoma

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Summary. *Objective:* Small cell glioblastoma is a high anaplastic variant of GBM characterized by a monomorphic proliferation of small or medium cells with oval nuclei and scanty cytoplasm. *Case study:* The cytologic findings of a small cell glioblastoma in 11-year-old male and histologic features of the tumor using immunocytochemistry are reported. *Conclusion:* The accurate preoperative diagnosis of a small cell glioblastoma is crucial to developing a curative surgical plan. Cytology- confirmed by histology- provides a convenient, safe and effective approach to solving a challenging differential diagnosis. (www.actabiomedica.it)

Key words: glioblastoma, cytology, histology

Introduction

Glioblastoma- WHO Astrocytoma grade IV is the most malignant glioma. It occurs most frequently in middle aged adults and is rare in children and young adults. Its most common sites are the frontal and temporal lobes but it may occur at any age and involve any part of the CNS. Glioblastoma arrives most commonly de novo (primary glioblastoma) or arrives by malignant transformation of low- grade astrocytoma (secondary glioblastoma).

Different molecular pathways have been described for tumor development in adulthood. In adults, the primary/de novo glioblastomas, are characterized by amplification of the epidermal growth factor receptor gene (EGFR) along with deletion or mutation of phosphate and tensin homolog tumor suppressor gene (PTEN). Secondary glioblastomas, often have mutations of the tumor suppressor gene TP53 but only infrequently have amplification of EGFR or alterations of PTEN. In pediatric de novo/primary glioblastomas, deletion of PTEN and EGFR amplification are rare similarly to their adult secondary counterparts (1).

Adult glioblastomas also show cytogenetic abnormalities: Loss of chromosome 10, deletion of the p16 gene in 9p21 amplification of the EGFR locus, and gain of chromosome 7 are commonly reported. in contrast to pediatric counterparts (2,3).

Primary glioblastomas are more common in older patients and are more aggressive. Survival from glioblastoma rarely exceeds one year. Postoperative irradiation and chemotherapy prolong survival minimally (4, 5).

Imaging shows a large mass of variable density with cavitation surrounded by a large area of edema. Glioblastoma has a wide range of histological appearance. Small cell glioblastoma is a primary glioblastoma, composed of poorly differentiated, uniform, small cells shows extensive ischemic necrosis, a higher proliferative index and high incidence of EGFR amplification (6, 7).

The cytology- immunocytology of small cell glioblastoma includes small cell anaplastic cells with typically irregular, hyperchromatic nuclei without nucleoli, mitoses, scanty cytoplasm, positive for cytoplasmic GFAP and S-100, MIB-1 greater than 10% and about one third cases are positive for p53.

Case report

An 11-year-old male was presented at University Hospital of Heraklion Crete with symptoms of encephalitis. A year ago was hospitalized for encephalitis due to Bartonella (Warthin Starry +) for Epstein- Barr lymphadenitis diagnosed by histology and in situ hybridism (EBER- 1, 2) with many small lymphocytes positive for EBV.

The MRI revealed a mass in the frontal lobe with cavitation and surrounding inflammation. A fine needle aspiration was performed. The cytologic diagnosis was suggestive of a small cell glioblastoma that confirmed by histology.

Material and methods

Cytology: The material obtained by FNAB from the cavitation of the tumor was smeared on glass slides. The air dried smears were used for Giemsa and Immunocytochemistry and the alcohol fixed for Papanicolaou 's method (Fig. 1).

Immunocytochemistry: In air dried smears immunocytochemistry was performed using the markers GFAP (Fig. 2). and S-100

Histology: In histological specimens fixed in 10% formalin after the biopsy of the tumor, the stain H&E was performed (Fig. 3).

Immunohistochemistry: The markers GFAP (Fig. 4), S-100, Vimentin, CD56, p53, NF, LCA, CD57, EMA and MIB-1 were used.

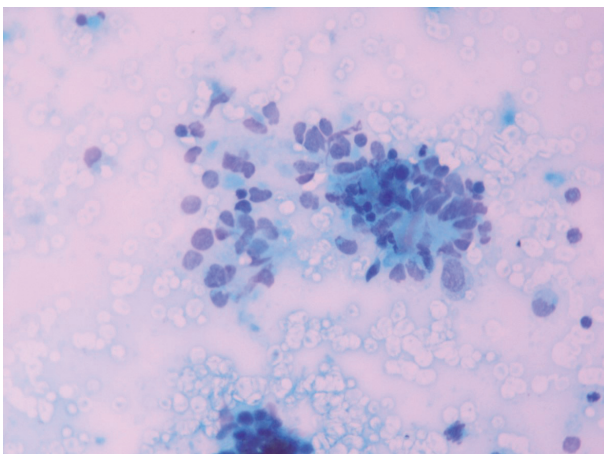


Figure 1. Glioblastoma, Fine needle aspirate. Large cluster of neoplastic cells. Papanicolaou stain X400

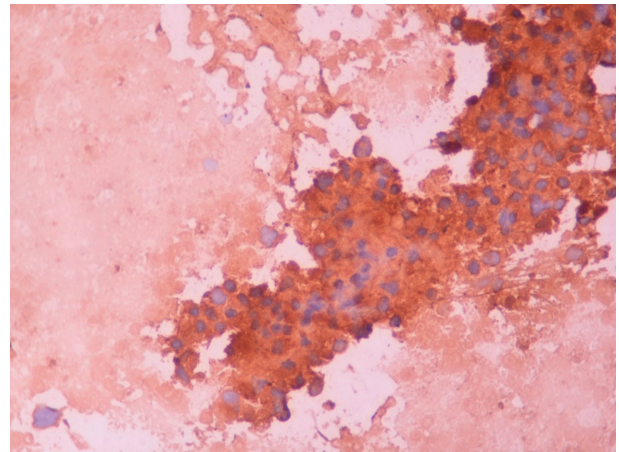


Figure 2. Glioblastoma, Fine needle aspirate. Large cluster of neoplastic cells. GFAP immunostain X400

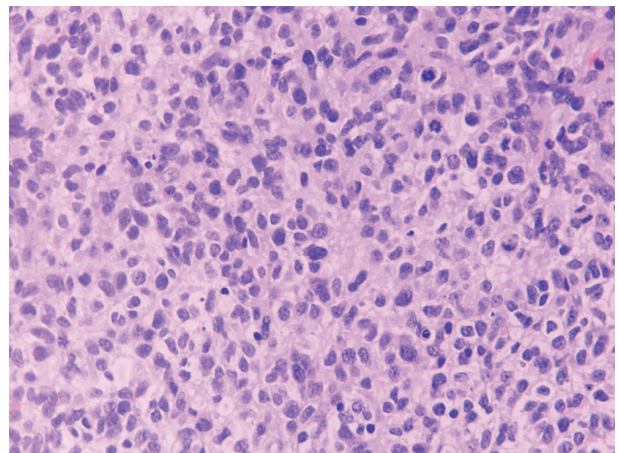


Figure 3. Glioblastoma. Tumor section. Hematoxyline-Eosin(H@E) stain X 400

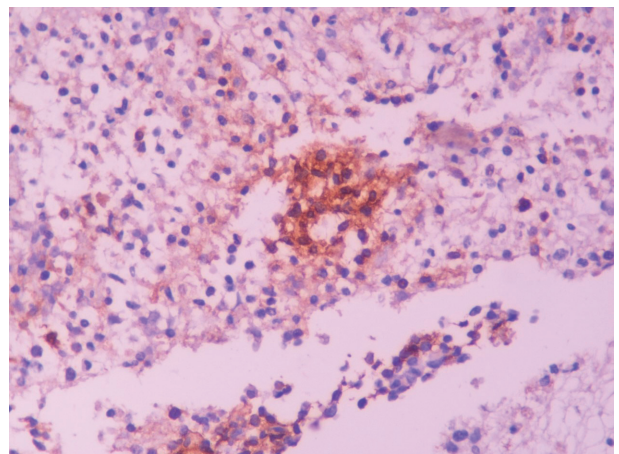


Figure 4. Glioblastoma. Tumor section. GFAP immunostain X 400

Results

Cytology: The slides showed abundant material with inflammatory deposits that comprised mainly of foamy macrophages, neutrophils, and in a lesser degree of small lymphocytes of T-cell type. Tumor cells were observed in between inflammatory infiltrates either isolated or in large clusters. The neoplastic cells were monomorphous small- medium in size, with scanty cytoplasm and oval hyperchromatic nuclei without prominent nucleoli. Mitotic figures were found as well.

Histology: Abundant material with glial neoplastic cells of medium size, nuclear atypia and many mitoses. Necrosis and palisade arrangement of the neoplastic cells was observed.

Immunocytochemistry: The majority of neoplastic cells were found cytoplasmic positive for GFAP and S-100 protein

Immunohistochemistry: The tumor cells expressed GFAP, S-100 protein, Vimentin, CD56 and p53 (60%).

The neoplastic cells were found to be negative for NF, LCA, CD57 and EMA markers. The index MIB-1 was found to be positive in 60% of tumor cells

Discussion

Glioblastoma multiforme (GBM), a grade IV astrocytoma as currently defined by the World Health Organization (WHO) classification, is the most common primary brain tumor with a median survival of approximately 1 year following current multi-modal treatments (8, 9).

Small cell glioblastoma may account for 10% of GBM diagnoses with another 11% showing focal, small cells features (10). Small cell glioblastomas despite the possibility of being mistaken for high- grade oligodendroglial tumors or lower grade astrocytomas, are- in all ages- aggressive lesions paralleling grade IV gliomas (11). However small cell glioblastoma tumors uniformly lacked 1p/19q deletion thus being distinguished from oligodendroglial tumors (12), showed EGFR amplification (13, 14).

Full understanding of the molecular biology underlying adult glioblastoma has been extended over

many years. On the contrary in children and adolescents the case is not the same. A large review has summarized all genetic alterations associated with epigenetic features and patients profile in both pediatric and adult tumors (15).

With regards to imaging in this specific case, the possible differential diagnosis with an infectious process makes it interesting. The differential diagnosis is that of a ring enhancement lesion and includes brain abscess: an abscess has a smooth inner wall, with satellite lesions, and a low intensity capsule in MRI (16,17).

Overall features to define that tumor include ring-enhancement and pseudopalisading necrosis, oval nuclei, high proliferative indices and thin GFAP- positive cytoplasmic processes are in agreement with our case.

In our case the small cell phenotype as outlined by another report (10) was defined by cytology on routine Papanicolaou and Giemsa stains and confirmed by histology on H&E stained sections by a prominent population of small, monomorphic, uniformly oval nuclei with minimal discernable cytoplasm and a high mitotic activity, given the otherwise bland nuclear cytology.

In our case the patient was pediatric, a male child 11 years-old, with a history of encephalitis due to Bartonella and a lymphadenitis due to Epstein- Barr. GBM is not a common tumor in pediatric patients and the differential diagnosis include glioblastomas with PNET- like foci tumors (small blue- cell tumor) but their cytologic features are quite different as primitive- appearing, hyperchromatic, rounded to carrot- shaped nuclei, often with molding.

The differential diagnosis of small cell glioblastoma also includes the anaplastic oligodendroglioma but SCG have oval rather than rounded nuclei, a high mitotic activity and very often have thin, GFAP- positive cytoplasmic processes. In contrast the anaplastic oligodendrogliomas more frequently have larger epithelioid cells with vesicular nuclei, prominent nucleoli and a greater degree of pleomorphism compared with small cell glioblastomas.

In conclusion small cell glioblastomas is a rare pediatric tumor and FNA cytology potentially provides a convenient, safe and effective approach to solving a challenging differential diagnosis but must be complemented by histopathology and immunohistochemistry.

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