Primitive neuroectodermal tumor of spine - A case report

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Abstract
Primitive neuroectodermal tumors (PNETs) are malignant soft tissue tumors of uncertain origin. They usually occur in the deep soft tissues. PNET of the spine are rare. We herein report a case of PNET occurring in thoracic region in an adult male. A 44-year-old male presented with acute onset lower extremity weakness and urinary retention. Magnetic resonance imaging revealed a mass lesion well defined moderately homogenously enhancing extradural lesion at D6. D7 and D8 level, extending into bony spinal canal and left neural foramina causing their widening at D6 and D7 level. On examination patient was conscious and oriented, higher mental functions are normal, cranial nerves normal. Paraplegia was seen with bowel and bladder fully involved. There was no sensation below D6 level. Deep tendon reflexes were absent. The patient's neurological examination improved dramatically after the surgery. The histopathological and immunohistochemical evaluations revealed PNET. Surgery remains the treatment of choice and immunohistochemistry is required for confirming the diagnosis.

Keywords: Primitive neuroectodermal tumor, Extradural, Thoracic region, Paraplegia.

Introduction
Primitive neuroectodermal tumors (PNETs) are extremely rare small round blue cell tumors of neuroectodermal origin. They are divided based on the tissue of origin into central PNET, Neuroblastoma and Peripheral PNET. They are also classified as a part of Ewing family of Tumors. Ewing Sarcoma is however more common in bone. Deep soft tissues of the extremities particularly upper thigh and buttock are the most common site for PNET.[1] Less commonly the tumor arises in the paravertebral soft tissues or the chest wall generally in close association with vertebrae or the ribs. It was first described by Hart and Earle in 1973.[2]

Case Report
A 44 years old male patient, residing in Bagalkot district, Karnataka was admitted to Hanagal Shri Kumareshwar Hospital with complaints of weakness, numbness and loss of sensations in both the lower limbs since twenty days. The weakness got worse day by day and was unable to stand and was bed ridden. The patient also complained of retention of urine. Patient had no history of pain, headache, seizures, vomiting, speech difficulty, facial weakness. He had no history of fever, trauma, weight loss, tuberculosis or any spinal injury. No history of similar complains in the past. He was a chronic alcoholic for 20 years with complete abstinence for 4 months, non-diabetic, non-hypertensive. The results of all laboratory tests, including complete blood count, renal, hepatic and coagulation profiles were normal.

On examination, patient was conscious and oriented. The higher mental functions were normal cranial nerve examination detected no abnormality. Paraplegia was seen with bowel and bladder fully involved. There was no sensation below D_6 level. Deep tendon reflexes were absent.

On MRI Imaging studies, a well-defined moderately homogenously enhancing extradural lesion at D6, D7 and D8 level, extending into spinal canal and left neural foramina causing their widening at D6 and D7 level. The lesion was also seen encasing left costo-vertebral junction at D7 level and extending posteriorly to involve paraspinal muscles on left side. It was causing compression and right anterolateral displacement of spinal cord. Features suggested of an aggressive malignant lesion. (Fig. 1). Abdominal and pelvic CT imaging and chest X-ray did not reveal any lesions. There was no evidence of ascites, or retroperitoneal or mesenteric lymphatic metastases. The patient subsequently underwent intraspinal neoplasm resection.

Intraoperatively the tumor was unencapsulated, firm to soft in consistency, partly rubbery, grey whitish in color and clearly separated from dura. Extension into the paraspinal area was noted. Intradural extension was not seen. and excision was done in toto.

Resected tumor mass in multiple fragments was received for histopathological examination. Grossly it showed multiple grey white soft tissue fragments, largest measuring 3X2X1cm and smallest measuring 0.5x0.5x0.3cms, rubbery in consistency and grey white on cut surface.

Microscopically multiple section studied from the mass showed tumor cells arranged in sheets, seen diffusely infiltrating into the adjacent neuromuscular tissue. Tumor cells were homogenous with small round nucleus, dispersed chromatin, inconspicuous nucleoli and scant eosinophilic cytoplasm, arranged around thin fibrovascular septae. Focal rosettes, frequent mitotic figures are seen. Diagnosis of PNET- Primitive neuroectodermal tumour was given. (Fig. 2 and Fig. 3).

Patient remained paraplegic for 7 days, later grade 1 to Grade II improvement was seen. But bowel/bladder did not improve even after 4 weeks.

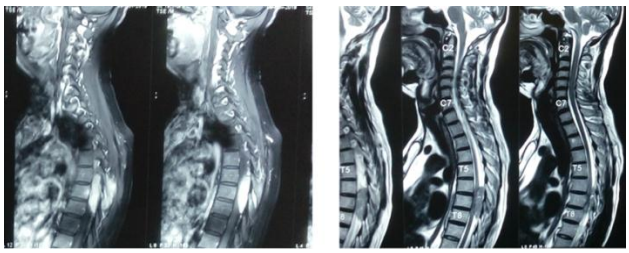

Fig. 3: well defined moderately homogenously enhancing extradural lesion at D6, D7 and D8 level, extending into bony spinal canal

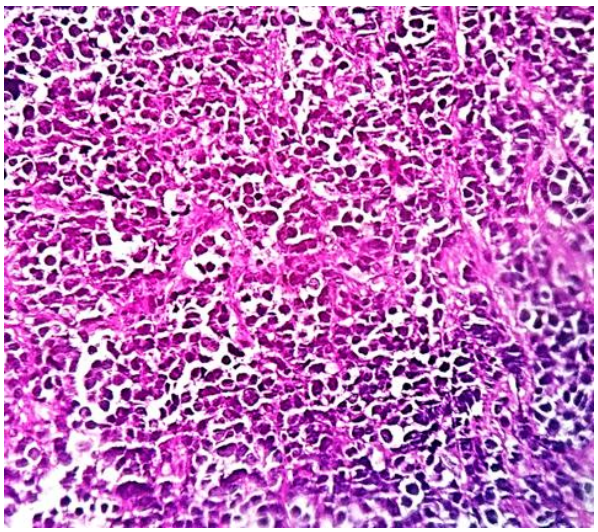

Fig. 2: Tumor cells arranged in sheets seen diffusely infiltrating into the adjacent neuromuscular tissue

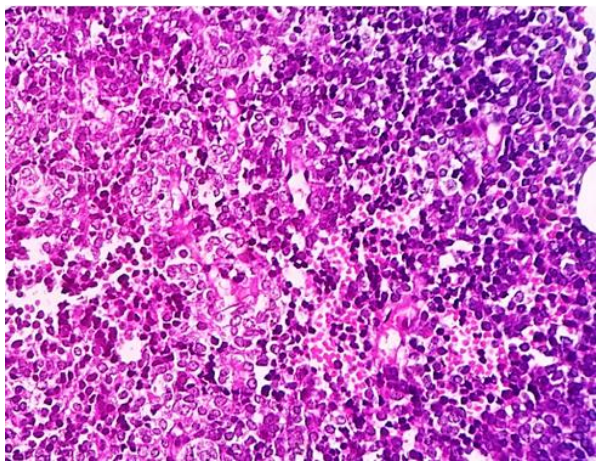

Fig. 3: Tumour cells were homogenous with small round nucleus, dispersed chromatin, inconspicuous nucleoli and scant eosinophilic cytoplasm.

Discussion

Primitive neuroectodermal tumors (PNETs) are malignant tumors of uncertain origin. They can be derived from central nervous system, autonomic nervous system or outside both. Stout first described these tumors which were thought to arise from nerves.[3] Tumors that are intimately attached to a major nerve may give rise to signs and symptoms related to diminished neurological function. Intraspinal PNET being are extremely rare.[4] Till date <100 cases have been documented. Its annual incidence ranges from 0.2-0.4 cases per 1,00,000.[5] They are rapidly growing soft tissue masses, which cause symptoms of nerve compression and pain. they are highly malignant and invasive, with a high rate of relapse and poor prognosis. Five year survival rate is 30-40%.[6]

Extradural spinal Primary Neuroectodermal Tumors (PNET) are extremely rare. According to study done by Kampman et al, 28 cases of intraspinal PNET were reported in the literature.[7] PNETs can be central or peripheral. Both differ in their clinical presentations. Extradural spinal PNETs has adult onset as compared to central PNET which occurs in children. The duration is often short, less than 4 months and can be short as 4 days.[8] Tumors can involve any level of the spine and location can be either intramedullary, intradural-extramedullary or epidural. Cranial symptoms are not a feature of primary intraspinal PNET which helps in distinguishing primary intraspinal PNET from spinal metastasis. The central PNET frequently disseminates via cerebrospinal fluid and rarely metastasize outside the CNS. Peripheral PNET disseminate to distant sites.

Grossly the excised tumors tend to be large, pale and soft, with extensive necrosis. In axial tumors, osseous involvement frequently occurs, and it is impossible to determine with certainty whether primary origin was in bone or soft tissue.[9] In our case, we received it in multiple fragmented grey white bits and there was no necrosis.

Diagnoses can be established by histopathological and immunohistochemical studies. Histopathological features include, a spectrum of appearances, which reflects the degree of neuroectodermal differentiation. They are predominantly lobular, or sometimes trabecular growth pattern associated with which is a prominent ramifying capillary network. Generally speaking little or no stroma is seen (although rare hyaline examples do occur), and a confluent or "filigree" pattern of necrosis is commonly found. Tumor cells at the poorly differentiated (Ewing) end of the spectrum have scanty, pale cytoplasm and round to ovoid open nuclei with a very finely distributed ("dusty") chromatin pattern, the presence of small nucleoli is variable. Some cases are composed of rather larger cells with discernible, often clear cytoplasm, but spindle cell morphology is exceedingly uncommon. At the opposite (so-called neuroepithelioma) end of the spectrum the cells may have somewhat eosinophilic cytoplasm, and the chromatin pattern may be coarser with more frequent nucleoli. It is significant that, at this better differentiated end of the morphologic continuum, numerous rosettes, usually of Homer Wright type, may occasionally be found, along with perivascular pseudorosettes. No cutoff point exists along this continuum; this explains why rare rosettes have been found for many years in otherwise typical cases of Ewing sarcoma.

Immunohistochemically, tumors at all points on the morphologic spectrum are linked by shared positivity for the CD99 antigen, a product of the MIC-2 gene on the X

chromosome that is best demonstrated by the antibodies O-13, MIC-2, or HBA-71,[10-12] most cases are also positive for β2-microglobulin and Fli-1. Antibodies to CD99 have proved to be especially useful in confirming a diagnosis of Ewing sarcoma/PNET.[13] In bona fide examples of Ewing sarcoma/ PNET the CD99 immunopositivity is diffuse and strikingly membranous. Aside from this, many tumors in the PNET spectrum show immunohistochemical evidence of neuroectodermal differentiation to a varying degree, as evidenced by positivity for antigens such as NSE, protein gene product 9.5 (PGP 9.5), neurofilament, Leu-7, and synaptophysin. It is important to note that 20% to 30% of cases in the Ewing sarcoma/ PNET spectrum show keratin positivity, which is often dot-like.

Gaining a complete resection of disease with negative margins is paramount in surgically treating PNETs. However complete surgical resection may not be possible when vital structures are involved. Because of limited number of cases in the literature, the treatment of spinal PNETs is not yet defined. Right now, surgery remains the mainstay of the treatment with the goal of both decompression and diagnosis. Chemotherapy and radiation are necessary aides in the treatment and they increase the survival by 2 years.[14]

Conclusion

Spinal extradural PNET are vere rare. Due to deficiency of clinical and radiological specificity, these tumors should be included in the differential diagnosis of extradural mass lesions. Histopathological and Immunohistochemical examination are required to confirm the diagnosis. Due to limited cases in literature, exact treatment of such tumors is not well formulated. Further research into the molecular pathogenesis of PNET and its probable application in immunotherapy is vital for development of more effective treatment for this condition.

Conflict of Interest: None.

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How to cite this article: RC Sasturkar, Deginal A, MH Prabhu. Primitive neuroectodermal tumor of spine - A case report. *J Diagn Pathol Oncol* 2019;4(2):156-158.