Int J Clin Exp Med 2019;12(4):4409-4413
www.ijcem.com /ISSN:1940-5901/IJCEM0079806

Case Report

Granular cell tumors in the human spinal canal: a case report and literature review

Jingling Xue[1], Honglei Chen[1], Yanlong Yang[2], Jun Hu[3], Guifang Yang[4]

[1]Department of Pathology, School of Basic Medical Science and Wuhan University Center for Pathology and Molecular Diagnostics, Wuhan University, Wuhan, Hubei, People's Republic of China; [2]Department of Dermatology, 195 Hospital of People's Liberation Army of China, Xianning, Hubei, People's Republic of China; [3]Demonstration Center for Experimental Basic Medicine Education, Wuhan University, Wuhan, Hubei, People's Republic of China; [4]Department of Pathology, Zhongnan Hospital and Wuhan University Center for Pathology and Molecular Diagnostics, Wuhan University, Wuhan, Hubei, People's Republic of China

Received May 17, 2018; Accepted December 10, 2018; Epub April 15, 2019; Published April 30, 2019

Abstract: Background: Granular cell tumors (GCTs) are uncommon benign tumors originating from primitive nerve cells. GCTs in human spinal canal are particularly rare, and a few cases have been reported. Case presentation: Here is reported a rare case of a 26-year-old female with a GCT in the L4 spinal canal and the related literature is reviewed. MRI indicated a benign nerve sheath tumor. Hematoxylin-eosin (HE) and immunohistochemistry staining revealed a benign GCT. Conclusion: GCTs in human spinal canal are rare and benign, causing clinical symptoms that vary because of their different locations.

Keywords: Granular cell tumors, benign, spinal canal

Introduction

Granular cell tumors (GCTs) are uncommon tumors with predilection toward the tongue, vocal cords, other areas in the head and neck, and the skin of the upper limbs and trunk. GCTs of the nervous system arise from peripheral nerves and the central nervous system (CNS). However, only 14 cases in the spinal canal have been reported [1-12]. Here, a case of a 26-year-old female with a GCT in the L4 spinal canal is presented and published cases of spinal GCT are reviewed.

Case presentation

A 26-year-old female presented to the Neurosurgical Outpatient Department of Zhongnan Hospital, Wuhan, Hubei, People's Republic of China with a 1-month history of pain without paresthesia in the lumbosacral region and in the left thigh. She reported that the pain exacerbated within the succeeding week without any cause, and the condition could not be alleviated when lying on her back and even at rest. The patient had no family history of neurofibromatosis and was previously well without regular medications. Examination revealed that the patient suffered from pain in the left pygal when she was percussed. Remaining findings of the neurological examination were normal. Magnetic resonance imaging (MRI) demonstrated a mildly enhancing mass in the L4 central canal (**Figure 1**). Expansion of the neural foramen suggested that a chronic process occurred, and the lesion with clear borders was likely a benign nerve sheath tumor. Surgery involved mass removal. A well-delineated soft gray-yellowish and brownish mass measuring 2 cm × 1 cm × 1 cm was present extramedullary within the spinal canal at the L4 vertebra. No postoperative complications were observed.

Histopathologically, the biopsy specimen showed sheets and nests of large polyhedral tumor cells separated by delicate fibrovascular tissues. Individual cells were round to polygonal, occasionally with distinct borders and abundant, indistinct, pale, finely granular, and acidophilic cytoplasm (**Figure 2**). The nuclei were

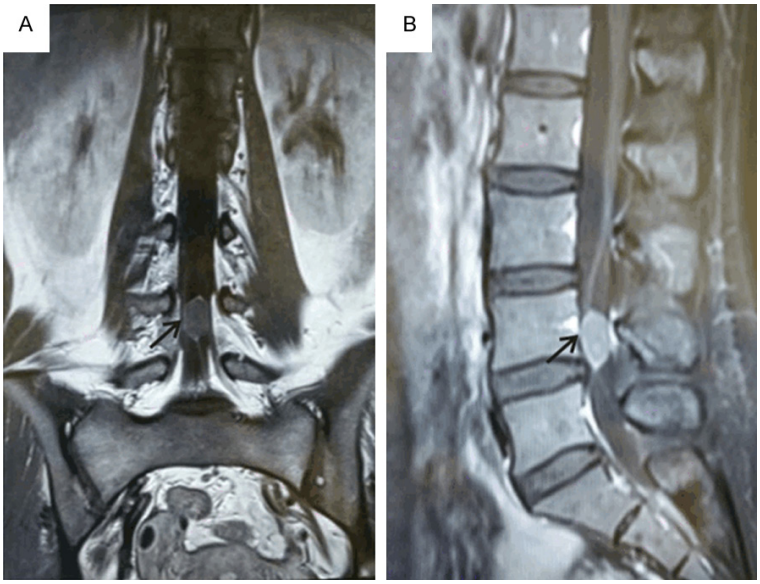

Figure 1. Magnetic resonance imaging demonstrates a mildly enhancing mass in the L4 central canal (A) Coronal plane (B) Sagittal plane.

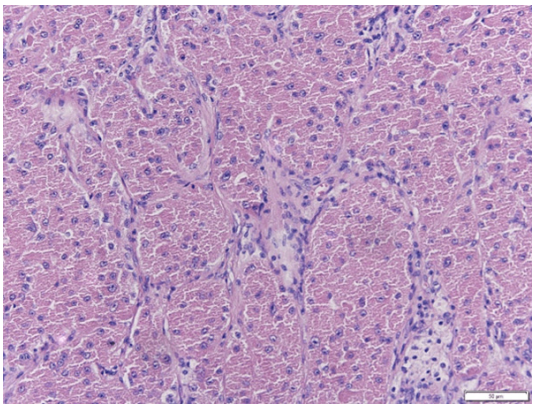

Figure 2. Sheets and nests of large polyhedral tumor cells separated by delicate fibrovascular tissue. Individual cells were round to polygonal, occasionally with distinct borders and abundant, indistinct, pale, finely granular, and acidophilic cytoplasm (HE 20 × 10).

round to oval and hyperchromatic to vesicular with an irregular nuclear membrane, but mitoses were lacking (10 random fields at 200-400 × revealed no mitotic figures). Additional sectioning, staining, and immunohistochemistry were conducted on a large mass fixed with 10% neutral buffered formalin. Staining with periodic acid Schiff (PAS) showed the coarsely dense positive staining of the diastase-resistant cytoplasm (**Figure 3**). Deep sectioning revealed clear association of the cauda equina with the outer connective tissue boundary of the mass (**Figure 4**). Immunohistochemistry showed that tumor cells were strongly and diffusely positive with S-100 protein (**Figure 5A**). No reaction with epithelial membrane antigen, glial fibrillary acidic protein (**Figure 5B**), human melanoma black-45, progestrone receptor, desmin, myoblast determination protein 1, myogenin, smooth muscle actin, calretinin, hepatocyte, and synaptophysin occurred. The Ki67 index was about 5% (**Figure 5C**). Overall, these findings were characteristic of a benign GCT. With operation of mass removal, a significant symptomatic/clinical improvement was achieved. As such, the patient was managed with a regular follow-up and is doing well up to the present date.

Discussion

GCTs are soft tissue tumors, which were initially reported as granular cell myoblastoma in 1926 by Abrinkossoff [13]. GCTs may occur in various parts of the body with a particular predisposition for the tongue [14], and several cases of tongue GCTs were analyzed in our previous report [15]. GCTs in the spinal canal are extremely rare. To enhance our understanding of these rare tumors, we reported a case and fully reviewed the previously published literature.

Since 1960, 15 cases of GCTs in the spinal canal, including the patient in our report, have been presented [1-12]. The details of these cases are summarized in **Table 1**. GCTs in the spinal canal preferably localize in the lower thoracic and lumbar area. Of the 15 cases, including the patient presented in this report, 4 were detected in the cervical area, 1 was found in the upper thoracic area (T1-6), 4 were observed in the lower thoracic area (T7-12), and 6 were identified in the lumbosacral area. GCTs in the spinal canal also have a preference for the extramedullae. Except the data of the case reported by Rickert [5] are unavailable, 4 intramedullary cases and 10 extramedullary cases

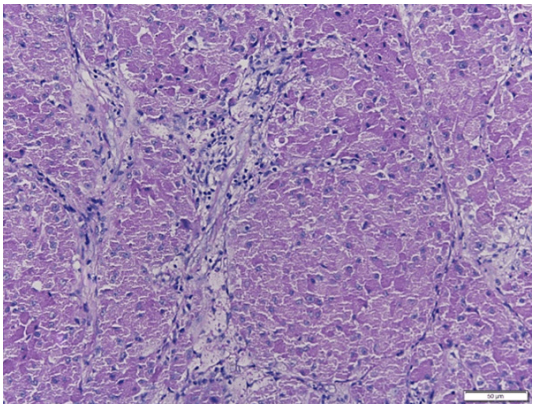

Figure 3. Staining with PAS shows coarsely dense positive staining of the cytoplasm that was diastase resistant (PAS 20 × 10).

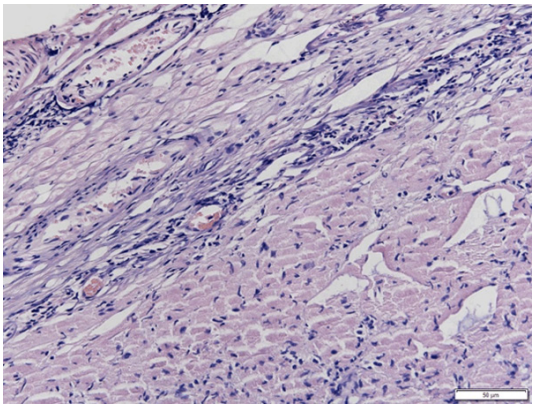

Figure 4. Deep sectioning reveals clear association of the cauda equina with the outer connective tissue boundary of the large mass (HE 20 × 10).

are described. Patients with GCTs in the spinal canal have an evident female predominance, and only two male patients have been reported. The age of these patients ranged from 9 years to 73 years (median age = 21 years).

The origin of GCTs has been debated since its original description was first presented. GCTs were previously termed myoblastic myomata to indicate their possible muscular origin, but electron microscopy and immunohistochemistry have revealed that they originate from Schwann cells and exhibit Schwannian differentiation. Granules in GCTs are usually positive for PAS and S-100 protein. However, the three cases reported by Markesbery [1], Rickert [5], and Qu [7] showed negative immunoreaction with S-100 staining. In contrast, 12 other GCT cases in the spinal canal, including our case, were positive for S-100 staining. The granules in our case were also PAS positive. Moreover, a transformation zone possibly existed between the cauda equina and the tumor in our case, indicating they likely arise from Schwann cells in a manner similar to their peripheral counterparts. Our case also shows that the patient manifested few clinical symptoms except pain without paresthesia in the lumbosacral region and in the left thigh, although the tumor was not small. Other cases, which were located above L1, suffered from some clinical symptoms, such as superficial sensations with paresthesia, difficulty in walking, and progressive swelling. In our opinion, the tumor in this case was located in the L4 level and the location was so low that only the cauda equina was found around the tumor. Thus, GCTs in different locations likely cause various clinical symptoms.

GCTs are potentially malignant, and they are rarely detected in less than 2% of cases with GCTs [16]. The histological criteria for the prospective diagnosis of malignancy in GCTs include tumor cell necrosis, tumor cell spindling, increased nuclear size, large nucleoli, mitotic activity, and nuclear pleomorphism. Features that suggest malignant GCTs include a history of local recurrence, rapid growth and large size (> 5 cm), metastasis, necrosis, and adjacent tissue involvement. Benign and malignant forms of GCTs may undergo local recurrence [17]. In previous reports, two GCT cases in the spinal canal experienced recurrence, but might not be diagnosed as malignant without enough histological manifestations. The other GCTs in the spinal canal cases, including our case, seemed to be benign. Our findings regarding these GCT cases in this rare location could help enhance understanding of this rare tumor.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Guifang Yang, Department of Pathology, Zhongnan Hospital and Wuhan University Center for Pathology and Molecular Diagnostics, Wuhan University, Wuhan, Hubei, People's Republic of China. Tel: +86-27-67812888; Fax: +86-27-6781289227; E-mail: guifangyang61@163.com

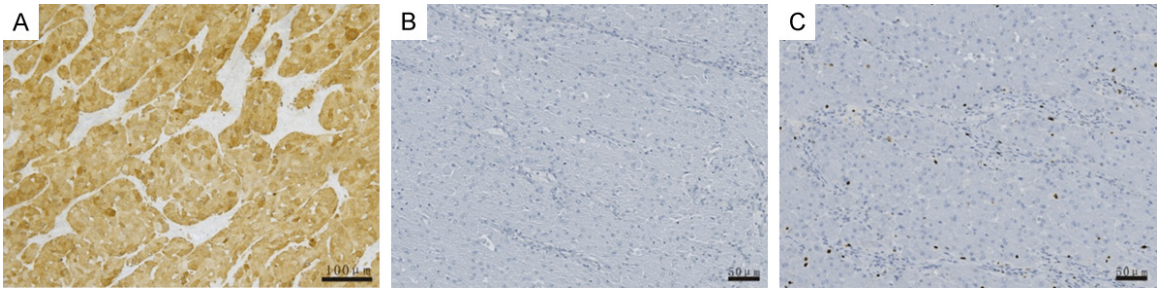

Figure 5. A. Cells that were strongly and diffusely immunoreactive with S-100 protein (SP 10 × 10). B. No reaction with glial fibrillary acidic protein (SP 10 × 10). C. Ki67 index of approximately 5% (SP 10 × 10).

Table 1. Clinical pathology data of the total fifteen cases

NO	Author	Year	Sex/Age	Level	Other	Recur	Add T x	S100	Intra/extramedullary
1	Markesbery	1973	F/73	C1	GI	None	None	N/A	Extramedullary
2	Stromblad	1987	F/10	T12	None	None	None	+	Intramedullary
3	Critchley	1997	F/17	T10	None	12 mon	Radiation	+	Intramedullary
4	Burton	1997	F/12	C1	None	7 mon	Rdiation	+	Intramedullary
5	Rickert	1997	F/10	L1	None	None	None	N/A	Unavailable
6	Takayama	2004	M/49	L1	None	None	None	+	Extramedullary
7	Qu	2009	F/16	T11	None	None	None	N/A	Extramedullary
8	Weinstein	2010	F/20	L1	None	None	None	+	Extramedullary
9	Lee	2013	F/22	T2	None	None	None	+	Extramedullary
10	Lee	2013	F/21	C5	None	None	None	+	Extramedullary
11	Vaghasiya	2014	F/13	L1-3	None	None	None	+	Extramedullary
12	Kilian	2015	F/13	C4/C5	None	None	None	+	Intramedullary
13	Li	2016	M/9	T11-12	None	None	None	+	Extramedullary
14	Li	2016	F/12	L1	None	None	None	+	Extramedullary
15	This report	2017	F/26	L4	None	None	None	+	Extramedullary

References

[1] Markesbery WR, Duffy PE, Cowen D. Granular cell tumors of the central nervous system. J Neuropathol Exp Neurol 1973; 32: 92-109.

[2] Stromblad LG, Brun A, Cameron R and Cronquist S. Spinal granular cell tumor with subarachnoid hemorrhage: case report. Neurosurgery 1987; 21: 230-233.

[3] Burton BJ, Kumar VG and Bradford R. Granular cell tumour of the spinal cord in a patient with Rubenstein-Taybi syndrome. Br J Neurosurg 1997; 11: 257-259.

[4] Critchley GR, Wallis NT and Cowie RA. Granular cell tumour of the spinal cord: case report. Br J Neurosurg 1997; 11: 452-454.

[5] Rickert CH, Kuchelmeister K and Gullotta F. Morphological and immunohistochemical characterization of granular cells in non-hypophyseal tumours of the central nervous system. Histopathology 1997; 30: 464-471.

[6] Takayama Y, Hasuo K, Takahashi N, Nishimiya M, Nonoshita T, Takita Y and Kuroki H. Granular cell tumor presenting as an intradural extramedullary tumor. Clin Imaging 2004; 28: 271-273.

[7] Qu J, Ma J, Luo L, Ai L, Li S and Dai J. Subdural granular cell tumor in thoracic vertebral canal. Neurol India 2009; 57: 679-681.

[8] Weinstein BJ, Arora T and Thompson LD. Intradural, extramedullary spinal cord granular cell tumor: a case report and clinicopathologic review of the literature. Neuropathology 2010; 30: 621-626.

[9] Lee CH, Hyun SJ, Lee JW and Rhim SC. Granular cell tumor of the intradural extramedullary spinal cord: report of two cases with respect to radiological differential diagnosis. J Korean Neurosurg Soc 2013; 53: 121-124.

[10] Vaghasiya VL, Nasit JG, Parikh PA and Trivedi PP. Intradural spinal granular cell tumor. Asian J Neurosurg 2014; 9: 96-98.

[11] Brown KG, Rao PJ, Oo TH and Fowler A. Granular cell tumors of the spinal canal: intramedullary case report and a review of the literature. J Spine Surg 2015; 1: 94-98.

[12] Li P, Yang Z, Wang Z, Zhou Q, Li S, Wang X, Wang B, Zhao F and Liu P. Granular cell tumors in the central nervous system: a report on eight cases and a literature review. Br J Neurosurg 2016; 30: 611-618.
[13] A AbrinkossoffÜber Myome, Ausgelend von der quergestreiften willkürlichen Muskulatur. Virchows Arch A Pathol Anat Histopathol 1926; 260: 215-233.
[14] Ordonez NG and Mackay B. Granular cell tumor: a review of the pathology and histogenesis. Ultrastruct Pathol 1999; 23: 207-222.
[15] Xue JL, Fan MW, Wang SZ, Chen XM and Li Y. A clinicopathological study of 14 cases of oral granular cell tumor. Zhonghua Kou Qiang Yi Xue Za Zhi 2005; 40: 302-305.
[16] Goldblum JR, Folpe AL, Weiss SW. Benign tumors of peripheral nerves. In: Enzinger and Weiss's Soft Tissue Tumors, editors. 6th edition. Philadelphia, PA: Elsevier Saunders; 2014. pp. 784-854
[17] Kaiserling E, Ruck P and Xiao JC. Congenital epulis and granular cell tumor: a histologic and immunohistochemical study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1995; 80: 687-697.