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CASE REPORT

An inflammatory pseudotumor in the thoracic epidural space presenting with progressive paraplegia: a histopathological diagnosis with clinical and radiological uncertainty. Case report with literature review

Vijayanth Kanagaraju[1] · Dinakar Rai[1] · Raghu Veer Chander Alluri[1] · C. Prasanna[1] · V. Shyam Sundar[1] · S. M. Arvind Kumar[1] · N. Venkatesh Kumar[1]

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Abstract
Introduction Inflammatory pseudotumors (IPTs) are benign lesions with unknown etiology, probably an immunological reaction to a traumatic or an infective insult or sometimes considered as an IgG4-related autoimmune disorder. It can occur as an isolated or multi-centric lesion and are reported to involve almost all parts of the human body. Although lung and orbital IPTs are reported commonly, central nervous system involvement is a rare occurrence. Only seven cases of spinal epidural IPTs have been reported to date. These are clinically and radiologically a diagnosis of exclusion. It is an exclusive histopathological diagnosis.
Case report We present here a 49-year-old female with 2 months history of progressive weakness in lower limbs, with no history suggestive of any traumatic, infective, inflammatory, or neoplastic pathology. Both clinical and radiological investigations were inconclusive. There was a mass lesion in the epidural space (predominantly in the posterior and right lateral space) at T1–T3 vertebral levels compressing the thoracic spinal cord. Considering the progressive nature of her neurological deficit, an emergency decompressive laminectomies of T1–T3 vertebrae were done with excision of the compressive mass lesion. Histopathological examination showed a rich lympho-plasmacytic cell infiltrates with storiform spindle cells and dense fibrosis, which was diagnostic of IPT. Post-operatively there was a rapid recovery in neurology and she became ambulatory at the end of 2 weeks. The purpose of this case report is to discuss the clinical, histopathological and radiological features, differential diagnosis, management, and prognosis of spinal IPT on the background of relevant literature review.

Keywords Inflammatory pseudotumor · Lympho-plasmacytic infiltrates · IgG4 · Fibro-inflammatory · Decompressive laminectomies

Case description

A 49-year-old female, presented in our neurology out-patient department with complaints of progressive weakness in lower limbs, developed over the past 2 months. Patient is a known diabetic since 14 years, on oral hypoglycemic medicines, with no other co-morbidities. The onset of weakness in lower limbs was spontaneous and acute in nature. There was no history of trauma or any constitutional symptoms or loss of weight and appetite. The weakness was preceded by numbness in the abdominal wall and lower limbs. Gradually, patient developed symptoms of gait instability and clumsiness while walking. The lower limb neurological status was gradually deteriorating and ambulation was restricted in the last 20 days. There was a rapid deterioration in her lower limb neurological status in the last 2 days, which forced her to consult here. The weakness was asymmetrical with right lower limb more involved than the left. On examination, the power in right lower limb was MRC grade 0/5 (Medical Research Council grading) and left lower limb was variable with hip flexors and adductors 3/5, knee extensors 4/5 and ankle and toe flexors and extensors 5/5. Her right side abdominal muscles were comparatively weaker than the left side, with absent superficial abdominal reflexes on both sides. Similarly, pin prick sensation on left side and light touch sensations on

✉ Vijayanth Kanagaraju
vijayanthorthospine@gmail.com

[1] Department of Orthopaedics and Spine Surgery, PSG Institute of Medical Sciences and Research, Coimbatore 641 004, India

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right side were impaired from lower anterior chest wall at around T4 dermatome, more like a Brown-Sequard syndrome picture. Deep tendon reflexes in lower limbs were exaggerated with bilateral plantar extensor response. She had no complaints of localized spinal pain or tenderness on examination. Her higher mental functions were normal. She showed no signs of respiratory distress and her breathing pattern were normal. She also had complaints of constipation but no urinary incontinence. Her peri-anal sensation was impaired but voluntary anal contraction was normal. She had facial puffiness with diffuse anterior neck fullness and her thyroid profile confirmed hypothyroid status.

Diagnostic imaging

After complete neurological assessment, patient underwent radiological evaluation. X-ray spine was normal but Magnetic Resonance Imaging (MRI) showed hypointense lesion in both T1- and T2-weighed images almost encircling (more in the posterior and right lateral epidural space) and compressing the dura and the thoracic cord opposite to T1, T2, and T3 vertebrae. There was no evidence of discovertebral signal intensity changes or pre-para vertebral collection (Fig. 1). With post-contrast T1-weighed image, the lesion was homogeneously enhancing (Fig. 2).

In view of thoracic compressive myelopathy and progressing neurological deficit, patient was shifted to orthopedic side for surgical management. A comprehensive clinico-radiological evaluation was done by us in consultation with our radiologists. But a precise preoperative diagnosis could not be established. The preoperative differential diagnosis that was considered included an epidural metastasis, lymphoma, myeloma, spontaneous epidural abscess, or hematoma. But none of the imaging findings and blood picture were conclusive.

Procedure done and histopathological findings

Since there was a progressive neurological deficit, we proceeded with surgery, wherein we did decompressive laminectomies of T1, T2, and T3 vertebrae, preserving the posterior facet joints. A pale brown fleshy mass measuring 0.9–3.5 cm and another small mass of 0.5 × 0.5 cm were excised from the posterior and postero-lateral epidural space. The mass was not infiltrative and was neither adherent to the dura mater nor to the bone and was relatively avascular. These intra-operative characteristics were suggestive of a non-malignant lesion. For our surgical convenience and to avoid cord manipulation, a small postero-lateral mass was excised separately from the main posterior mass, which was excised in toto. The excised specimen was sent for histopathological examination (HPE) (Fig. 3). HPE showed an un-encapsulated fibro-inflammatory lesion, extending focally into the surrounding fat (Fig. 4). The inflammatory components were predominantly lymphoplasmacytic in nature with an admixture of neutrophils, foamy histiocytes, and eosinophils. The connective tissue component varied in cellularity consisting of spindle cells in storiform pattern and a dense pattern of collagen with hyalinization. Lymphoid aggregates and blood vessels were scattered in the lesion, with no evidence

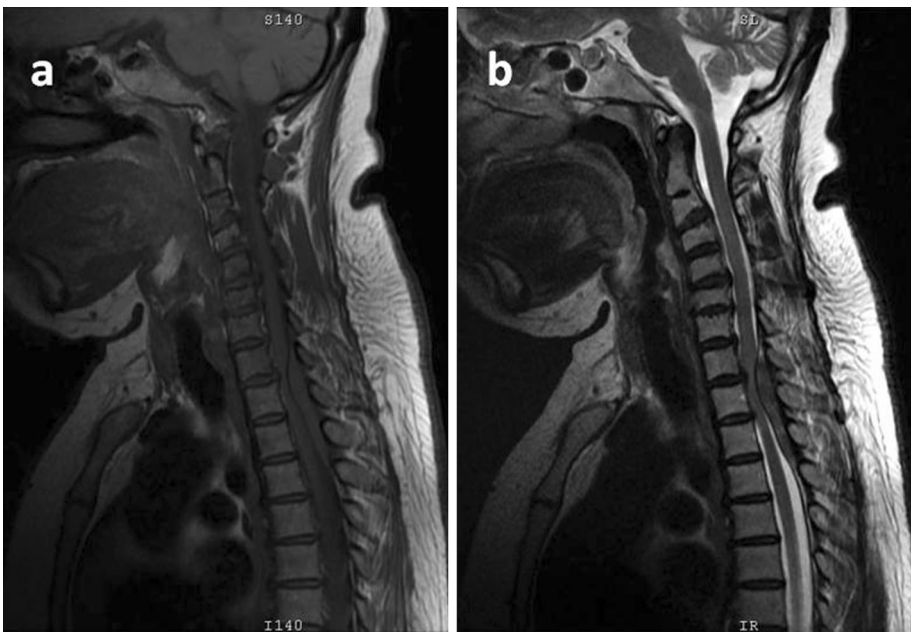

Fig. 1 Homogeneously hypointense epidural lesion in T1-weighted sagittal MRI sequence (**a**) and heterogeneously lesion in T2-weighted sagittal sequence (**b**)

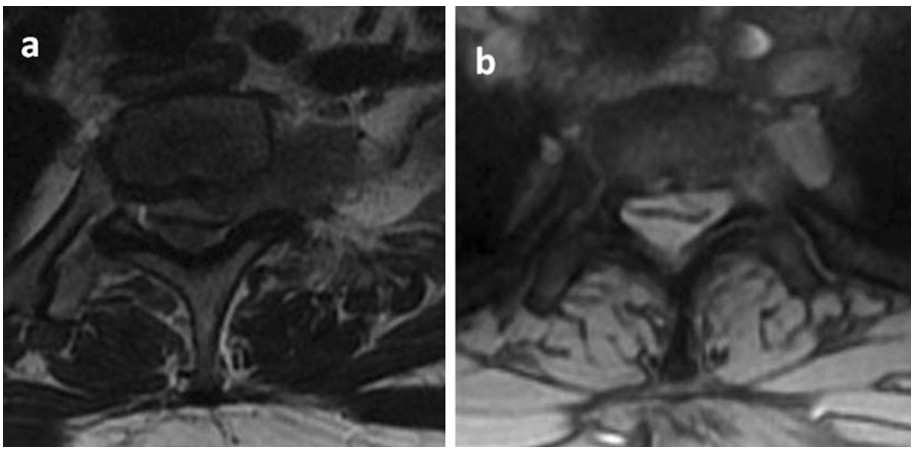

Fig. 2 T1 axial MRI image showing hypointense epidural lesion encircling and compressing the dura (**a**) and becomes homogeneously hyperintense on T1 post-contrast

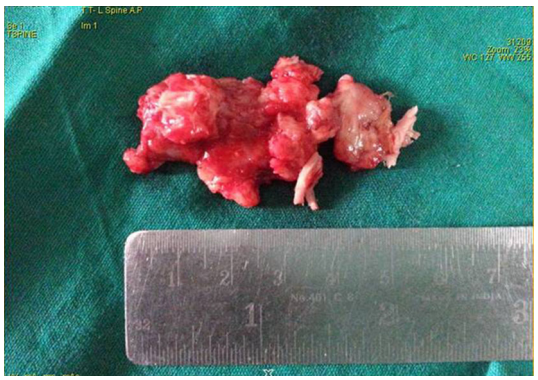

Fig. 3 A *pale brown* fleshy mass measuring 0.9–3.5 cm and another small mass measuring 0.5 × 0.5 cm were excised from the postero-lateral epidural space

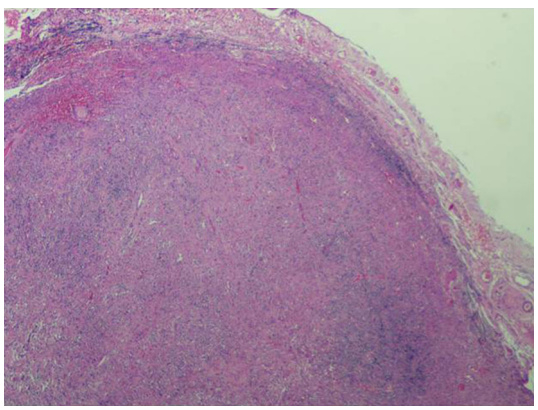

Fig. 4 4 × 10 magnified view shows a thin capsule with inflammatory cell collection

of occlusive phlebitis or mitotic activity or nuclear atypia (Fig. 5). The pathological diagnosis was inflammatory pseudo tumor (IPT). Search for lesions in other areas of the body by ultrasound and MRI turned out to be negative. Her serum IgG4 levels were normal, and IgG4 staining of plasma cells in the histopathological specimen was also negative. Post-operatively, fine needle aspiration cytology (FNAC) of thyroid mass under ultrasound guidance was done and showed no evidence of malignancy or thyroiditis. She was also given a course of oral steroids for 2 months till her neurology became normal and later-on gradually tapered. Steroids were given to take care of small residual lesions and to prevent recurrence as it was proved to be useful in other extra-spinal IPTs [1, 3, 24].

Historical review of the condition, epidemiology, diagnosis, pathology, differential diagnosis

IPT is a rare, histologically benign condition that mimics a malignant lesion clinico-radiologically, but usually are non-fatal. It was first observed by Brunn in 1939 as a lesion in lung and was named as IPT by Umirker in 1954. It most commonly involves lungs and orbit but also reported to occur in any site or organ system [1].

Etiology is still unknown. IPT has been considered as either a primary immunologic lesion or a fibro-genetic disorder or a specific reaction secondary to infectious agents, adjacent necrosis, or neoplasm [2]. Some IPTs have been associated with IgG4-related sclerosing disease, a systemic disease in which there is extensive IgG4-positive plasma cells and T cell infiltration of various tissues. This has been found commonly with autoimmune pancreatitis [3]. It is possible that many different etiologies might produce the same histological pattern. In other words, the features of IPT might depend not on its causal agent, but rather on the modality of response to the agent [4]. IPT is also reported in literature by various terminologies like plasma cell granuloma and inflammatory myofibroblastic tumor (IMT). Although IMT has a histology similar to IPT, it is considered as a different entity recently and recognized as a spindle cell neoplasm related to anaplastic lymphoma

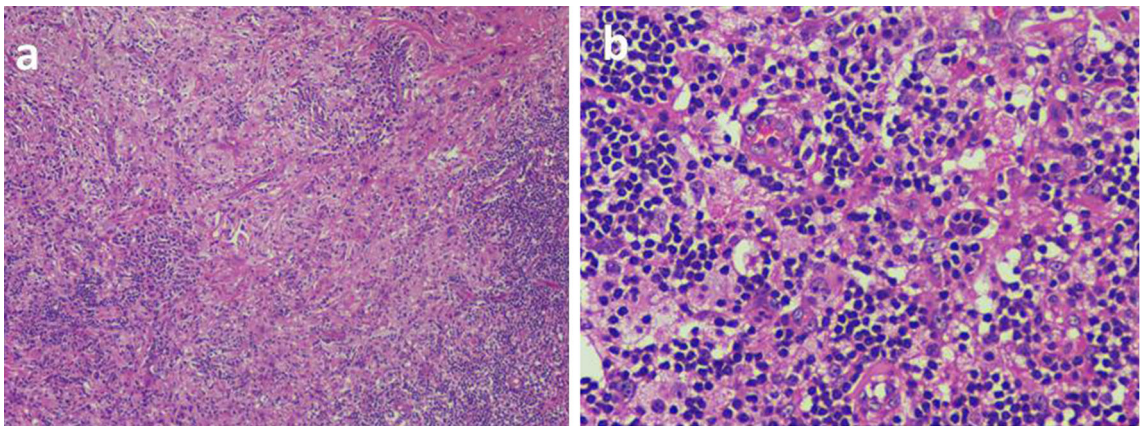

Fig. 5 **a** 10 × 10 magnified view shows lymphoid aggregates and inflammatory cell infiltrate. **b** 40 × 10 magnified view shows rich lymphoplasmacytic infiltrates (plasma cells, eosinophils, macrophages, and lymphocytes) with storiform arrangement of spindle cells and dense fibrosis

kinase (ALK) receptor tyrosine kinase gene located on 2p23 chromosome [5].

There is no distinguishing MRI diagnostic feature suggestive of IPT. It is basically a diagnosis of exclusion. Usually, IPTs are hypointense in both T1- and T2-weighed MRI images showing strong enhancement with gadolinium contrast, as seen in our patient (Fig. 1). But this was not uniform in all reported cases. Seol et al. have speculated that the signal intensity on T2-weighed images is dependant on the degree of inflammatory cell population and fibrotic lesion within the IPT. The areas with abundant inflammatory cells could be hyperintense on T2-weighed images; on the contrary pauci-cellular and fibrotic areas might be hypointense [6].

When the preoperative MRI reveals an epidural mass with no bony destruction and a normal fatty marrow, as in our patient, consider IPT in the differential diagnosis. The common differential diagnosis for a spinal epidural IPT includes lymphoma, metastatic tumors, multiple myeloma, meningioma, epidural abscess, and hematoma. Biopsy and HPE are diagnostic. Lymphoma usually consists of single lineage lymphocytes, either T cells or B cells, whereas IPTs consist of both T cells and B cells. Also lymphoma, metastasis, and myeloma show hypo-intensity on T1 and inhomogeneous hyper-intensity on T2-weighed images with signal intensity changes in the vertebrae with or without bony destruction. Meningiomas are mostly iso-intense with spinal cord on both T1- and T2-weighed images with moderately homogeneous enhancement with contrast. Most meningiomas show a dural tail sign [6]. Epidural abscesses are hypointense on T1 and hyperintense on T2-weighed images with a peripheral rim enhancement on contrast administration [7], and acute spinal epidural hematoma is iso-intense on T1 and heterogeneously hyperintense with focal hypo-intensity on T2 weighed images and shows peripheral enhancement with contrast [8].

Histologically, an IPT contains cells associated with both acute and chronic inflammation such as lymphocytes, plasma cells, myofibroblastic spindle cells, and collagen fibers [3]. Recently in the consensus statement on the pathology of IgG4-related IPTs, experts have formulated a criteria for its diagnosis based in HPE which includes dense lympho-plasmacytic infiltrates, storiform fibrosis, and obliterative phlebitis. With two out of the above three HPE findings is considered diagnostic for IgG4 related IPT [9]. The HPE finding in our patient well suited these diagnostic criteria, showing rich lympho-plasmacytic infiltrates with storiform arrangement of spindle cell and dense fibrosis (Fig. 5).

To date in literature, only seven cases of spinal epidural IPT have been reported [6, 10–14]. Among the seven cases of IPTs, two were reported in the cervical spine [11, 13] and five in the thoracic spine [6, 10, 12–14]. One patient had an association with multifocal fibro-sclerosis [11], another associated with polymyalgia rheumatica [14], two cases reported to be associated with giant cell arteritis [13], whereas other three cases presented denova with no association with any systemic inflammatory disorders [6, 10, 12]. Our patient presented with IPT at upper thoracic level and was associated with hypothyroidism, but FNAC of the thyroid mass has not proven any inflammatory pathology, so it was considered co-incidental. Few cases of intra-dural IPTs have also been reported [15–24].

Rationale for treatment and evidence-based literature

Surgical excision is the best way to reach a precise diagnosis, as radiological findings cannot differentiate the IPTs from other epidural space-occupying lesions. Other treatments such as steroid therapy, antibiotics, radiotherapy,

chemotherapy, or carbon-di-oxide laser have been tested on extra-spinal IPTs, with variable results [24]. Orbital IPTs have been reported to regress with high doses of systemic steroids alone [1, 3]. But in case of progressive neurological deficit, surgical excision of the spinal epidural compressive lesion (IPT) is mandatory to establish a histopathological diagnosis and simultaneously decompress the spinal cord from mass effect and to allow neurological recovery [14]. Chance of neurological recovery after excision and decompression of spinal epidural IPT is reported to be excellent [10–14]. Cyclophosphamide-induced remission in steroid-resistant cases of epidural IPTs was also reported [25]. Although IPTs are benign, literature has shown it to recur in 20–25 % of cases in extra-spinal locations [1, 3].

Outcome, follow-up

Her neurological recovery after surgery was excellent. Post-operatively physiotherapy was started. She showed signs of neurological recovery by the fifth post-operative day, which gradually improved. She started ambulating with support by 2 weeks post-operatively and independent by 2 months. At final follow-up after 1 year, she was asymptomatic, though radiological or MRI evaluation was not done to prove recurrence.

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Conflict of interest None of the authors have any potential conflict of interest.

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