

# Case Report: A Rare Case of Pediatric Conus Medularis Glioblastoma Multiforme

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### INTRODUCTION

Despite astrocytomas being the most common primary central nervous system (CNS) neoplasm they rarely occur in the spinal cord. Intramedullary spinal cord (IMSC) astrocytoma can occur in any age group but it is rare among those more than 60 year old. In the pediatric age group, 59% of IMSC lesions are astrocytomas with a slight male predominance. Most (85-90%) IMSC astrocytomas are low grade lesions with glioblastoma multiforme (GBM) accounting for only about 1-3% of all IMSC primary astrocytomas. There have been less than 200 cases of IMSC GBM reported. IMSC astrocytomas are more frequent at the cervical and thoracic region than the lumbar and conus region. Therefore, GBM of the conus medullaris is an extremely rarity.

There are 12 reported conus GBM cases to the best of our knowledge (table 1). Two cases have been female and ten cases male, giving a male to female ratio of 5:1. Among the adult population (age >18 year old) there were six cases, all the patients were male. This skew may be due to the limited cases reported.

There were six cases in the pediatric age group, four boys and two girls, a male to female ratio of 2:1. The age among pediatric patients ranges from 12 – 16 year old. That makes the case illustrated, a nine year old girl, most probably the youngest documented conus GBM case.

We report this case of conus glioblastoma multiforme (GBM) treated with surgical excision, radiotherapy and temozolomide as denovo high grade intramedullary spinal cord glioma because it is not commonly seen and its occurrence in the conus medullaris is an extreme rarity and the management of this disease is difficult.

### CASE REPORT

A nine year old girl presented with low back pain associated with progressive lower limbs weakness & numbness of five months duration. Subsequently she developed urinary and bowel incontinence one month prior to admission and she was bed bound on admission.

Physical findings showed near symmetrical hypotonic hyporeflexic paraparesis with power of 2/5 and hypesthesia from L1 dermatome downward.

Pre-operative MRI (Fig 1 A&B) revealed a conus expanding intramedullary mass which is heterogenous with ill defined margin. Contrast CT brain was normal.

T11-L2 laminotomy and near total tumor excision was performed. Tumor was within the conus, it appear reddish with moderate vascularity, friable with ill defined margin (Fig 1 C&D).

The histopathology findings showed area of hypercellularity with pleomorphic cells, mitotic figure of 15-20 per high power field, areas of necrosis and haemorrhage with pseudopalisading, and endothelial hyperplasia consistent with Glioblastoma Multiforme, WHO grade IV tumor (Fig 2). Post operative she remained bed bound and power was 2/5 on both lower limbs. The symptom of incontinence persisted and she underwent adjuvant therapy with radiotherapy & Temozolomide. The patient came for clinic follow up for the next six months but was wheel chair bound with neurological deficit confined to lower limbs and urinary & bowel incontinence.

### DISCUSSION

Conus GBM is a rare disease entity and its management is challenging. The clinical presentation are of conus medullaris syndrome, which may include back, leg pain and sciatica which the symptoms may mimic lumbar disc herniation<sup>2</sup>, lumbar level sensory loss or saddle anaesthesia, lower limbs weakness, urinary & bowel incontinence and erectile dysfunction in male patient<sup>3,4,5</sup>. The paraesthesia, lumbar & saddle region, and paraparesis are usually near symmetrical in distribution. The ankle reflex may be hyper, hypo or areflexia depending on extent of conus involvement. The knee jerks are affected only when the conus lesion is cranially extensive or when the L3, 4 rootlets are compressed by the expanding conus. The anal tone may be lax on rectal examination.

Imaging of conus lesion is important as the management strategies and prognosis are drastically different between benign and aggressive lesion. The current best available modality is the spinal MRI. Careful interpretation of imaging is needed as case initially noted as lumbar disc herniation has being reported<sup>2</sup>.

On the MRI the conus is expanded by the GBM. It is heterogenous due to the presence of hemorrhage, area of

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Table I: Reported cases of conus GBM

Authors	Age/Sex	Presentation	Metastases	Treatment	Duration of survival
O'Connell <i>et al</i> (1946)	16/ M	Right leg pain	Subarachnoid space, ventricle	Radiation	16 months
Tashiro <i>et al</i> (1976)	12/F	Right leg pain	Subarachnoid space, cerebellum, hypothalamus, thalamus, brain stem	Surgery	11 months
Andrews <i>et al</i> 1978	45/M	Back pain, paraparesis, saddle anesthesia	Septal region, ventricle	Surgery, radiation	13 months
Cohen <i>et al</i> 1989	1) 16/F 2) 14/M	(1 & 2) quadriplegic	1) Septum 2) Intracranial	(1&2) surgery & radiotherapy	1) 6 months 2) 4 months
Kawanishi <i>et al</i> 1993	50/M	Gait instability, below T11 sensory loss	Cerebellum, sylvian fissure, cingulate gyrus	Surgery	Unknown
Scarrow <i>et al</i> 2000	62/M	Right sciatica	Nil	Surgery, radiotherapy	Unknown
Medkhour <i>et al</i> 2002	20/M	Back pain, paraparesis & paraesthesia	Ventricle, posterior fossa	Surgery, radiotherapy + Surgery	10 months
Stecco <i>et al</i> 2005	14/M	Paraparesis, urinary disturbance, perineal hypoesthesia	Posterior fossa	Surgery	Unknown
Elsamaloty <i>et al</i> 2006	20/M	Lower back pain, left leg numbness, urinary & erectile disturbance	Ventricle, cerebellar, brainstem	Surgery, radiotherapy	10 months
Bonde <i>et al</i> 2008	16/M	Back pain, paraparesis, urinary disturbance	Simultaneous cervical-medullary lesion	Surgery, radiotherapy	6 months
Choi <i>et al</i> 2009	46/M	Back pain, paraparesis	Unknown	Surgery, radiotherapy, temozolomide	Unknown
Gee <i>et al</i> (this case 2009)	9/F	Back pain, paraparesis, urinary disturbance	T6-T8 vertebral bodies.	Surgery, radiotherapy, temozolomide	10 months

M indicate Male; F, female. +: incomplete radiotherapy

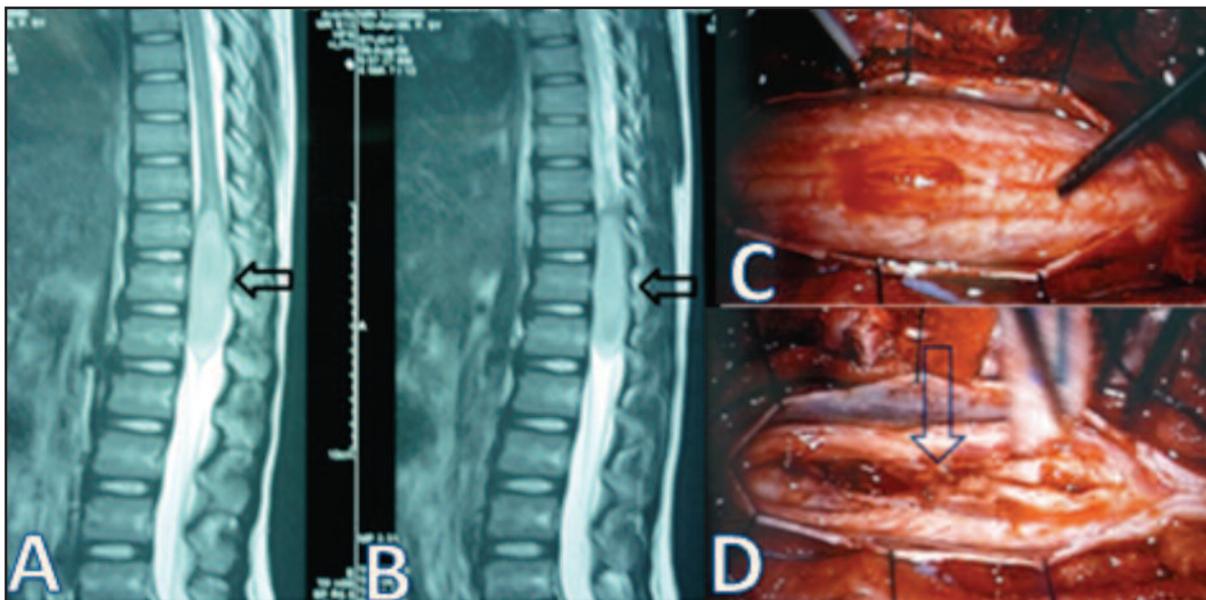
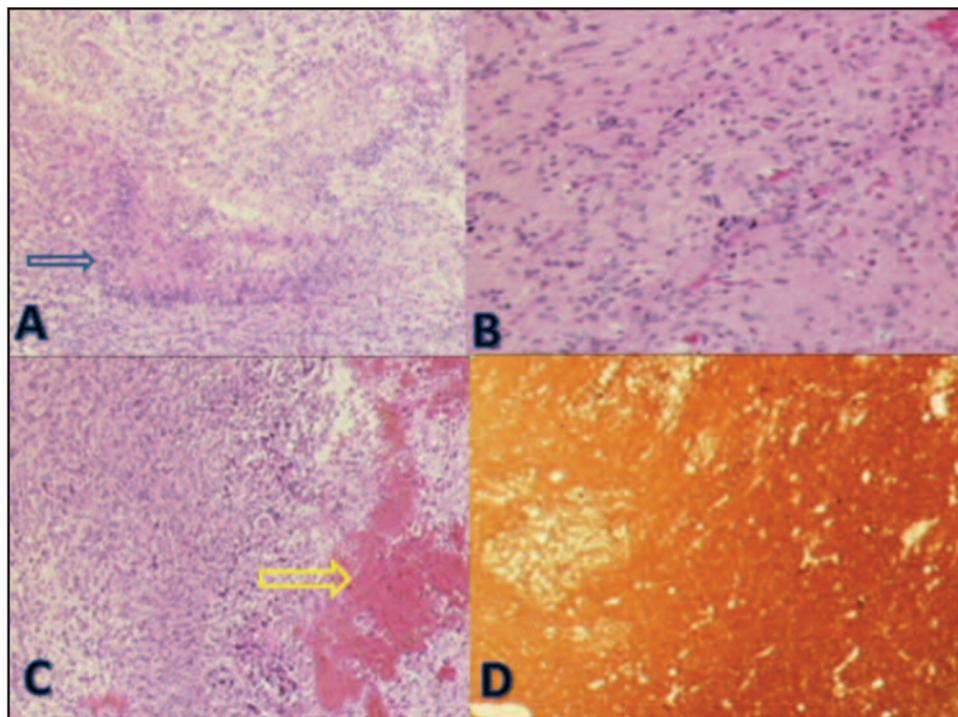


Fig. 1: A & B: T2WI sagittal view MRI at presentation showing heterogenous conus expanding lesion (black arrow) measured about 6.4 cm extended from T11 to lower end of L1 level.

C: The midline dura opening made after T11-L2 laminotomy. The cord appeared full and expanded; there was no extension of mass towards the cord dorsal surface.

D: The tumor appeared reddish, jelly like and friable. The tumor margin was ill defined with moderate vascularity.



**Fig. 3:** Histological slides.  
 A: Hemotoxylin & Eosin stain (H&E), magnification 4x, histological hallmark of pseudopalisading pattern (blue arrow) around a centre of necrosis.  
 B: H&E, magnification 10x, pleomorphic tumor cells with anaplastic features, hyperchromatic nuclei with variable cytoplasm.  
 C: H&E, magnification 2.5, showed area of hypercellularity and haemorrhage (yellow arrow).  
 D: Glial fibrillary acidic protein immunohistochemical stain, magnification 2.5x, showed GFAP immunoreactivity, establishing the tumor as a glioma.

necrosis, cyst and cellular debris. The viable solid component of the GBM enhances with Gadolinium and the margin is often ill defined with some having surrounding hypointense edematous white matter on T1 weighted image<sup>3</sup>. Benign lesions like ependymoma usually are homogenous on MRI with presence cranio-caudal peripheral cyst and clear imaging demarcation.

Intraoperatively GBM lesions have ill defined margins with moderate-high vascularity. Areas of haemorrhage and necrosis can be seen under the operating microscope. Upon encountering such findings and correlation of clinical-imaging findings of high grade lesion, with aid of frozen section cytology surgical intervention can be confined to biopsy and less radical surgical resection.

The diagnosis is confirmed by histological findings of pleomorphic cells arranged in pseudopalisading pattern with hypercellularity. Areas of necrosis, angiogenesis and hemorrhage are evidence with prominence mitotic figure and high Ki-67 indices. These glial cells are positive for GFAP staining. Reduction in GFAP expression correlate with glioma progression but it has limited prognostic value<sup>4</sup>.

The outlook of conus GBM is grim, the duration of survival range from 4-16months with median survival of 12 months<sup>4</sup>. Few cases of IMSC malignant astrocytoma survive for more than 4 years duration.

Current treatment regime fails to produce promising results. Some advocate radical surgery for diagnosis and cytoreduction for maximal result and pain reduction with adjuvant therapy<sup>1</sup>; while others prefer biopsy or partial resection for fear of worsening functional status with emphasis on post operation quality of life in a patient with markedly reduce survival duration<sup>2,3</sup>.

Almost all cases received adjuvant radiotherapy unless patient unable to tolerate the therapy<sup>4</sup>. Chemotherapy such as intrathecal interferon  $\beta$  is recommended in conjunction with cranio-spinal irradiation. Recently, temozolomide is also used in the treatment of this disease entity<sup>2</sup>.

Most patients succumb to the progression of the disease, intracranial and spinal dissemination<sup>1,3,4,5</sup>, respiratory failure<sup>3,4</sup>, orthostatic pneumonia secondary to immobility and immunosuppression through malnutrition or post adjuvant therapy and deep vein thrombosis with complicating pulmonary embolism. Duration of symptoms and histological grade predict the prognosis and post intervention survival duration<sup>1</sup>. The pre operative neurological status is a good functional prognosticating factor for the outcome of surgery. This patient succumbs to cranial and spinal dissemination 10 months post surgical intervention.

Recently, new strategies are being employed in the treatment of high grade IMSC astrocytomas. New chemotherapy agent

such as Temozolomide<sup>2</sup> and gene therapy<sup>4</sup> are under study in the treatment of this disease entity. The long term result is pending and positive result of new therapy is much awaited in battling this grave disease.

#### CONCLUSION

CNS malignant astrocytoma has a descending frequency of occurrence according to site; moving from intracranial to cervical-medullary, thoracic, lumbar and extremely rare in the conus medullaris. IMSC glioblastoma are rare and de novo conus medullaris GBM is an extreme rarity. The duration of symptoms is short and the neurological & clinical deterioration are rapid. Despite aggressive treatment via surgery and radiotherapy IMSC & conus GBM still carry a grim and fatal prognosis. This is a strong motivation for developing new treatment strategy. New treatment modality like Temozolomide & gene therapy is currently in under study and long term result is under study and review.

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