CASE REPORT

Ganglioglioma of conus medullaris in a patient of neurofibromatosis type 1: A novel association?

Ilangovan Vijay Sundar, Manish Jaiswal, Devendra Purohit, R. S. Mittal
Department of Neurosurgery, SMS Medical College and Hospital, JLN Marg, Jaipur, Rajasthan, India

ABSTRACT

Ganglioglioma of the conus region is quite rare with only 12 reported cases. Ganglioglioma shares biologic features with neurofibromatosis leading to suggestions that the co-existence of the two diseases may be more than coincidental. We report a case of ganglioglioma of the conus medullaris in a patient of neurofibromatosis and explore the possible association of the two diseases.

Key words: Adolescent, conus medullaris, ganglioglioma, neurofibromatosis

Introduction

Ganglioglioma is a slow-growing tumour composed of a mixture of neuronal and astrocytic elements with both cell types showing a broad spectrum of histological features. Most affect the temporal lobe and are rare in the spinal cord. They are more frequent in the cervicothoracic region,[1] the conus medullaris being an extremely uncommon site. Only 12 cases of ganglioglioma of the conus medullaris have been reported of which only one was associated with neurofibromatosis.[2,3] We report a case of intramedullary spinal cord ganglioglioma involving the conus medullaris in a 16-year-old male.

Case History

A 16-year-old male presented to us with difficulty in walking and urinary incontinence since 5 months. On examination the patient had deformity of left foot with clawing of the toes and wasting of intrinsic muscles of left foot, intact motor power at all levels except weakness of left ankle dorsiflexion, and tone was normal. He had diminished sensation over the saddle area and posterior aspect of both legs. Ankle reflex was diminished bilaterally. He had multiple [more than 6] hyper pigmented macules over trunk and right lower limb whose size was well over 15 mm in greatest diameter [Figure 1]. The patient also had axillary freckling. There was no history suggestive of such a disease in maternal or paternal side of patient family. The patient was investigated and on MRI spine there was intramedullary lesion in lower dorsal cord and conus at D11 to L1 level [Figure 2]. D11 to L1 laminectomy done, mass was infiltrated in cord substance from D 11 to L1 level, soft in consistency with normal vascularity and pinkish white in color. Microscopic near total excision of intramedullary mass was done. The postoperative period was uneventful and the patient was discharged in satisfactory condition. Histopathological examination revealed a biphasic pattern where there was combination of neuronal and glial cell element. The neurons were dysplastic with features of low grade astrocytoma with excessive calcification along with a prominent capillary network. The ganglion cells were positive for synaptophysin, neurofilament, and chromogranin with focal expression of CD34 [Figure 3]. GFAP was positive in the astrocytic element. A final diagnosis of ganglioglioma (WHO grade-1) was made. At 2 month follow up, the patient had regained bowel and bladder control and power of his left ankle joint had improved.

Access this article online	
Quick Response Code:	Website: www.asianjns.org
	DOI: 10.4103/1793-5482.145088

Address for correspondence:
Dr. I. Vijay Sundar, No 6, Bharathi Nagar First Street, North Usman Road, T.Nagar, Chennai, Tamil Nadu, India.
E-mail: drvijaysundar@gmail.com

Discussion

First described by Courville and Anderson in 1930 and once regarded as a hamartomatous lesion, it is now widely believed that ganglioglioma is a true neoplasm of a relatively benign nature, which probably forms as a result of the maturation of tumors originally composed of primitive neuroblastic cells.

Many confusing synonyms such as ganglioglioneuroma, neuroastrocytoma, ganglionic glioma, and neuroglioma exist. They are currently classified as gangliocytoma where the tumor consists solely of large relatively mature neoplastic neurons or

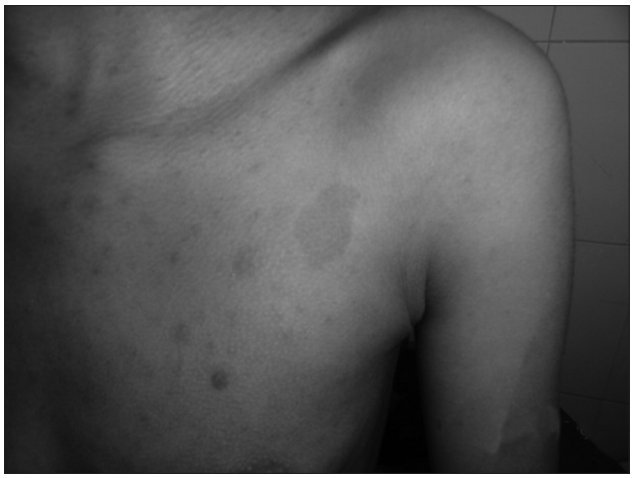

Figure 1: Clinical photograph showing multiple macules

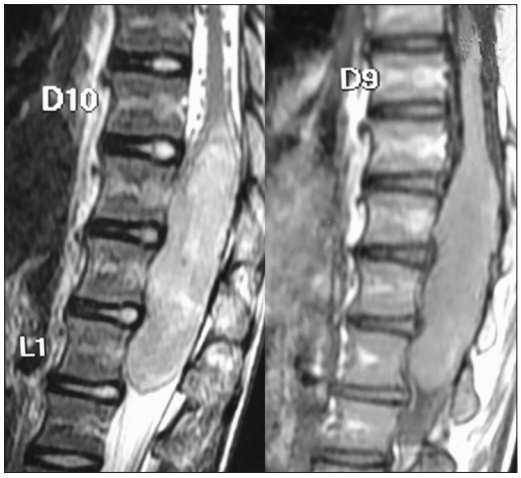

Figure 2: Magnetic resonance imaging showing intramedullary lesion

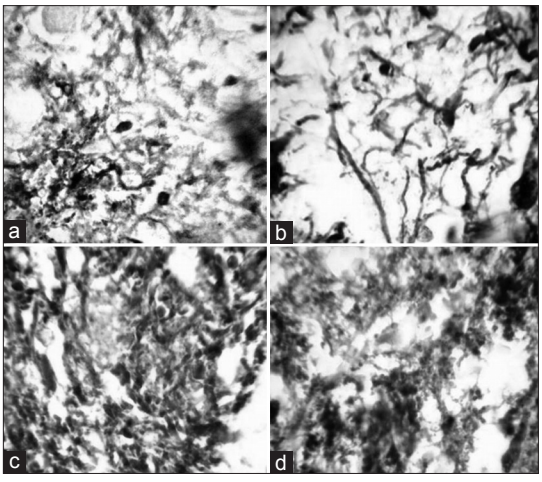

Figure 3: (a) Histopathological image showing positivity for CD34; (b) GFAP; (c) NF1 and (d) synaptophysin

ganglion cells, ganglioglioma which has an additional presence of a neoplastic astrocytes and ganglioglioneurocytoma with additional features, such as a substantial population of small neoplastic mature neurons.[4]

Gangliogliomas most commonly occur in the temporal lobes and in the cerebellar hemispheres in the brain. Gangliogliomas arising in the spinal cord are extremely rare and probably represent 1.1% of all intra-medullary spinal neoplasms.[5] It has a slight male predominance, a median age at diagnosis of 6 years[1] and a mean duration of symptoms until diagnosis of 12 months. Most frequently, mass lesions were located in the cervical or thoracic regions and involved 4 to 8 vertebral segments.[2] Clinical presentation varies according to the level of the lesion.

Neurofibromatosis 1 (NF1) is an autosomal dominant disorder with an incidence of 1 in 4000 which is associated with a variety of benign and malignant lesions such as café au lait spots, neurofibromas, phaeochromocytomas, pilocytic astrocytomas, and malignant peripheral nerve sheath tumors. NF1 is caused by genetic alterations of the NF1 gene located on 17q11.2.

Spinal tumors cause neurological symptoms in about 2% of NF1 patients and can be detected in 40% of NF1 patients by magnetic resonance imaging (MRI). Neurofibromas and rarely astrocytomas are the most common tumors in the spinal canal of patients with NF1. Spinal tumors in NF1 cause symptoms mainly in older patients (mean age 32.8 years).[6,7] In children with NF1, the optic chiasm may be involved by ganglioglioma.

The association of ganglioglioma of the conus medullaris and NF1 has been described in only one case previously[3] though NF1 has been found in patients with ganglioglioma located elsewhere in the spine.[8] Interestingly, NF1 is considered by many to be a disorder of glial cells and neurons, which are also the main histologic components found in gangliogliomas.[9]

MRI is the diagnostic modality of choice and the findings most suggestive of ganglioglioma are long tumor segment, scoliosis and bony erosion, mixed signal on T1-weighted MR images, prominent tumoral cyst, patchy enhancement after contrast, and the absence of edema.[10]

The main elements found in gangliogliomas are atypical neurons, astrocytes, and a fibrovascular stroma. Ganglioglioma may be suspected when an otherwise astrocytic neoplasm contains a component of large cells potentially representing neurons which may display atypical or dysplastic features, such as binucleation, calcification, background desmoplasia, and perivascular lymphoplasmacytic infiltration.[4,9] Neoplastic neurons are irregularly arrayed or clustered and lack the polarity of normal pyramidal neurons. Most have large nuclei with prominent nucleoli as well as the basophilic Nissl.

Immunohistochemically, the tumor neurons are positive for synaptophysin, neurofilament protein, neuron-specific enolase, and chromogranin A and the glial elements express glial fibrillary acidic protein. Perivascular collars of lymphocytes are present.[11]

Proliferation markers such as bromodeoxyuridine, flow cytometry, and antibodies against Ki-76 help assess the growth kinetics of these tumors. Slow growth rate is seen in gangliogliomas with a low number of positive cells (1- 6%).

Ganglioglioma is usually discernible from astrocytoma provided adequate sampling has been done particularly in large specimens. However, when a diagnosis of astrocytoma (especially anaplastic astrocytoma) is made from hematoxylin eosin stains of limited tissue samples, there is a significant chance that the tumor is actually a ganglioglioma, because it can be difficult to distinguish large tumor astrocytes from neoplastic neurons[4] or find neurons in small samples or separate neoplastic from trapped native neurons.[4,12]

Because of the above points some authors report the incidence rate up to 14%, that would put ganglioglioma the second most common intramedullary tumor after astrocytomas under the age of 10 years.[8]

Malignant transformation is rare in ganglioglioma and in one series is reported to be about 10%. In the rare malignant gangliogliomas, it is the astrocytic component that is responsible for their malignancy. The significance of anaplastic astrocytes is uncertain as many anaplastic gangliogliomas lack a clear clinical aggressive behavior;[13] therefore, the biological behavior of most of these tumors is not predicted by their histology.

Microsurgical techniques greatly facilitate total removal of the tumor which is the treatment of choice. Its relatively good demarcation from the surrounding normal tissue allows complete surgical resection. Radical extirpation is associated with minimal morbidity and an excellent long-term prognosis. Presently, postoperative radiotherapy is not believed to play any role in the management of completely resected gangliogliomas. Only in those tumors that show anaplastic features or a high proliferation index should radiotherapy be considered.

Conclusion

Ganglioglioma should be suspected whenever a child presents with a tumor involving a considerable length of the spinal cord. It is usually well demarcated from the surrounding normal tissues, which greatly facilitates surgical excision. As a result of their favorable prognosis correct diagnosis is important to avoid progressive neurological deficit and unnecessarily aggressive therapy.

Acknowledgement

All authors have participated equally in the preparation of this manuscript.

References

1. Jallo GI, Freed D, Epstein FJ.Spinal cord gangliogliomas: A review of 56 patients. J Neurooncol 2004;68:71-7.
2. Costa J, Ruivo J, Miguéns J, PimenteJ. Ganglioglioma of conus medullaris. Acta Neurochir (Wien) 2006;148:977-80.
3. Hayashi Y, Nakada M, Mohri M, Murakami H, Kawahara N, Hamada JI. Ganglioglioma of the thoracolumbar spinal cord in a patient with neurofibromatosis type 1: A case report and literature review. Pediatr Neurosurg 2011;47:210-3.
4. Miller DC, Lang FF, Epstein FJ. Central nervous system gangliogliomas, 1: Pathology. J Neurosurg 1993;79:859-66.
5. Satyarthee GD, Mehta VS, Vaishya S.Ganglioglioma of the spinal cord: Report of two cases and review of the literature. J Clin Neurosci 2004;11:199-203.
6. Lee M, Rezai AR, Freed D, Epstein FJ.Intramedullary spinal cord tumors in neurofibromatosis. Neurosurgery 1996;38:32-7.
7. Thakkar SD, Feigen U, Mautner VF. Spinal tumours in neurofibromatosis type 1: An MRI study of frequency, multiplicity and variety. Neuroradiology 1999;41:625-9.
8. Park CK, Chung CK, Choe GY, Wang KC, Cho BK, Kim HJ. Intramedullary spinal cord ganglioglioma: A report of five cases.Acta Neurochir (Wien) 2000;142:547-52.
9. KluweL, TatagibaM, FünstererC, Mautner VF. NF1 mutations and clinical spectrum in patients with spinal neurofibromas. J Med Genet 2003;40:368-71.
10. PatelU, PintoRS, MillerDC, HandlerMS, RorkeLB, EpsteinFJ, *et al*. MR of spinal cord ganglioglioma. AJNR Am J Neuroradiol 1998;19:879-87.
11. Wolf HK, Muller MB, Spanle M, Zentner J, Schramm J, Wiestler OD. Ganglioglioma: A detailed histopathological and immunohistochemical analysis of 61 cases. Acta Neuropathol 1994;88:166-73.
12. Isimbaldi G, Sironi M, Tonnarelli GP, Roncoroni M, Declich P, Galli C. Ganglioglioma: A clinical and pathological study of 12 cases. Clin Neuropathol 1996;15:192-9.
13. Hamburger C, Buttner A, Weis S. Ganglioglioma of the spinal cord: Report of two rare cases and review of the literature. Neurosurgery 1997;41:1410-6.

How to cite this article: Sundar IV, Jaiswal M, Purohit D, Mittal RS. Ganglioglioma of conus medullaris in a patient of neurofibromatosis type 1: A novel association?. Asian J Neurosurg 2016;11:455.

Source of Support: Nil, **Conflict of Interest:** None declared.