Brief Report: Anaplastic Pleomorphic Xanthoastrocytoma Invading the Skull in a Child

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Abstract

We present a case of a tumour in a 12-year-old mentally normal girl, who presented with a painless forehead swelling. Imaging studies demonstrated a large lesion within the right frontal lobe with erosion through the frontal bone. Histological diagnosis met all the criteria of glioblastoma with evidence of florid bone invasion. DNA methylation analysis, however, demonstrated features consistent with anaplastic pleomorphic xanthoastrocytoma. This skull invasion is a very uncommon presentation of gliomas, especially in children, and only a handful of cases have previously been described.

Keywords: CNS tumors; Neuro-pathology; Tumors; Brain; Cancer genetics; Surgery; Neuro-oncology

Abbreviations: MRI: Magnetic Resonance Imaging; GFAP: Glial Fibrillary Acidic Protein; S100: S100 protein; AE1/3: Cytokeratin AE1/3 stain; DNA: Deoxyribonucleic Acid; MIB-1: E3 ubiquitin protein ligase 1; EMA: Epithelial Membrane Antigen; CDKN2A: Cyclin-dependant kinase inhibitor 2A; BRAF V600E: B-RAF proto-oncogene; ACNS: Trial number; WHO: World Health Organisation

Introduction

Pleomorphic xanthoastrocytoma is a rare World Health Organization (WHO) grade II tumour typically found in the temporal lobes in children and young adults. It has rarely been described with anaplastic features [1]. We present the first report of a previously healthy 12-year-old girl initially diagnosed histologically with frontal Glioblastoma with florid bone invasion through the skull. DNA methylation analysis subsequently showed features more consistent with anaplastic pleomorphic xanthoastrocytoma.

Case Report

The patient presented with a palpable, painless, non-pulsatile mass in the right supra-orbital region, which had developed over a 2-week period. She did not complain of headache and parents did not report any change in behaviour. Magnetic Resonance Imaging (MRI) scan demonstrated an ill-defined, avidly enhancing, and mass of heterogeneous signal intensity in the right frontal lobe causing 15 mm of midline shift (Figure 1). There was destruction of adjacent calvarium with extension into the sub-galeal soft tissue along with evidence of breach of the orbital roof with extension of the mass inferiorly into the orbit. MRI spine was unremarkable. At surgery, a grey-brown necrotic mass was seen protruding from the frontal bone. The orbital roof breach was explored, necrotic-appearing bone was resected and the abnormal tissue removed from the orbit. The remainder of the tumour was debulked and the orbital roof reconstructed. The frontal bone was replaced after excising a 1 cm margin at the defect. The patient awoke with no obvious deficits and an MRI day 1 post-operatively demonstrated no complications with a small enhancing area at the sylvian fissure (Figure 1).

Histopathologic examination revealed a tumour with a range of phenotypes, the predominant component being sheets of cells with oval to spindled nuclei and a coarse chromatin pattern but no obvious nucleoli. These cells showed moderate amounts of eosinophilic cytoplasm and mitotic figures were readily identified. Appearances were suggestive of meningothelial differentiation, however there were no clearly defined whorls, the nuclei lacked pseudo-inclusions and there was evidence of endothelial proliferation and florid pseudo-palisading necrosis (Figure 2A). The tumour showed extensive leptomeningeal spread and invasion into bone (Figure 2B). Stains for glial fibrillary acidic protein (GFAP), S100 protein, vimentin and, focally, for synaptophysin were positive. The E3 ubiquitin protein ligase (MIB-1) showed a proliferative index of 9%. AE1/3 immunostain highlighted a focal collection of rhabdoid cells. The epithelial membrane antigen (EMA) immunostain was negative, as were the immunostains for cytokeratin marker (CAM 5.2), cadherin, progesterone receptor and myogenin. Chromosome analysis showed gains of chromosomes 3,7,9,11,14,17&21. Loss of heterozygosity was not detected at 1p19q. While histologic diagnosis met all the criteria of Glioblastoma, the unusual finding of florid bone invasion, prompted further analysis using DNA methylation profiling using the Illumina 450 k array (Illumina Human Methylation 450 k Array and Internal Classifier V7.0.). This revealed focal homozygous deletion of chromosome 9p, including the locus for cyclin-dependant kinase inhibitor 2A (CDKN2A).
has been rarely described in malignant gliomas, having been reported in only a few case reports restricted to adult patients [10-12] and has never been reported in children with pleomorphic xanthoastrocytoma with anaplastic features.

Conclusion

The diagnosis of high grade glioma should be considered in cases where bony erosion and subgaleal extension is seen on imaging, especially if the tumour appears intra-axial. DNA methylation analysis had a significant clinical impact by enabling the accurate diagnosis of a very rare tumour entity. Our case highlights the need to establish a classification system which combines clinical, histopathological characteristics and also incorporates molecular analysis, such as DNA methylation profiling, to more accurately diagnose tumor entities.

Conflict of Interest Statement

The authors declare that they have no conflict of interest in regards to this case.

References