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Neuropathological Spectrum of Pilocytic Astrocytoma – an Indian Series of 120 Cases

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Pilocytic astrocytomas (PAs) are generally well circumscribed, slowly growing, cystic tumors, occurring in the pediatric age group. Our aims were to retrospectively analyze the neuropathological spectrum of PA, and correlate it with various clinicopathological features. A total of 120 PAs, diagnosed and managed at this center during a 5-year period, were included. The study population had a mean age of 18.9 years, with male predominance (68.3%), and demonstrated predilection for posterior fossa (61.7%). On histopathology, biphasic pattern (89.2%) along with Rosenthal fibers (66.7%) and eosinophilic granular bodies (60%) were present in the majority of cases. Vascular features were characterized by perivascular hyalinization (51.7%), angiomatous proliferation (21.7%) and glomeruloid changes (21.7%). Hemosiderin-laden macrophages were noted in 37.1% of cases. Further, 60.8% showed lymphoplasmacytic infiltration, while atypia and necrosis were present in 25.8% and 1.7% of cases, respectively. Statistical evaluation revealed significant correlation of angiomatous proliferation with age (≤12 and >12-year age groups) (p=0.011); and of hemosiderin deposition with angiomatous proliferation (p=0.006), perivascular hyalinization (p=0.035), and age (≤12 and >12-year age groups) (p=0.028). This study emphasizes that though PAs generally display classical histomorphology, diagnosis may be challenging in patients with unusual clinicopathological features, e.g. in older patients, uncommon location, absence of biphasic pattern, or presence of nuclear atypia, mitotic figures and necrosis, and also in cases of small biopsies. In the absence of diagnostic histology enumerated above, vascular features like angiomatous proliferation, glomeruloid changes and perivascular hyalinization, along with hemosiderin-laden macrophages and perivascular lymphocytic infiltration should be considered as surrogate histological markers of PA. (Pathology Oncology Research Vol 12, No 3, 164–171)

Key words: Pilocytic astrocytoma, vascular spectrum, angiomatous proliferation, glomeruloid vessels, perivascular, hyalinization, hemosiderin

Introduction

Pilocytic astrocytoma (PA) is a common type of slowly growing, grade I brain tumor[6,19] generally found in children and young adults. PA can affect the entire neuraxis, although the cerebellum and the region around the third ventricle are the most common sites of origin.[6,19] Typically, it is a well-circumscribed, often cystic tumor composed of variable portions of loose and compact tissue, along with presence of Rosenthal fibers in compact areas and eosinophilic granular bodies (EGB) in microcystic foci. Other features that are variably present in PA include sclerotic vessels, vascular proliferation, calcification[7,11,14,24,27,28,30] and chronic inflammation,[7,14,27] while nuclear pleomorphism, mitosis and necrosis are rare. Owing to the differences in prognosis and therapeutic options, it is vital to distinguish PA from diffuse astrocytoma, and in the presence of mitosis / necrosis from other high-grade neoplasm.

Occasionally, the classical biphasic pattern may not be quite evident, especially when one pattern predominates over the other, and in case of an uncommon location, making a differential diagnosis with diffuse astrocytoma especially challenging. This problem is further compounded in cases of small biopsies.[15] The presence of Rosenthal fibers and EGB, although useful in diagnosis,

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Table 1. **Incidence of pilocytic astrocytoma in reference to ICT and glial tumors and mean age / age range during the study period (1998-2002)**

Year	*ICT*	*Glial tumor*	*Pilocytic astrocytoma*	*Ratio of GT: PA*	*Mean age/range*
1998	572	185 (32.3%)	32 (5.6%)	5.8	20.2y (7m-81y)
1999	525	187 (35.62 %)	33 (6.3%)	5.6	19.4y (4y-75y)
2000	744	242 (35.53 %)	37 (5%)	7.1	16.4y (6m-57y)
2001	793	275 (34.69 %)	53 (6.7%)	5.2	19.3y (4y-67y)
2002	652	210 (32.21 %)	46 (7%)	4.6	18.7y (2.5y-60y)
Total	3286	1099 (33.4%)	201 (6.1%)	5.5	18.8y (7m-81y)

ICT: intracranial tumors; GT: glial tumors; PA: pilocytic astrocytoma; y: years; m: months

is not invariable, especially in the setting of occasional mitotic figures, necrosis, nuclear pleomorphism and vascular proliferation.

The present study was therefore undertaken to retrospectively evaluate the neuropathological spectrum in PA, and analyze the diagnostic significance of various clinicopathological features, which could be suitably utilized in the absence of classical histology of PA.

Materials and Methods

The study included surgically obtained specimens from PAs managed at the Neurosciences Center of this institute, between 1995 and 2004, where slides and blocks were both available. Repeat biopsies of index cases were excluded. Relevant clinical details e.g. age at surgery, sex and site were noted.

Resected tissues from all cases were fixed in 10% neutral buffered formalin, routinely processed and embedded in paraffin. Five-micron-thick sections were stained by hematoxylin and eosin (H&E). Four histopathologists (AM, CS, PD and MCS) independently reviewed H&E slides along with relevant immunohistochemical / histochemical stains [glial fibrillary acidic protein (GFAP), leukocyte common antigen (LCA), Perl's stain, periodic acid Schiff (PAS), myelin], and reconfirmed the original diagnoses, as per the criteria of WHO classification of CNS tumors (2000).[20]

The evaluated neuropathological spectrum included the presence of predominant architectural pattern (compact or microcystic), Rosenthal fibers, EGB, mitoses, nuclear pleomorphism, calcification, necrosis, chronic inflammation, hemosiderin-laden macrophages, multinucleated giant cells, ganglion cells, and vascular changes like perivascular hyalinization, angiomatous proliferation and glomeruloid changes. Mitotic counts were evaluated as the single highest count per 50 high-power fields (HPF: x400), in the most mitotically active area of the tumor.

Statistical analysis using Pearson's χ^2 test was performed to correlate vascular features e.g. angiomatous proliferation, glomeruloid change and perivascular hyalinosis with age (≤12 years vs. >12 years), site (posterior fossa vs. non-posterior fossa) and hemosiderin deposition (absence vs. presence). Furthermore, the latter feature was also correlated with site of origin using similar statistical method.

Results

Incidence

A total of 3,286 intracranial tumors (ICT) were diagnosed at this center, between 1998 and 2002. Of this, 1,099 (33.4%) cases were glial tumors (GT) including 201 (6.1%) pilocytic astrocytomas. Of these, 120 cases (59.7%) in which slides and blocks were available were included in the present study.

There was mild variation in the incidence of PA and glial tumors during the study period, which ranged from 5-7% (mean 6.1%), and 32.3-35.6% (mean 33.4%), respectively. The ratio of PA and glial tumors during the same period was comparable, and ranged between 4.6:1 and 7.1:1 (mean 5.5) (*Table 1*).

Using Pearson's χ^2 test, no statistically significant change in the trend in incidence of PA was found in this center, during the study period.

Clinical features

Age and sex ratio: The age range for PA was 7 months to 81 years, with a mean, median and mode of 18.9 years, 10 years and 18 years, respectively. Most of the cases (61.7%) were in the age group ≤18 years, with 40.8% of the cases were under 12 years of age. The mean age of cases during each of the 5-year study periods ranged between 16.4 years and 20.2 years (*Table 1*). Cases included in the study showed a male preponderance (2.2:1).

Location: Posterior fossa was the commonest location (61.7%), while other affected areas included supratentorium (10.8%), optic nerve (6.7%), brainstem (5.8%), sellar/suprasellar area (5.8%), ventricles (5%) and spinal cord (4.2%).

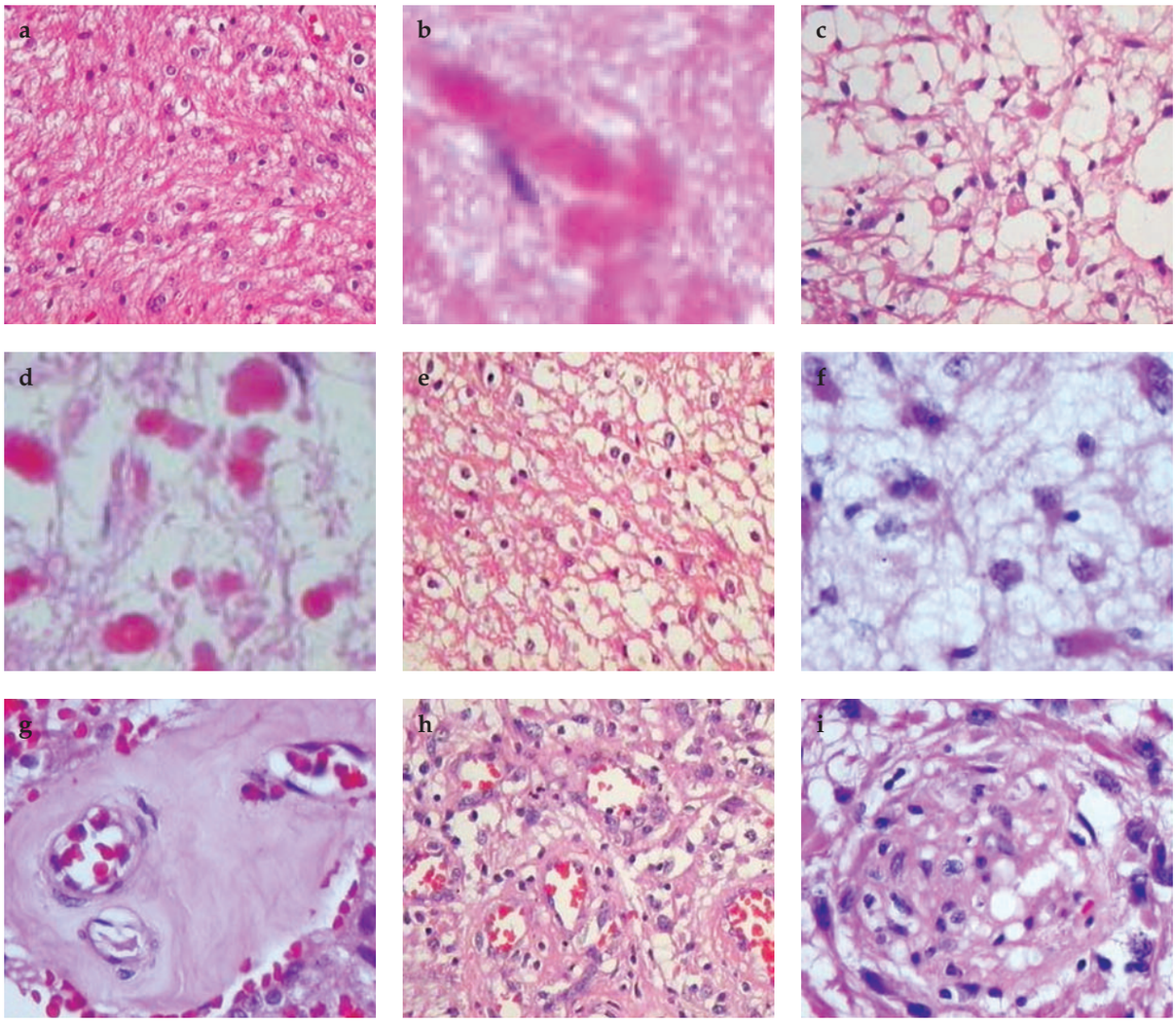

Figure 1. *Pilocytic astrocytoma characterized by biphasic architecture, composed of compact piloid areas (**a:** HE x200) containing Rosenthal fibers (**b:** HE x400), and loose microcystic component (**c:** HE x200) with interspersed eosinophilic granular bodies (**d:** HE x400). In many cases adjacent areas showed oligodendroglial component (**e:** HE x200), with few showing presence of minigemistocytes (**f:** HE x400). Vascular features were characterized by perivascular hyalinization (**g:** HE x400), angiomatous proliferation (**h:** HE x200) and glomeruloid change (**i:** HE x400).*

Histopathology

All biopsies showed an astrocytic tumor characterized predominantly by two organizational patterns, e.g. loose glial tissue reticulated by extensive cystic change, and dense piloid tissue *(Figure 1a)*. The latter were composed of islands or sheets of compact, elongated bipolar fibrillary piloid cells associated with Rosenthal fibers (beaded, sausage- to corkscrew-shaped hyaline bodies of varying sizes) *(Figure 1b)*. The loose-textured microcystic areas *(Figure 1c)* were composed of astrocytic cells with small cell body and relatively short, cobweb-like processes. These areas were typically associated with eosinophilic granular bodies (EGB) *(Figure 1d)*.

The majority (79 of the 120 cases, 89.2%) showed a characteristic biphasic pattern of PA, of which 20 biopsies displayed a predominance of microcystic areas, while 8 cases had predominance of the compact component. The remaining 13 cases (10.8%) were monophasic, of which 9 had compact architecture, while 4 were microcystic. In 19 cases, tissues adjacent to typical PA areas showed either oligodendroglioma-like foci (16 cases) *(Figure 1e)* or diffuse astrocytoma-like areas (3 cases). However, all these biopsies were considered as PA, since the coexisting changes were focal in nature.

Rosenthal fibers, characteristically associated with the compact areas, were present in 66.7% of cases. In 55

biopsies these were scant, while in 3 cases they were abundantly distributed. EGBs *(Figure 1d)*, typically present in the microcystic areas *(Figure 1f)*, were seen in 60% of cases.

The most prominent vascular changes were in the form of closely packed sclerotic vessels resembling a cavernous angioma, most of which (51.7%) showing perivascular hyalinization *(Figure 1g)*. Other vascular changes were identified as angiomatous proliferation (21.7%) *(Figure 1h)* with formation of a subluminal layer of hyperplastic capillaries in the cyst walls mimicking capillary hemangioma, and also as glomeruloid changes of vessels (21.7%) *(Figure 1i)*. Thirty-eight (31.7%) biopsies showed presence of hemosiderin-laden macrophages.

Other histological features apparent in these cases were the presence of nuclear atypia (31 cases) *(Figure 2f)*; chronic mononuclear inflammatory cell infiltrate affecting both parenchymal *(Figure 2a)* as well as perivascular areas (73 cases) *(Figure 2b)*, most of which were lymphocytes on IHC staining with anti-LCA antibody *(Figure 2c)*; multinucleated giant cells (25 cases) *(Figure 2g)*, cholesterol clefts *(Figure 2d)*, calcification (21 cases) *(Figure 2e)* and the presence of ganglion-like cells (5 cases). All these features suggested degenerative changes in long-standing lesions.

Evidence of mitotic activity was noted in 10 cases *(Figure 2h)*. In most cases these were focal and sparse [around 1-2 per 50 high-power fields (HPF)]. The exception was of

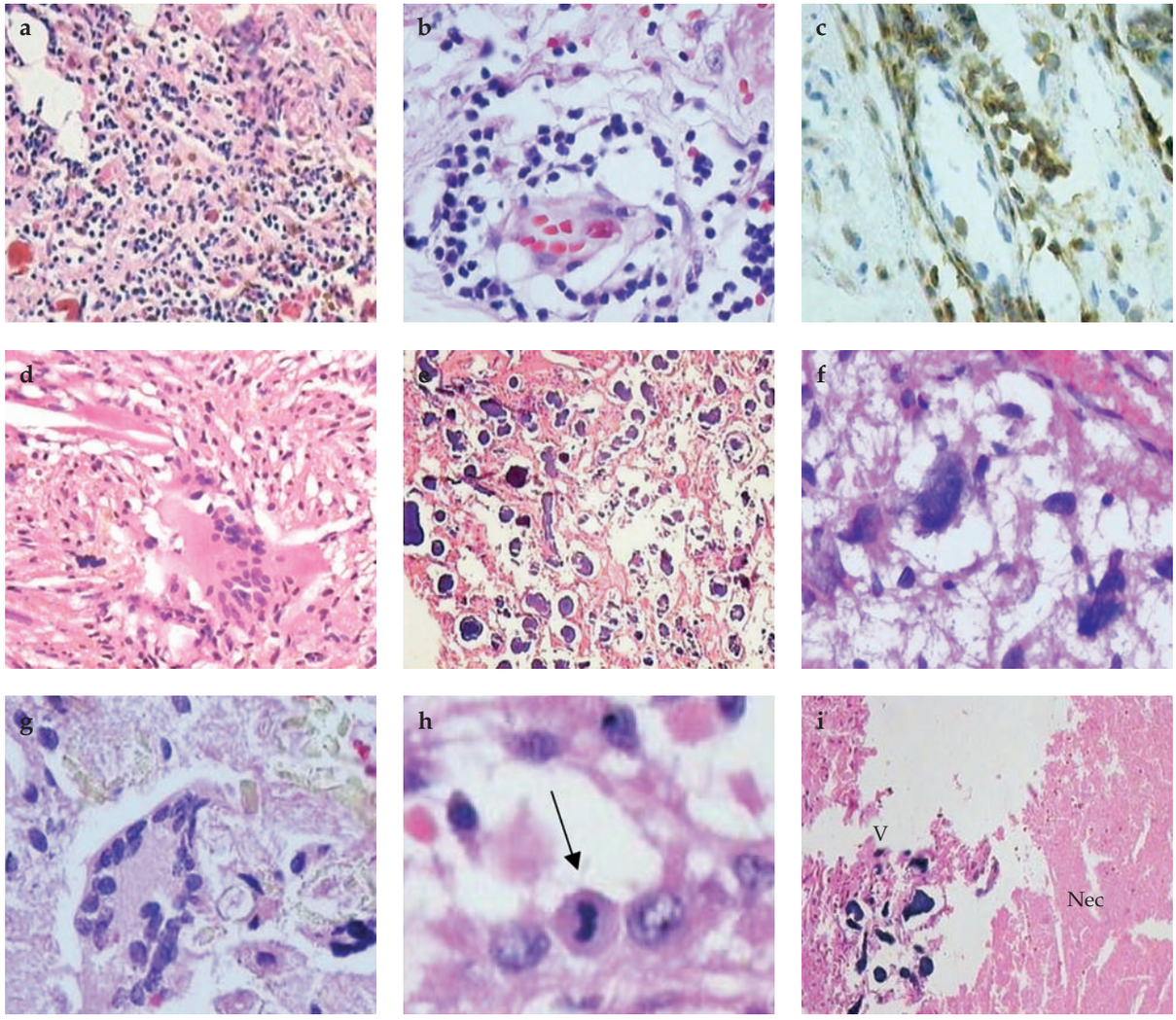

Figure 2. *Degenerative changes were marked by parenchymal (**a:** HE x200) and perivascular (**b:** HE x400) lymphocytes infiltration (**c:** LCA x400), with cholesterol clefts (**d:** HE x200) and calcification (**e:** HE x40). Occasional cases however showed nuclear pleomorphism (**f:** HE x400), with multinucleated giant cells with nuclei arranged in a 'pennies on a plate' fashion (**g:** HE x400), presence of mitotic activity (arrow) (**h:** HE x400) and necrosis (Nec : necrotic foci, V: viable area) (**i:** HE x100) .*

a tumor in a 32-year-old male, which showed abundant mitotic figures (5-6/50 HPF), along with necrosis and calcification, with absence of nuclear atypia and microvascular proliferation. Necrosis was also seen in the case of an 18-year-old male with recurrent cerebellar tumor, biopsy of which did not reveal any mitotic activity, nuclear atypia or microvascular proliferation. However, necrosis in both cases was infarct-like without associated perinecrotic palisading *(Figure 2i)*.

Statistical evaluation using Pearson's χ^2 test revealed a significant correlation between angiomatous proliferation and age (≤12 years vs. >12 years age groups) (p=0.011), and between hemosiderin deposition and angiomatous proliferation (p=0.006), perivascular hyalinization (p=0.035), or age (≤12 years vs. >12 years age groups) (p=0.028).

Discussion

Pilocytic astrocytomas (PAs) are slowly growing, well-circumscribed, often cystic tumors, corresponding to WHO grade I, which are generally associated with a favorable prognosis. They generally affect the pediatric age group[7] and constitute 10% of cerebral and 85% of cerebellar astrocytomas.

In the present series, PA constituted 6.1% of all intracranial tumors and 18.3% of all glial tumors during a 5-years study period, which was similar to the 5.5% incidence among 987 astrocytomas, in the 15-year population-based study conducted by Burkhard et al[8] in the canton of Zurich, Switzerland. However, these were considerably less as compared to the 18% noted by Rosemberg and Fujiwara[32] in their series of 1,195 tumors in children between 0 and 21 years of age, and the 23.5% observed by Rickert and Paulus[31] in their series of 340 primary CNS tumors in children under 17 years of age.

Though no clear evidence of increased incidence of PA among any racial or ethnic group is available,[17,29] some reports[17,23] have noted an increased incidence of PA among Caucasians as compared to black or Asian population. However, Ohgaki and Kleihues[29] have concluded that this may probably be a reflection of the differences in their socio-economic status and under-ascertainment in some regions, rather than a significant difference in genetic susceptibility.

The mean age of patients (N=120) included for assessment of histological spectrum was 18.9 years (range, 7 months-81 years), while the mean age of children ≤18 years (N=124) among the entire population of 201 PA cases diagnosed during the study period was 10.6 years (range, 5 months-18 years). This was in contrast to the 18 months mean age (range, 2-84 months) noted by Komotar et al[21] in their series on childhood PA (N=42).

PAs commonly occur in the first two decades of life,[6,19] with few cases being reported in the >30-year age group,[2,3] while occurrence beyond 50 years is exceptional.[4-6,16,18,19,25] However, in the current study 29 (14.4%) patients were in the >30-year, with 7 (3.5%) being in the >50-year age group. The rarity of PA in the >30-year age groups is highlighted by Bell et al[2] who noted 10 such cases during a 6-year period, with an incidence of 0.49 cases per million population per year.

Generally PA does not show any gender predilection.[6] However, a male preponderance (2.2:1, 68.7%) was noted in the present study, which was similar to the male predominance (64.2%) reported by Komotar et al,[21] but different from the mild female predominance (56%) noted by Machen and Prayson.[27]

PA has been reported to arise from various locations in the neuraxis, with preference for the optic nerve, optic chiasma, hypothalamus, cerebellum, brain stem, thalamus, basal ganglia and cerebral hemispheres.[6] In the present series posterior fossa (61.7%) was the commonest location, which was similar to that noted by Machen and Prayson.[27] Usually, spinal cord and brainstem are less frequent, but not uncommon, sites of occurrence.[6] However, with the refinement of available neurosurgical techniques, brainstem pilocytic astrocytomas are increasingly being resected.[1,23,33] The incidence of PA among brainstem gliomas ranges between 11%[1] and 52.6%.[33] In the current study 7 cases (5.8%) originated from the brainstem, while 5 cases (4.2%) affected the spinal cord. Though 8.3% of PAs reported by Machen and Prayson[27] affected the brainstem, none were localized to the spinal cord.

On histology, PA is typically identified by the classical biphasic pattern, composed of compact areas admixed with microcystic component. Though this dramatic and instantly recognizable biphasic pattern was present in the majority (89.2%) of the cases in this study, unfortunately it is identified in only a minority of cases[7] and is not essential to the diagnosis of PA. Further, biopsies displaying monophasic pattern (present in 10.8% biopsies in the present series), or showing predominance of the compact or microcystic component of biphasic pattern, may resemble diffuse astrocytoma, and differentiating the two may become increasingly difficult. This diagnostic dilemma may be further compounded by unusual clinicopathological features, e.g. older patients (beyond the second decade), unusual location (brainstem or spinal cord), and uncommon histology (necrosis, mitoses, nuclear pleomorphism, vascular proliferation).

Although the presence of Rosenthal fibers and EGB are useful histological parameters for the identification of PA, these are not absolute. Rosenthal fibers, occurring principally in compact areas, may be scant to abundant in distribution. Although these are easily identified on H&E stain, Masson trichrome or Luxol fast blue staining may be required for better visualization. Rosenthal fiber-rich areas are a common feature of long-standing piloid gliosis asso-

ciated with craniopharyngioma in the hypothalamus and cyst wall of cerebellar hemangioblastoma, and thus are not diagnostic of PA. Similarly, the PAS-positive EGB or 'protein droplet' may also be seen in association with gangliooglioma and pleomorphic xanthoastrocytoma, and serve as markers of slow-growing, low-grade, prognostically favorable neoplasm. In the present study Rosenthal fibers and EGB were present in 66.7% and 60% cases respectively, while Machen and Prayson[27] and Forsyth et al[12] noted a higher incidence of 83.3% and 76%, and 75% and 74%, respectively. A semiquantitative scoring of Rosenthal fibers, on a 1+ (scant) to 3+ (abundant) scale, found the majority of cases (68.8%) to be 1+ while only 3 cases had a scoring of 3+.

The histologic parameters that are conventionally assessed during evaluation of an astrocytic tumor are nuclear pleomorphism, mitotic activity, vascular proliferation and necrosis, features associated with more aggressive behavior. Focal nuclear changes like hyperchromasia or multinucleated cells with nuclei arranged in a 'pennies on a plate' fashion, identified in 25.8% and 20.8% cases respectively, can be seen in PA, and are generally considered as degenerative changes, with no prognostic significance.[7,27] These changes are generally seen in 'older' individuals, i.e. those >25 years of age, in conjunction with other histological features like vascular hyalinization, hemosiderin-laden macrophages and chronic inflammation,[7] which were present in 51.7%, 31.7% and 60.8% cases, respectively. Further corroborative evidence for PA in such cases may be evident from a review of the clinical profile, radiological images, and histologic evidence of vascular hyalinization along with lack of proliferative activity.[7]

One may also encounter occasional mitotic activity or tumor cell necrosis, as seen in 8.3% and 1.7% cases in this study. Solitary mitotic figures (1-2/50 HPF), as seen in this series, may be seen in approximately 30% of PA.[13] Necrosis may be present in up to 10.4% of all PA,[7,26] but these are generally infarct-like, and associated with low proliferative activity and lack of perinecrotic palisading,[7] similar to that observed in the current series. Generally these patients have a history of recent surgery or radiotherapy, and do not have a poor outcome.

The standard grading system applicable for fibrillary astrocytomas seems to be misleading in PA and should not be done.[26] PAs generally begin and remain as grade I lesions, with rare cases necessitating descriptors like 'atypical' and 'malignant',[7] when worrisome histological features like necrosis, mitoses and vascular proliferation are encountered. PA is designated as 'atypical' when seen in conjunction with nuclear atypia and increased cellularity, although no clinical significance could be elucidated.[32] The term 'malignant' has been reserved for the rare cases where mitotic figures are expressed per high power fields, in association with microvascular proliferation with or without necrosis. To date, no consensus has been reached regarding the utility of grading and criteria on which it should be based. Though 3 of the 10 cases displaying focal mitotic activity were associated with presence of nuclear atypia, and qualified as 'atypical' PA, none fitted the description of 'anaplastic' PA described by Tomlinson et al.[33]

Pilomyxoid astrocytoma (PMA) is a recently described type of brain neoplasms, sharing similar features with PA.[10,21-23] It remains controversial whether this represents an aggressive variant of classical PA or is an entirely distinct clinicopathological entity. When compared with the typical biphasic histology of PA, this neoplasm demonstrates small, compact, piloid, and highly monomorphous cells in a loose fibrillary and markedly myxoid background, without Rosenthal fibers or EGB, both characteristic of PA. Tumor cells are often arranged radially around vessels in a pattern that resembles the perivascular rosettes seen in ependymomas. Rare mitotic figures may be seen occasionally. Furthermore, PMA may be responsible for the clinical variability associated with PA. Thus it is imperative that in the absence of classical histology in PA, cases should be assessed for PMA, for accurate diagnostic classification and prognosis. However, none of our cases showed histology compatible with PMA.

Vascular changes associated with PA are seen either as vascular hyalinization where closely packed sclerotic vessels resemble cavernous angioma,[7] or occasionally as microvascular proliferation. The latter is typically glomeruloid in pattern, forming a subluminal layer of hyperplastic capillaries in cyst walls. This pattern is more common in PA, although in isolation should not prompt a diagnosis of high-grade neoplasm. The other form of microvascular proliferation, hyperplasia of endothelial cells within larger vessels, is rarely seen in PA. In the current series, vascular changes were seen as perivascular hyalinization (51.7%), angiomatous proliferation (21.7%) and glomeruloid changes (21.7%). Statistical evaluation revealed a significant correlation between angiomatous proliferation and age (≤12 years vs. >12 years age groups) or hemosiderin deposition. Machen and Prayson[27] noted vascular hyalinization and proliferation in 56.2% of cases each. Hemosiderin-laden macrophages were present in 31.7% biopsies, which showed a significant statistical correlation with angiomatous proliferation, perivascular hyalinization and age (≤12 years vs. >12 years age groups).

The presence of mononuclear inflammatory cell infiltration was another important histological feature of pilocytic astrocytoma observed by most investigators.[7,14,27] Gilles et al[14] have noted parenchymal and perivascular lymphocytic infiltrates as distinctive histological features which were more likely to be observed in older children. Machen and Prayson[27] noted focal chronic inflammation (predomi-

nantly lymphocytes) in 71% of cases, while in the current series it was observed in 60.8% of biopsies. Though this has been described as a feature suggestive of senescence,[7] the exact role of these cells in tumor immunology and their significance in relation to tumor progression and response to therapy needs further evaluation.

Although a minority of PA undergoes calcification,[7] suggesting chronicity of the lesion, Machen and Prayson[27] noted this in 29.2% of biopsies, while it was present in 17.2% of cases in this study. Gilles et al[14] noted parenchymal calcification more among older children, while Philipson et al[30] observed calcification and ossification in a case of PA involving spinal nerve root in a 39-year-old woman. Dierssen et al[11] also described extensive calcification in a case of pontine PA. Maruyama et al[28] and Lee et al[24] reviewed the CT and MR characteristics of juvenile pilocytic astrocytomas and noted tumor calcification in occasional cases.

Ganglion-like cells have been noted in 5 cases, all of which were located in the cerebellum. It has been suggested that these, generally affecting cerebellar PA, are either entrapped normal neurons, possibly Purkinje cells, or neurons of the dentate nuclei. Controversy arises when these are dysmorphic and constitute part of the neoplasm, in which case these should be considered as gangliogliomas instead of PA.[7]

Occasionally areas adjacent to classical PA foci may display oligodendroglial or diffuse astrocytoma component[6,19] as seen in 16 and 3 cases, respectively in the present series. Recently Kan et al[18] reported a rare case of frontal oligodendroglioma coexisting with cerebellar juvenile pilocytic astrocytoma. Molecular analysis, however, detected deletion of chromosome 1p36 in the former component only.

Although pilocytic astrocytoma is a common tumor in children, located in the posterior fossa, and has a classical radiological appearance with a typical histomorphology, diagnostic dilemma on resected specimen can often arise either if the biopsy is small and not representative, or if it lacks the classical compact and microcystic architecture, Rosenthal fibers and EGB. Owing to the differences in prognosis and therapeutic options, it needs to be differentiated from diffuse astrocytoma. Generally a radiological correlation is imperative where one looks for contrast enhancement unassociated with perilesional edema, as well as presence of a cystic component, as features of PA.[9]

Pilocytic astrocytoma may histologically mimic other discrete, contrast-enhancing neoplasms like ganglioglioma (GG) or pleomorphic xanthoastrocytoma (PXA). Though GG may show microcystic areas with Rosenthal fibers and EGBs, its distinctive feature lies in the dysmorphic neurons which are immunopositive for neurofilament. PXA on the other hand is distinguished by the presence of increased cellularity, marked pleomorphism, partially fascicular structure, reticulin-rich morphology, perivascular lymphocytes and lack of Rosenthal fibers and perivascular hyalinization or glomeruloid vascular proliferation.[6,7]

Monophasic PA may often resemble diffuse astrocytoma, especially if it lacks Rosenthal fibers and EGBs. In such cases radiology plays a vital role, where a tumor with a cystic component along with contrast enhancement unassociated with perilesional edema generally supports the diagnosis of PA. On histology it generally lacks the cellular pleomorphism and has less even distribution of nuclei as seen in diffuse astrocytoma. However, in the presence of vascular proliferation and necrosis PA may resemble glioblastoma multiforme (GBM), distinction from which bears definite therapeutic and prognostic connotation. In such situations vascular features of the tumor play an important role in differentiating the two entities. Vascular changes in PA are usually in the form of glomeruloid proliferation and less often as proliferation of endothelial cells within large vessels, unlike GBM which is generally associated with the latter type.[6,7]

Apart from mimicking neoplasms, PA frequently needs to be distinguished from areas of piloid gliosis, owing to their dense fibrillary morphology associated with Rosenthal fibers. These are generally found in the cerebellum around hemangioblastoma and around long standing PA, around craniopharyngiomas in the hypothalamic regions, and also around subpial zone around any chronic lesions. Piloid gliosis is a reactive process which on histology lacks the microcystic component and vascular changes of PA.[6,7]

This study highlights that apart from low mitotic activity and absence of necrosis, vascular changes like angiomatous proliferation, glomeruloid changes and perivascular hyalinization, along with hemosiderin-laden macrophages and perivascular lymphocytic infiltration should be considered as surrogate diagnostic features of PA. These features in conjunction with collateral clinical, histologic and imaging parameters may facilitate diagnosis and guide subsequent management protocol, especially in a setting of uncommon location, older age group and small fragmented biopsies.

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