Int J Clin Exp Pathol 2012;5(5):458-462
www.ijcep.com /ISSN: 1936-2625/IJCEP1203006

Case Report

Giant cell ependymoma-report of three cases and review of the literature

Jian Yi Li[1], Jose I Lopez[2], Suzanne Z Powell[3], Stephen W Coons[4], Gregory N Fuller[5]

[1]Department of Pathology and Lab. Medicine, North Shore and Long Island Jewish Health System, Lake Success, Hofstra North Shore-LIJ School of Medicine, NY, USA; [2]Department of Pathology, Hospital Universitario de Cruces, The University of the Basque Country (UPV/EHU), Barakaldo, Bizkaia, Spain; [3]Department of Pathology and Genomic Medicine, The Methodist Hospital, Houston, TX, USA; [4]Division of Neuropathology, Barrow Neurological Institute, Phoenix, AZ, USA; [5]Department of Pathology, The Univ. of Texas, M. D. Anderson Cancer Center, Houston, TX, USA

Received March 11, 2012; accepted April 21, 2012; Epub May 5, 2012; Published June 30, 2012

Abstract: Ependymomas constitute the most common type of primary spinal cord tumors, and are subclassified as myxopapillary ependymoma, classic ependymoma, and anaplastic ependymoma. Ependymomas can be further subclassified based on morphologic phenotype: cellular, papillary, tanycytic, clear cell, pigmented and epithelioid. Giant cell ependymoma (GCE), a rare variant, has recently been described. Reported cases have exhibited a wide anatomic distribution, including spinal cord, cerebrum and cerebellum. We report here three cases of GCE, arising from cerebrum in a 5-year-old girl, spinal cord in a 34-year-old female and cerebellum in an 86-year-old female respectively. Histologically those cases showed prominent pleomorphic giant cells with focal perivascular pseudorosettes in all cases. Tumor cells were immunopositive for GFAP and EMA. Only the first case was qualified for anaplastic ependymoma. No recurrence was noted in these three cases after 57, 46 and 6 months of follow-up respectively. By reviewing the literature, GCEs arising from spinal cord and cerebellum tended to have low-grade morphology while supratentorially located GCEs tended to have anaplastic features. GCEs were preferentially located in extraventricular regions. Anaplastic GCEs in adult population seemed to pursue a more aggressive behavior. Gross total resection should still be the main treatment for GCEs.

Introduction

Ependymomas are slow growing tumors of children and young adults, which account for 3-9% of all neuroepithelial tumors. Ependymomas are the most common primary intramedullary spinal cord neoplasms, accounting for 50 to 60% of spinal cord gliomas [1]. They consist of myxopapillary ependymoma (WHO grade I), classic ependymoma (WHO grade II), and anaplastic ependymoma (WHO grade III). WHO grade II ependymomas have four variants: cellular, papillary, tanycytic and clear cell [1]. Since the extent of tumor removal is the most significant prognostic factor for long-term survival, the gross total resection should be the primary treatment goal. In 1996, the first two cases of giant cell ependymoma of the filum terminale were described by Zec et al [2]. In recent years, another 17 cases of giant cell ependymoma have been reported, which were located in spinal cord, cerebrum and cerebellum [3-17]. We report three cases of giant cell ependymoma (GCE) arising from cerebrum, spinal cord and cerebellum respectively. To our knowledge, this represents the largest case serials of giant cell ependymomas.

Case report

Case 1

A 5-year-old girl with a history of headache and left side weakness. The Magnetic resonance imaging (MRI) showed an extraventricular heterogeneously enhanced solid and cystic mass in the right parietal lobe (**Figure 1**). The gross total resection was achieved. The histologic diagnosis was anaplastic ependymoma, WHO grade III (**Figure 1**). No recurrence was noted after 57

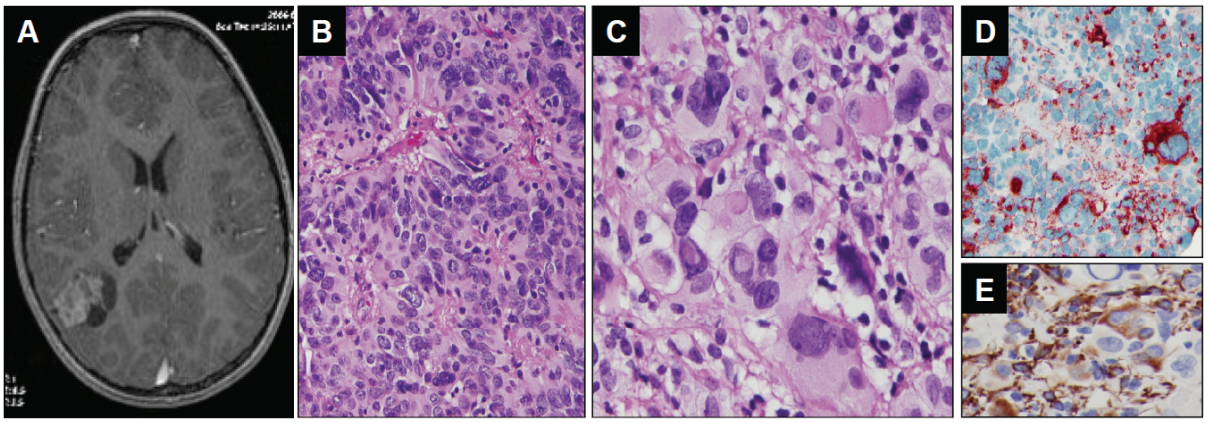

Figure 1. Neuroimaging and histological findings of the tumor from case 1. A. Axial gadolinium-enhanced T1-weighted MRI image demonstrated a heterogeneously enhanced solid and cystic mass in right parietal lobe. B. Perivascular pseudorosette (Hematoxylin and eosin 200X). C. The giant cell with eosinophilic cytoplasm, eccentrically located single or multiple nuclei with prominent nucleoli, and intranuclear cytoplasmic inclusions (Hematoxylin and eosin, 400X). D. EMA immunohistochemical stain showed perinuclear dot-like or ring pattern. E. GFAP immunohistochemical stain showed positivity of tumor cells.

months of follow-up.

Case 2

A 34-year-old female with a history of tingling and numbness in the right side of body and with recent progressive weakness in the right side of body. The MRI showed well-defined, slightly T1-hypointense, intramedullary enhancing lesion of the cervical spinal cord. T2-weighted imaging revealed a cystic caudal region with both rostral and caudal parenchyma edema. The gross total resection of the tumor was performed. The histologic diagnosis was ependymoma, WHO grade II (**Figure 2**). There was no recurrence after 46 months of follow-up.

Case 3

An 86-year-old female with a history of vertigo and abnormal gait. The MRI showed a heterogeneously enhancing solid and cystic lesion in the right cerebellum hemisphere. The tumor was grossly totally resected. The histologic diagnosis was ependymoma, WHO grade II (**Figure 2**). No recurrence was seen after 6 months of follow-up.

All cases showed prominent pleomorphic giant cells with abundant eosinophilic cytoplasm and distinct cell borders (**Figure 1** and **2**). Typical perivascular pseudorosettes were seen focally in all cases. Focal ependymal epithelial surfaces were identified in the case 3. There were strong cytoplasmic positivity for GFAP and perinuclear dot-like immunopositivity for EMA in tumor cells for all three cases (**Figure 1**). The case 1 exhibited hypercellularity, increased mitotic activity, including the presence of atypical bizarre mitotic figures, and florid microvascular proliferation, consistent with anaplastic ependymoma (WHO grade III).

Discussion

In present report, we described three ependymal tumors with abundant giant cells with focal perivascular pseudopapillary pattern. Giant cell glioblastoma, pleomorphic xanthoastrocytoma (PXA), subependymal giant cell astrocytoma (SEGA), and atypical teratoid/rhabdoid tumor (AT/RT) should be considered in the differential diagnosis on the H&E sections. Giant cell glioblastoma, the major differential diagnosis, is characterized by prominent micovascular proliferation and pseudopalisading necrosis [18]. Those features did not present in all our cases. PXA is composed of pleomorphic astrocytic cells and occasional lipdized cells with perivascular lymphocytic infiltration and prominent eosinophilic granular bodies [18]. PXA usually occurs in the superficial location of cerebrum with frequent meningeal involvement. SEGA is almost exclusively associated with tuberous sclerosis and also located around the lateral ventricle. Well-formed perivascular pseudorosette usually

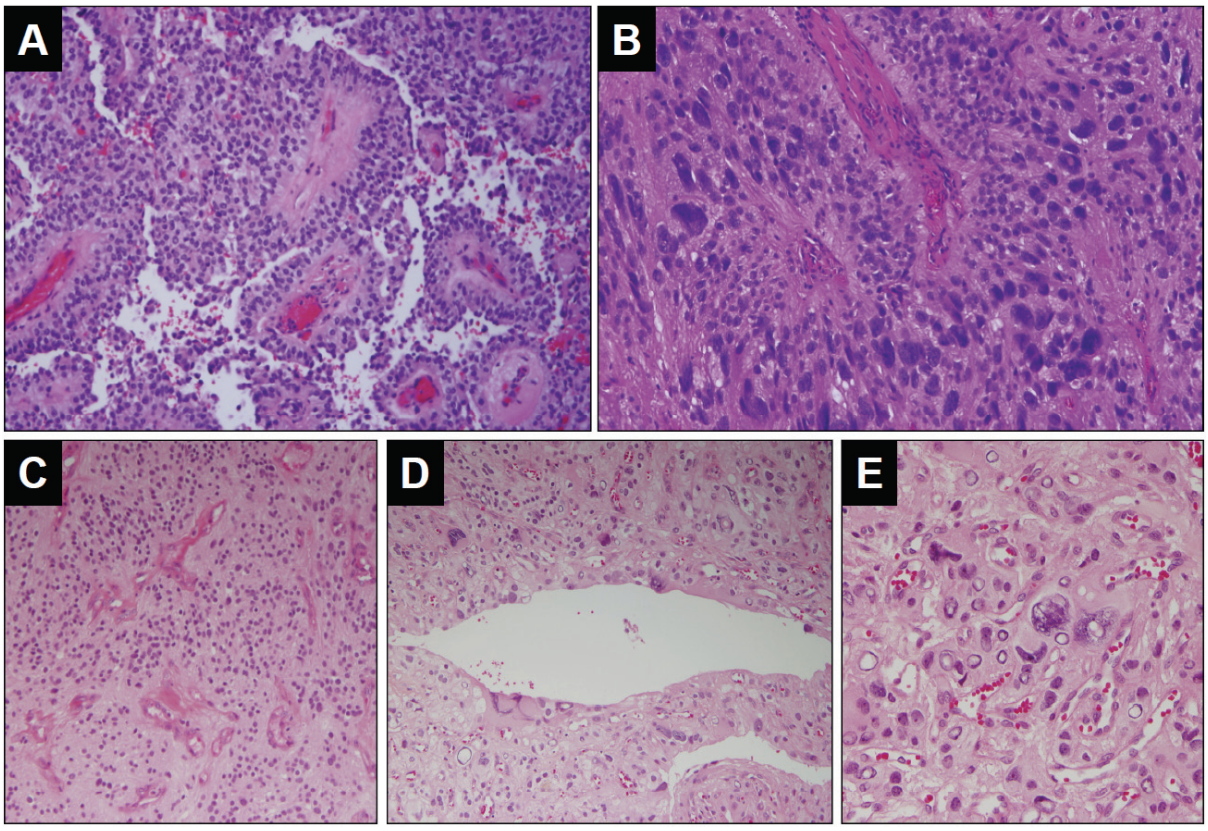

Figure 2. Histological findings of the tumor from case 2 and case 3. A-B for case 2: A. Low power view of perivascular pseudorosette and pseudo-papillary structure (Hematoxylin and eosin 200X). B. Perivascular pseudorosette formed with pleomorphic tumor cells (Hematoxylin and eosin, 400X). C-E for case 3: C. Low power view of perivascular pseudorosette in well-differentiated area of this tumor (Hematoxylin and eosin 100X). D. Ependymal epithelial surfaces formed with pleomorphic tumor cells (Hematoxylin and eosin, 200X). E. Pleomorphic giant tumor cells. (Hematoxylin and eosin, 400X).

does not present in SEGA [19]. In the third case, there were focal rhabdoid cells, raising the possibility of AT/RT. The immunohistochemical stain for INI1 was performed and demonstrated diffuse immmunoreactivity of tumor cells to INI1 antibody. Typically AT/RT tumor cells are negative for INI1 [20, 21]. In our three cases, tumor cells were strongly positive for GFAP, and prominent EMA positivity was present in perinuclear dot-like and ring patterns, diagnostic of ependymoma.

Besides our present three cases, 18 cases of giant cell ependymoma have been described in the literature [2-17]. Five out of 21 (23.8%) cases occurred in children and 16 out of 21 (76.2 %) occurred in adult. The median age of these 21 patients was 34 years ranging in age from 5 to 89 years. The male to female ratio was 1.1:1 (**Table 1**) [2-17]. The clinical presentations were non-specific and depended on the location of tumor. Ten out of 21 cases (47.6 %) were located in spinal cord. Six cases occurred at cervical spinal cord, two at thoracic spinal cord and two at filum teminale. Seven out of 21 cases (33.3%) were supratentorially located. Two cases occurred in temporal lobe, and one in frontal lobe, parietal lobe, occipital lobe, temporo-parietal lobe and suprasellar region respectively (**Table 1**). All supratentorial giant cell ependymomas were originated at extraventicular regions. Only one case occurred in the frontal lobe and extended to the lateral ventricle. Four out of 21 cases (19.1%) occurred in cerebellum (Three were extraventricular while one was in the 4th ventricle) (**Table 1**) [2-16]. Fifteen out of 21 cases (71.4%) had low grade (WHO grade II) histology, among which eight were arising from spinal cord; four from cerebellum and one from fourth ventricle [2, 6, 8-13, 16, 17].

Table 1. Clinical and pathologic features of giant cell ependymomas

Age	5-89 years (median =34 years)
Sex	11 male : 10 female (ratio = 1.1:1)
Location	Spinal cord : 10 cases (6 at cervical spinal cord, 2 at filum teminale, and 2 at thoracic spinal cord) Supratentorial: 7 cases (2 in temporal , 1 in frontal, 1 in parietal, 1 in occipital, 1 in temporo-parietal and 1 in suprasellar region) (All are extraventricular and 1 extends to the lateral ventricle) Cerebellum: 4 cases (3 are extraventricular and 1 in 4th ventricle)
WHO grade	WHO grade II: 15 cases WHO Grade III: 6 cases
Treatment	Gross total resection in 17 cases and subtotal resection in one case Radiation therapy for 3 cases after surgery Chemotherapy and radiation therapy for 3 cases
Follow-up time and prognosis	1.5-35 months (median = 7 months) 5 patients had recurrence (4 WHO grade III and 1 WHO grade II) 1 patient died of anaplastic ependymoma (WHO grade III) 1 patient with WHO grade II ependymoma died of surgical complication

Six cases out of 21 cases (28.6%) had anaplastic features (WHO grade III), among which five were arising from the cerebrum and one from cerebellum [3-5, 7, 15]. Five out of seven supratentorial giant cell ependymomas were high grade tumors [3-5, 15].

Besides one autopsy case, seventeen patients were underwent gross total resection and one case underwent subtotal resection [2-16]. Three anaplastic ependymoma cases were treated with radiation therapy after gross total resection [3, 4, 15]. Two anaplastic ependymoma cases and one supratentorial ependymoma case were treated with the combination of chemotherapy and radiation therapy after surgery [5, 7, 10]. Eighteen cases have been followed-up ranging from 1.5 to 57 months with the median of 15.5 months [2-10, 12-16]. Five patients with anaplastic ependymoma and one patient with WHO grade II ependymoma developed recurrent tumor [3, 5-7, 15]. The patient with anaplastic ependymoma in the temporal lobe died of disease after 20 months of follow-up even though she was treated with gross total resection, and the combination of radiation and chemotherapy [5]. One of two patients with ependymoma (WHO grade II) in the thoracic spinal cord died of complications after surgery [13].

Giant cell ependymomas arising from spinal cord (all cases 100%) and cerebellum (3 out of four cases, 75%) tended to have low-grade morphology [2, 6-9, 11, 13, 14, 16, 17]. GCEs arising from supratentorial locations (5 out of 7 cases, 71.4 %) tended to have anaplastic features [3-5, 10, 12, 15]. Anaplastic GCEs in general had a higher chance to recur compared to WHO grade II GCEs. However, two suparatentiorial anaplastic GCEs in children had no recurrence after 46 and 57 months of follow-up respectively. Although the majority of patients with anaplastic ependymoma were treated with radiation therapy with/without chemotherapy after surgery, gross total resection should still be the treatment of choice for GCEs.

In conclusion, we report here three cases of GCE, which occurred in cerebrum, spinal cord and cerebellum respectively. These tumors have prominent pleomorphic giant cells as well as focal ependymal differentiation. Their ependymal origin is confirmed by immunohistochemistry. By reviewing all published cases, extraventricular regions of cerebrum and cerebellum are the preferential location for GCEs. GCEs in spinal cord and cerebellum tend to be WHO grade II morphology while supratentorially located GCEs tend to have anaplastic features. Anaplastic GCEs in adult population most likely have a more aggressive behavior. Gross total resection still remains as the first line treatment for GCEs.

Address correspondence to: Dr. Jian Yi Li, Department of Pathology and Lab. Medicine, North Shore-Long Island Jewish Health System, 6 Ohio Drive, Suite 202, Lake Success, NY 11042, USA Tel: +1 516-304-7240; Fax: +1 516-224-8586; E-mail: jli2@nshs.edu

References

[1] Wiestler O, Schiffer D and Coons S. Ependymal tumor. 2000; 71-79.
[2] Zec N, De GU, Schofield DE, Scott RM and Anthony DC. Giant cell ependymoma of the filum terminale. A report of two cases. Am J Surg Pathol 1996; 20: 1091-1101.
[3] Brown DF, Chason DP, Schwartz LF, Coimbra CP and Rushing EJ. Supratentorial giant cell ependymoma: a case report. Mod Pathol 1998; 11: 398 -403.
[4] Pimentel J, Kepes JJ, Moura Nunes JF, Bentes C, Miguens J and Antunes JL. Supratentorial giant cell ependymoma. Clin Neuropathol 2001; 20: 31-37.
[5] Moritani S, Kushima R, Bamba M, Kobayashi TK, Oka H, Fujimoto M, Hattori T and Okabe H. Highly anaplastic extraventricular ependymoma arising in an adult, mimicking metastatic adenocarcinoma with heavy stromal inflammation and emperiporesis. Pathol Int 2003; 53: 539-546.
[6] Fourney DR, Siadati A, Bruner JM, Gokaslan ZL and Rhines LD. Giant cell ependymoma of the spinal cord. Case report and review of the literature. J Neurosurg 2004; 100: 75-79.
[7] Jeon YK, Jung HW and Park SH. Infratentorial giant cell ependymoma: a rare variant of ependymoma. Pathol Res Pract 2004; 200: 717-725.
[8] Pal P, Fernandes H and Ellison DW. Woman aged 24 years with fourth ventricular mass. Brain Pathol 2005; 15: 367-368, 373.
[9] Cooper PB, Katus M, Moores L, Geyer D, Smirniotopoulos JG, Sandberg GD and Rushing EJ. Rare giant cell ependymoma in an octogenarian. Case report and review of the literature. J Neurosurg 2006; 105: 908-911.
[10] Adamek D, Dec M, Sobol G, Urbanowicz B and Jaworski M. Giant cell ependymoma: a case report. Clin Neurol Neurosurg 2008; 110: 176-181.
[11] Szpak GM, Lewandowska E, Schmidt-Sidor B, Pasennik E, Modzelewska J, Stepien T, Zdaniuk G, Kulczycki J and Wierzba-Bobrowicz T. Giant cell ependymoma of the spinal cord and fourth ventricle coexisting with syringomyelia. Folia Neuropathol 2008; 46: 220-231.
[12] Sangoi AR, Lim M, Dulai M, Vogel H and Chang S. Suprasellar giant cell ependymoma: a rare neoplasm in a unique location. Hum Pathol 2008; 39: 1396-1401.
[13] Shamji MF, Benoit BG, Perry A and Jansen GH. Giant cell ependymoma of the thoracic spine: pathology case report. Neurosurgery 2009; 64: E566-E567.
[14] Barbagallo GM, Caltabiano R, Parisi G, Albanese V and Lanzafame S. Giant cell ependymoma of the cervical spinal cord: case report and review of the literature. Eur Spine J 2009; 18: 186-190.
[15] Dahlback HS, Brandal P, Krossnes BK, Fric R, Meling TR, Meza-Zepeda LA, Danielsen HE and Heim S. Multiple chromosomal monosomies are characteristic of giant cell ependymoma. Hum Pathol 2011; 42: 2042-2046.
[16] Trivedi P, Gupta A, Pasricha S and Patel D. Giant cell ependymoma of a cervical spinal cord. Indian J Pathol Microbiol 2011; 54: 201-203.
[17] Gessi M, Kuchelmeister K, Lauriola L and Pietsch T. Rare hitological variants in ependymomas: Histopathological analysis of 13 cases. Vichows Arch 2011; 459: 423-429.
[18] Martinez-Diaz H, Kleinschmidt-DeMasters BK, Powell SZ and Yachnis AT. Giant cell glioblastoma and pleomorphic xanthoastrocytoma show different immunohistochemical profiles for neuronal antigens and p53 but share reactivity for class III beta-tubulin. Arch Pathol Lab Med 2003; 127: 1187-1191.
[19] Sharma MC, Ralte AM, Gaekwad S, Santosh V, Shankar SK and Sarkar C. Subependymal giant cell astrocytoma–a clinicopathological study of 23 cases with special emphasis on histogenesis. Pathol Oncol Res 2004; 10: 219-224.
[20] Biegel JA, Fogelgren B, Zhou JY, James CD, Janss AJ, Allen JC, Zagzag D, Raffel C and Rorke LB. Mutations of the INI1 rhabdoid tumor suppressor gene in medulloblastomas and primitive neuroectodermal tumors of the central nervous system. Clin Cancer Res 2000; 6: 2759-2763.
[21] Judkins AR, Mauger J, Ht A, Rorke LB and Biegel JA. Immunohistochemical analysis of hSNF5/INI1 in pediatric CNS neoplasms. Am J Surg Pathol 2004; 28: 644-650.