IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 15, Issue 3 Ver. VI (Mar. 2016), PP 53-56
www.iosrjournals.org

Spontaneous Anaplastic Transformation in Cerebellar Pilocytic Astrocytoma: A Case Report and Review Of Literature.

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Abstract: *Pilocytic atrocytoma(PA) is a World health organization (WHO) grade I astrocytoma. It most commonly develops during first two decades of life with predilection for infratentorial region. The tumor shows a favorable behavior and patients usually have excellent long term improvement. Histologic progression and features of anaplasia is a rare event in pilocytic astrocytomas and is commonly seen with the history of radiation and is associated with aggressive behavior. Malignant or anaplastic pilocytic transformation has only been mentioned in the WHO classification of CNS tumors, however it has not been assigned a grade. Nevertheless, the literature has a number of case reports and few series which describes definite anaplastic transformation in PAs. We herein report a rare case of progression of anaplasia within 11months of primary diagnosis without antecedent radiotherapy.*

Keywords: *Pilocytic astrocytoma, Anaplastic transformation, radiotherapy*

I. Introduction

Pilocytic atrocytoma(PA) is a World health organization (WHO) grade I astrocytoma. It most commonly develops during first two decades of life with predilection for infratentorial region. The tumor shows a favorable behavior and patients usually have excellent long term improvement. Though histologic progression of grade II tumors, which is also grouped in as low grade glioma, to higher grades of anaplasia is well known phenomenon with clear mapping of the temporal genetic and molecular events, the same is quite rare event with grade I tumors, especially pilocytic astrocytomas. Histologic progression and features of anaplasia is a rare event in pilocytic astrocytomas and is commonly seen with the history of radiation and is associated with aggressive behavior.[1, 2, 3] We herein report a rare case of progression of anaplasia within 11months of primary diagnosis without antecedent radiotherapy.

II. Case Report

A 20 year old male presented in October 2011 with occipital headache, visual blurring, vomitings and gait ataxia for a duration of 15 days. Neurological examination revealed pailledema and right cerebellar signs. There were no cranial nerve deficits. CT scan of brain revealed a 3x4x4 cm, hypodense lesion in the vermian region extending into the right cerebellar parenchyma, with a speck of calcification and nonvisualisation of the fourth ventricle. There was peripheral enhancement of the lesion on contrast administration. Magnetic resonance imaging (MRI) of brain revealed a lesion of size 3x4x4 cms occupying the cerebellar vermis and right lobe, hypointense on T1, hyperintense on T2W images, squashing the fourth ventricle. On Gadolinium contrast T1W images the lesion had a heterogeneously enhancing solid and peripherally enhancing cystic lesion (Figure 1). A suboccipital craniectomy and near total excision of the lesion was performed. Peroperatively the lesion was soft to firm, moderately vascular, nonsuckable with no clear plane of gliosis from the surrounding cerebellum. The lesion was seen entering the middle cerebellar peduncle and was left back. The postoperative period was uneventful.

The histopathology showed a characteristic biphasic pattern with occasional granular bodies and Rosenthal fibers. Part of the tumor showed oligodendroglial areas. The Ki67 labelling index was 1%. The morphologic features were consistent with a diagnosis of pilocytic astrocytoma. Lost to followup, the patient landed in the emergency department after eleven months, in altered sensorium and huge swelling in the suboccipital region. The MRI showed recurrence of tumor measuring 5x5x4cms extending upto the tentorium, and the subcutaneous region through the post-operative bony defect causing compression of the fourth ventricle. The lesion was hypointense on T1 and hyperintense on T2W images with heterogenous, brilliant enhancement of the tumor. Re-exploration and gross total excision was performed on emergency basis.

Histopathology:

The histopathology sections showed varied morphologic features. A part of the tumor showed characteristic features of pilocytic astrocytoma with many Rosenthal fibers and eosinophilic granular bodies (EGBs). However the rest of the tumor showed marked hypercellularity with brisk mitosis. Palisading necrosis and microvascular proliferation was seen. The Ki67 labelling index was 40%. The cells showed strong positivity for GFAP and weak p53 nuclear expression was seen in more than 50% of cells. These features were consistent with anaplastic change in pilocytic astrocytoma. The patient developed hydrocephalus and a ventriculoperitoneal shunt was placed. The patient was further referred for radiotherapy and is doing well on eight months of postsurgical follow up.

III. Discussion

Pilocytic astrocytoma is a WHO grade I type of circumscribed astrocytoma. The 5 and 10 year survival rates are more than 95% after surgical resection alone. [4, 5] Malignant or anaplastic pilocytic transformation has only been mentioned in the WHO classification of CNS tumors however has not been assigned a grade. [10] Nevertheless, the literature has a number of case reports and few series which describes definite anaplastic transformation in PAs. [1-3,7-10] The published literature on this entity spans a long period with the earliest report by Alpers et al.[11] Most of these reports have mentioned presence of hypercellularity, brisk mitotic activity and or presence of palisading necrosis as the defining features of anaplasia in pilocytic astrocytoma. However the exact mitotic count has not been mentioned. Areas resembling the classic PA with EGBs and Rosenthal fibers are must for diagnosis of anaplastic PA particularly for tumors without a precursor lesion. Rodriguez et al [10] has published a largest case series including 34 cases. There was male predominance; cerebellum being the most common location. Eleven percent of these were irradiated for a precursor lesion. The median interval from the original diagnosis was 14 years with a range of 4 months to 40 years. Diffuse fibrillary astrocytomas require presence of atleast more than one mitosis to upgrade to anaplastic astrocytoma and presence of palisading or geographic necrosis is equated to glioblastoma. Unlike this the anaplastic PAs can show areas of pseudopalisading necrosis. Rodriguez et al have mentioned a cut of mitotsis of 4/10 hpf to distinguish conventional WHO grade I PA from anaplastic PAs.[10] So was the case in our patient where mitotic activity was 6/10 hpf with areas of necrosis. PA with anaplastic features with necrosis tend to behave like a grade 3 astrocytomas.

The importance of MIB-1 labelling indices in deciding outcome is not well established. The value of more than 2% is known to have shortened progression free survival in partially resected tumors. Rodriguez has mentioned median index of 24.7% in anaplastic component however the association with survival is not discussed. The conventional PAs usually do not show p53 expression. However the anaplastic component has consistently shown weak or strong expression of p53. [10,12] similarly the tumor in our patient also showed expression of p53 in more than 50% of the tumor cells. Stuer et al [13] has mentioned that anaplastic transformation occurs more frequently in adult patients. Similarly, most of the patients in published reports were also adults. Rodriguez et al has shown a median age group of 35 years. This is in keeping with the findings of our patient (20 years).

History of irradiation is a important finding in majority of these patients commonly in cerebellar PAs. Zoeller et al [14] has reported a single case of optic pathway PA with anaplastic transformation without prior irradiation**.** Radiation is an established cause of anaplastic transformation in diffuse astrocytomas and benign tissues following DNA mutations. [14] Tomlinson et al [13] has reported that incidence of spontaneous malignant transformation was seen in 0.9% whereas radiation was the factor in 1.8%. Contrary to this, Rodriguez et al [10] found prior irradiation in only 11% of cases. The biologic behavior of anaplastic PAs induced after irradiation is different from the denovo or spontaneous anaplasia. Prior irradiation is known to confer poor prognosis to these patients. Apart from the diagnostic issues, anaplasia in PA is now established as a definite marker of aggressive behavior in these tumors. Prior irradiation, necrosis and increased mitosis are supposed to confer shorter survival. Thought the patient in our study did not have previous irradiation, a close clinical follow up is required along with chemoradiotherapy.

IV. Conclusion

This is an addition of a rare case of cerebellar anaplastic astrocytoma without prior irradiation to the existing literature. Anaplastic transformation of a pilocytic astrocytoma must be kept in mind in case of recurrence of tumor following near total excision, notwithstanding antecedent radiotherapy.

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Legends:

Figure1- Preoperative images showing a hypodense lesion in the right side of the cerebellum with nonvisualisation of the fourth ventricle, enhancing peripherally on the contrast CT Scan axial images (A,B). MR imaging shows a heterogenous lesion hypointense on T1W images (C), hyperintense on T2W images (D), with heterogenous contrast enhancement depicting a solid-cystic lesion (E,F).

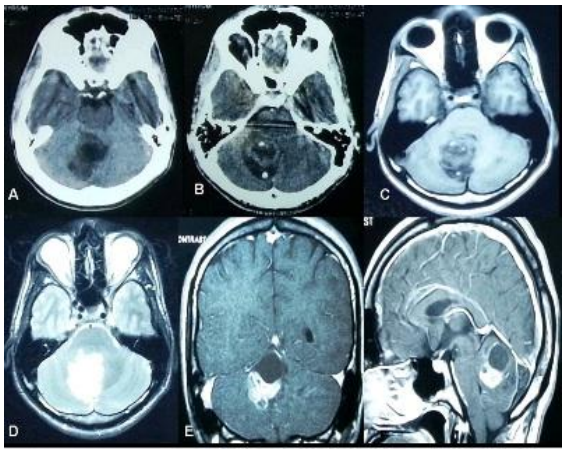

Figure 2- Postoperative MR imaging (at recurrence) a lesion in the right lobe of cerebellum, extending from the tentorium superiorly till the foramen magnum, dorsally into the subcutaneous tissue, heterogeneously hypointense on T1W, hyperintense on T2W and FLAIR images, demonstrating enhancement with contrast administration.

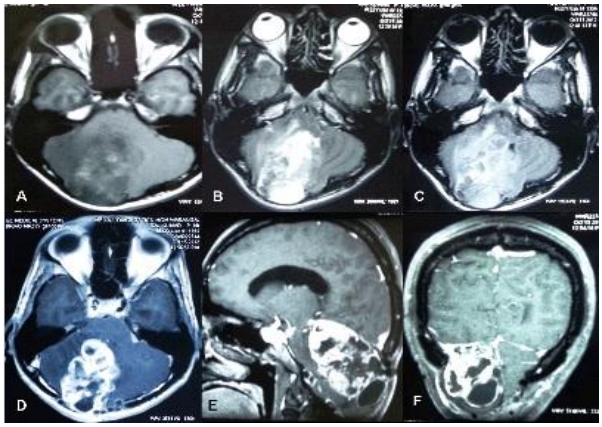

Figure 3: The microphotograph of the primary tumor showing (A,B) the characteristic biphasic pattern with EGBs. The recurrent tumor showing increased mitosis with high Ki67 as inset (C), Areas showing palisading necrosis and endothelial proliferation (D, E). Focal perivascular pseudorosettes (F).