CASE REPORT

Astroblastoma – reviewing literature and one case report

DANIEL MIHAI TELEANU1), ANDREEA ILLIESIU2), ADRIAN FLORIAN BALAŞA3), RALUCA IOANA TELEANU4), NICOLAE-ŞTEFAN BOGACIU5)

1) Department of Neurosurgery, Emergency University Hospital of Bucharest, Romania; Department of Neurosurgery, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
2) Department of Pathology, Emergency University Hospital of Bucharest, Romania
3) Department of Neurosurgery, Emergency County Hospital, Tîrgu Mureş, Romania; Department of Neurosurgery, University of Medicine, Pharmacy, Sciences and Technology of Tîrgu Mureş, Romania
4) Department of Pediatrics and Pediatric Neurology, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
5) Department of Neurosurgery, Emergency University Hospital of Bucharest, Romania

Abstract

Background: Astroblastoma is a poorly defined central nervous system (CNS) tumor, included along with polar spongioblastoma and gliomatosis cerebri in the group of neuroepithelial tumors of uncertain origin in the June 2016 World Health Organization (WHO) Classification of tumors of the CNS. They are rare neoplasms that affect primarily patients of young ages. The purpose of this research is to highlight the uniqueness and rareness of this pathology and to emphasize on the particularities of one case managed in our Clinic. Case description: We present the case of a 54-year-old patient with a history of seizures since the age of six years old, who presented on admission with progressive worsening and unresponsiveness to treatment, starting six months prior to presentation. Brain imaging shows a right frontal mass compressing neighboring structures. Gross total resection of the tumor was performed, and histopathological examination of the surgical sample together with immunohistochemistry highlighted the presence of a low-grade astroblastoma. Conclusions: We summarized data from the literature in order to highlight aspects of this affliction: clinical presentation, imagery, surgical treatment and pathology, hoping that this will aid physicians in finding useful information on this subject, which can guide them to a good outcome. We also discussed differential diagnosis, as this type of tumor shares common features with ependymoma, meningioma, astrocytoma, etc.

Keywords: astroblastoma, low grade, ependymoma, astrocytoma.

Introduction

Astroblastoma is a type of tumor classified as being of uncertain origin in the 2016 World Health Organization (WHO) Classification of tumors of the central nervous system (CNS) [1]. They are a rare type of tumors comprising of less than 3% of all neuroglial brain tumors (0.45–2.8%) [2]. Demographic characteristics of patients suffering from this disease show a young age (children and young adults) and female predominance [3], but older patients have also been reported. Tumor characteristics can take the evolution of the patient in two directions: low-grade – good prognosis after gross total resection, high-grade – uncertain prognosis with features merging with those of GBM. Major histopathological (HP) features of the astroblastoma are perivascular processes and vascular hyalinization. The lesion appears large and lobulated on standard magnetic resonance imaging (MRI) evaluation [4]. On occasion, even in the presence of malignancy features, good clinical evolution comes to contradict the poor prognosis stated by HP examination [5].

Astroblastoma has not been studied in an exhaustive manner due to its low incidence rate, which does not allow for large studies to be conducted. A search for the term “astroblastoma” in the titles of articles indexed on PubMed shows only 101 results, the majority of which are case reports.

Aim

The aim of this paper is to present a rare occurrence in the neurosurgical pathology and highlight an uncommon manifestation found in our presented case: tumor bleeding. A review of the existing cases in literature has also been performed.

Case presentation

A 54-year-old woman with a history of epilepsy since the age of six years old, with the last seizure reported four years prior to admission, presented with a 6-month history of progressive headache and dizziness. Clinical examination showed a temperature of 36.8°C, heart rate 70 beats/minute, blood pressure 110/70 mmHg, respiratory rate 18 breaths/minute, 99% oxygen saturation while breathing ambient air. Patient had anicteric sclerae, oro-pharynx with no lesions and a supple neck. Heartbeat was regular with no murmures, abdomen was nontender with no hepatomegaly or splenomegaly, no adenopathy was discovered. Patient was alert and oriented, had no cranial nerve deficit, normal motor strength, non-altered sensory function, normal reflexes with no higher mental function disturbances. The patient declared no allergies and no significant family history. Usual laboratory blood tests were in normal range. The patient was admitted in...
the Department of Neurosurgery of Emergency University Hospital of Bucharest, Romania, with elevated intracranial pressure for further investigation. A MRI analysis was performed, pointing out the presence of an intracranial mass localized in the right frontal lobe, with mass effect on adjacent structures. The mass was well defined, with mixed cystic-solid content, septated and hyperintense on T1- and T2-weighed imaging and abnormally low apparent diffusion coefficient (ADC) values on diffusion-weighted imaging (DWI) (Figure 1).

Imagistic features suggested a tumor with possible differential considerations, which included astroblastoma, teratoid tumor or glioma (ependymoma, astrocytoma ranging from low to high grade: GBM, diffuse grade II astrocytoma, oligodendroglioma, pleomorphic xanthoastrocytoma). Usually, astroblastoma appear in the supratentorial space with iso-to hypointense T1 sequence and heterogeneously hyperintense T2. Teratoid tumor frequently presents as a tumor of the posterior fossa in children, iso-to hyperintense on T1 and hyperintense on T2. GBM appears as a hypo- to isointense mass on T1 and hyperintense on T2; the centre of the mass is heterogenic suggesting necrosis. Ependymoma appears iso- to hypointense on T1 and hyperintense on T2. Pleomorphic xanthoastrocytomas have a mixed solid-cystic appearance with a low signal cystic component and iso- to hypo-intense solid component on T1 and hyperintense signal of both cystic and solid components on T2. Oligodendroglioma usually presents as hypointense on T1 and hyperintense on T2 with intratumoral calcifications.

The patient was prepared for surgery, and in the morning of the event, she accused worsening of the headache. During surgery, when the tumor was exposed, the surgical team discovered remarkable hemorrhaging at the site, which caused dissection of the mass from the brain, subsequently being easily removed as it was pushed out of place by the expanding brain. The tumor was rubbery, highly vascular and well demarcated from the surrounding brain. The specimen was sent for HP examination and hemostasis was achieved.

HP examination revealed a papillary architecture (Figure 2) composed of gemistocyte-like cells organized around hyalinized vessels, creating areas of pseudorosettes (Figure 3). Tumor cells contained abundant cytoplasmic mass, large nuclei and prominent nucleoli and were sending thick and short processes towards vessel walls (Figure 4). No fibrillar component and no mitotic figures were identified. Immunohistochemistry (IHC) highlighted positivity to vimentin (monoclonal mouse anti-vimentin antibody, clone V9, 1:50 dilution, Dako) (Figure 5), S100 protein (polyclonal rabbit anti-S100 antibody, 1:1000 dilution, Dako) (Figure 6), glial fibrillary acidic protein (GFAP) (monoclonal rabbit anti-GFAP antibody, clone EPR1034Y, 1:150 dilution, Abcam) (Figure 7) and negativity to progesterone receptor (PR), epithelial membrane antigen (EMA), p53, bcl-2 and neuronal...
nuclei (NeuN) (polyclonal rabbit anti-NeuN antibody, 1:1000 dilution, Abcam) markers (Figure 8). Ki67 proliferation index was 4% (monoclonal mouse anti-Ki67 antibody, clone MIB-1, 1:50 dilution, Dako) (Figure 9).

Although gemistocytic cells are occasionally found in different types of gliomas, a gemistocytic astrocytoma and other gliomas (fibrillary astrocytoma, oligodendroglioma) do not have pseudorosettes, which are commonly found in ependymomas, but ependymomas do not present gemistocytic-like cells. Therefore, based on these findings, the tumor was reported as a low-grade astroblastoma.

Figure 2 – Overall image of the tumor showing the papillary appearance of tumor architecture [Hematoxylin–Eosin (HE) staining, ×100].

Figure 3 – Gemistocytic-like cells predominantly arranged as perivascular rosettes (HE staining, ×200).

Figure 4 – Tumor cells features showing abundant cytoplasmic mass and large nuclei (HE staining, ×200).

Figure 5 – Gemistocytic-like cells with intense vimentin reaction (Anti-vimentin antibody immunomarking, ×200).

Figure 6 – Gemistocytic-like cells with intense S100 protein reaction (Anti-S100 antibody immunomarking, ×200).

Figure 7 – Tumor cells with intense glial fibrillary acidic protein reaction, similar to astrocytes (Anti-GFAP antibody immunomarking, ×200).
Postoperative, the patient had a favorable evolution, the headache and dizziness resolved, and there were no neurological deficits or seizures. A computed tomography (CT) scan with contrast enhancement was performed after surgery, which showed no pathological contrast enhancement.

The patient did not receive oncological treatment after surgery because evidence suggested a low-grade tumor, rather than a higher-grade one, which would have needed more aggressive treatment.

Follow-up MRI was performed at one month showing no tumoral residues, but only slight signal alteration due to cerebral scarring at the site from where the tumor was excised (Figure 10).

After almost one year, the patient is in good condition, with no neurological signs and no tumor recurrence.

**Discussions**

Astroblastoma was firstly depicted by Bailey & Cushing [6] and further detailed by Bailey & Bucy [7] at the beginning of the 20th century, who believed that astroblastomas originated from astroblasts, an intermediate stage between glioblasts and astrocytes. Further studies using ultrastructural and immunohistochemical investigations proved that tumor cells express features of a tanycyte, a special type of ependymal cells, suggesting a possible origin from here [8]. Another idea is an abnormal...
Astroblastoma – reviewing literature and one case report

The prevalence of all astroglial primary brain tumors [2, 9], but it could be even lower than that [10], considering the fact that very few cases are reported every year. Most cases are diagnosed in the first three decades of life [11], older patients being rare but not exceptional, as our case report indicates, with ages on diagnosis ranging up to 70 years old, as it is reported in another review [12].

Large series have not been studied due to the paucity of this pathology; one study consisting of 23 cases being the largest we found so far [13]. A 2014 review [14] asserts the existence of roughly 230 reported cases, while others, even more recent ones [11, 12], found less. There is a clear predominance in females [11, 12, 14–17], although some did not come to this conclusion [17–19].

Most astroblastomas are supratentorial cerebral tumors and while superficial locations are more frequent, profound locations are also reported [11]. The frontal lobe is the preferred site of tumor development, followed by the parietal and temporal lobe. Other locations are infrequent, but still manageable: occipital lobe [20], brainstem, corpus callosum, ventricular system, etc. Most of the times, these tumors are very large when discovered, suggesting that they have a slow growth, non-infiltrating pattern, which allows the brain to accommodate the lesion for a long time until it gets so large that it causes neurological signs and symptoms.

Clinical presentation depends, as other lesions of the CNS, on localization with headaches and seizures being the most frequent complaints.

Astroblastomas are usually very well delineated on neuroimaging studies and may be confused with extraaxial tumors, especially if there are bone structure alterations at the site of the tumor [12]. Characteristics found on CT scan consist of mixed cystic and solid components, hyperattenuated in most of the cases [12, 17], which give it a heterogeneous appearance, sometimes completed by microcalcifications. MRI findings show heterogeneous lesions, iso-to hypo-intense on T1 sequences, hyper-intense on T2 sequences and heterogeneous enhancement on T1 contrast-enhanced images, while perilesional edema might be present, but reduced most of the times [3, 12, 15]. Perilesional edema is usually low in astroblastoma including high-grade variants, unlike in other high-grade tumors. Magnetic resonance spectroscopy (MRS) is non-specific, showing elevated choline with decreased N-acetylaspartate levels, also found in other CNS tumors [5, 12, 21]. Sometimes, sudden onset of symptoms suggests hemorrhage, which may be discovered on imaging studies and taken as being of vascular origin, rather than of tumor origin [22]. Based on the imaging studies, the differential diagnoses for astroblastoma include pilocytic astrocytoma, oligodendroglioma, high-grade astrocytoma, primitive neuroectodermal tumor, ependymoma.

Histologically, astroblastoma is defined by the presence of perivascular pseudorosettes and perivascular hyalinization [19]. The key in distinguishing them from other glial neoplasms is lack of fibrillarity, meaning that perivascular processes are not fibrillar and stroma shows no fibrillarity. A papillary architecture is created with radially arranged cytoplasmic processes towards the central thickened and hyalinized blood vessels. Tumor cells have eosinophilic cytoplasm and the processes are short and thick.

Concerning the differentiation degree, there are two distinct histological degrees: a low-grade and a high-grade type. Low-grade type expresses a better differentiation pattern with uniform perivascular pseudorosettes, low mitotic figures, minimal cellular atypia, sclerosis of vascular walls, absence of spontaneous palisading necrosis and absence of endothelial proliferation. The average Ki-67 index is around 3%. It has a favorable postoperative prognosis. On the other hand, high-grade type shows more anaplastic features such as high mitotic index (>5 mitoses/10 high-power fields), cytological atypias, high cellularity, microvascular proliferation, necrosis with palisading. Ki-67 proliferating index is over 10% [1]. Another particularity in high-grade variants, perilesional edema is less observed at imaging analysis in comparison to other high-grade tumors [23]. It has a poor prognosis associated with recurrences and shorter length of postoperative survival [13], although some studies reported no recurrence after radical surgery of high-grade astroblastomas [5]. Also, some low-grade variants may recur after total gross excision [13, 24]. One case found in the literature reported suprasellar, spinal and pineal region metastasis of an astroblastoma 20 months after radical surgery of the primary tumor. The primary tumor was a low-grade astroblastoma, while metastasis exhibited high-grade features. Interestingly, immunoreactivity to GFAP was partially lost in the metastasized cells, but oligodendrocyte transcription factor-2 (OLIG-2) positivity increased, in comparison to primary tumor, when GFAP was strongly positive with only focal expression of OLIG-2. Besides, an arteriovenous malformation coexisted with the primary tumor, found at the first CT–angiography investigation. The malformation was microscopic confirmed by distribution of the vessels in a tortuous fashion [20].

Adjuvant radiotherapy is not necessary in low-grade types, while in high-grade it is highly recommended. Immunoreactivity for astroblastoma cells is typically positive for GFAP, vimentin and S100 protein, as in our case.

Positive diagnosis of astroblastoma is often difficult as it expresses common characteristics with other CNS tumors. Therefore, differential diagnosis is very important.

A first entity to differentiate from is ependymoma, intracerebral type. Imaging examinations showed that, unlike astroblastoma, which is superficial supratentorial localized with a bubbly appearance in the solid form, ependymoma usually occurs infratentorially in close proximity to ventricles. When it is localized supratentorially, it presents as a cystic mass. Solid type lacks that aforementioned bubbly appearance [17, 25]. As for histology differences, ependymoma can also display pseudorosettes, but the cytoplasmic processes are more fibrillated and thinner than those in astroblastoma [26]. The nuclei in astroblastoma are larger and vascular sclerosis is not usually exhibited in ependymoma [27]. Immunopositivity to GFAP, vimentin and S100 overlaps in both tumors, but there may be a more intense expression of GFAP in ependymomas [25]. Also, GFAP is more variable in other elements of the tumor such as rosettes and papillae than
in pseudorosettes. OLIG-2 expression is sparse in ependymomas, correlated with intense GFAP positivity [18].

Because astroblastoma shares features both of ependymoma and astrocytoma, the latter should also be considered. An astrocytoma has a clinical behavior closely correlated with pathological description, while an astroblastoma could manifest clinical follow-up in contradiction with its microscopic findings of malignancy. MRI imaging showing aspects of astrocytoma can mislead the diagnosis in some cases [2, 26]. For example, if the radiological finding of an anaplastic astrocytoma is a cystic appearance, it is caused by central necrosis. It also associates peritumoral T2 hyperintensity [17]. Gemistocytic-like cells and pseudorosettes presence, as in our case, can easily misguide to a gemistocytic astrocytoma diagnosis. GFAP-positive gemistocytic cells with thick processes around vessel walls can also be present in oligoastrocytoma, where fibrillary component is missing. The presence of gemistocytic-like cells in our case could be a mark of long-term prognosis. It is thought that the presence of gemistocyte in a low-grade astrocytoma is a sign of a rapid transformation to an anaplastic astrocytoma [28]. It is questionable if the poor prognosis seen in gemistocytic astrocytoma can also be attributable to an astroblastoma.

An astroblastoma, high-grade type, can also be confused with a pleomorphic xanthoastrocytoma due to presence of pleomorphic cells (frequent nuclear inclusions and cytoplasmic xanthomathous change). Xanthoastrocytoma is usually located superficially with leptomeningeval involvement and is positive to GFAP, S100, reticulin and negative to chromogranin and p53 (or focal positive). It has been described that the general form of appearance on CT and MRI in a pleomorphic xanthoastrocytoma is that of an enhancing mural nodule within a single large cyst [17].

Another entity that should be considered is extra-axial solid tumor, particularly papillary meningioma. This is often a misdiagnosis in case of a superficially placed astroblastoma, in close contact to dura mater [29]. Specific CT and MRI features of meningioma such as tumor touching the inner surface of the skull or erosion of the inner table and diploe may be present also in case of an astroblastoma, as reported in the literature [30]. Microscopically, papillary meningioma is connected to the meninges and the perivascular pattern is similar to pseudorosettes of ependymoma [31]. Immunohistochemical features of glial markers make the difference between them. Papillary meningioma is usually positive to cytokeratin and EMA, but negative to GFAP, while the EMA expression in astroblastoma is focal [5, 32].

An interesting case of astroblastoma with signet ring-like cells was reported in the literature. It was histologically similar to a classical astroblastoma with papillary pattern, hyalinized vessels and perivascular arrangements. Signet ring-like cells were GFAP positive and formed areas of islands. It was questionable if these cells were an incidental finding or attributed to biological characteristics [33].

Other cases were published, describing rhabdoid morphology. Rhabdoid cells were described as cuboidal or elongated with eccentric nuclei, prominent nucleoli and eosinophilic cytoplasm. All the other classical components of astroblastoma were present. The importance of differential diagnosis with other rhabdoid morphological tumors was highlighted [34–36].

Management of astroblastomas is poorly defined because of the rarity of this disease. Surgical treatment is ideal with complete resection being possible in almost all cases. This is because this tumor is expansive in nature, rather than infiltrative, and it is very well demarcated from the cerebral tissue. Radiotherapy has shown some success, especially when used in high-grade astroblastomas. For low-grade variants, surgical treatment solely, with follow-ups, is better accepted, while for high-grade ones, more aggressive management (including radiotherapy and chemotherapy) is useful, but still there is no conclusive information on this subject [3, 11, 14, 16, 37].

Clinical manifestations of astroblastomas are nonspecific, usually patients presenting with elevated intracranial pressure and neurological signs specific to the location of the tumor. Peripheral localization of the tumor, as we have seen in this case is most often seen in astroblastomas [3]. The typical bubbly appearance on MRI studies was suggestive for this type of tumor, but common imagistic features shared with other brain tumors: glioma, teratoid tumor, ependymoma account for an imagistic differential diagnosis. Histopathological diagnosis in our case is consistent for astroblastoma with elongated glial cells with eosinophilic cytoplasm (gemistocytic-like cells) and processes extended towards a centrally hyalinized vessel. Immunophenotype was positive for GFAP, S100, vimentin and negative for epithelial membrane antigen as defined in the literature.

Tumor bleeding is an unusual occurrence in astroblastomas, but it is possible and it may be an aiding feature in the early stages of the diagnosis as observed in other cases [38]. Also, sudden exacerbation of the symptomatology, as presented in our case, is a “red flag” for possible bleeding and warrants for immediate action.

Conclusions

We presented a typical case of a rare brain tumor but with an unusual feature that we found to be clinically important. Tumor bleeding is a highly uncommon manifestation of astroblastoma, but when it appears it gives more information for the differential diagnosis. Bleeding was found to be peritumoral in our case as opposed to gliomas were bleeding, when it occurs, is usually intrallesional. This feature might be used to distinguish between the two types when present on initial imagistic studies. Hemorrhage has been shown in our case to exacerbate the symptomatology. Sudden aggravating neurological signs or symptoms may be a witness for tumoral bleeding and warrant for immediate action: emergency imaging studies and surgical treatment. Peritumoral bleeding may help the surgeon by dissecting the mass from the adjacent brain, having considered that astroblastoma is usually located peripherally as in our case, but it may also have serious consequences by creating a mass effect on the brain, which again, is mandatory to be managed as soon as possible.

Conflict of interests

The authors declare that they have no conflict of interests.
Astroblastoma – reviewing literature and one case report

References


Received: October 2, 2017
Accepted: February 7, 2019

Corresponding author
Daniel Mihai Teleanu, Lecturer, MD, PhD, Department of Neurosurgery, “Carol Davila” University of Medicine and Pharmacy, 37 Dionisie Lupu Street, Sector 2, 020021 Bucharest, Romania; Emergency University Hospital, 169 Independenţei Avenue, Sector 5, 050098 Bucharest, Romania; Phones +4021–318 07 19, +4021–318 05 23, e-mail: daniel.teleanu@umfcd.ro