A Young Male with Paraplegia, Massive Cervical Adenopathy and Nondiagnostic Biopsy Specimens

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Abstract
An 18-year-old man presenting with paraplegia due to spinal epidural infiltration at D6-D7 underwent laminectomy and spinal decompression followed by near-complete resolution of neurological symptoms; but this resolution was followed by progressively enlarging cervical lymph nodes. Leucocytosis, an elevated erythrocyte sedimentation rate, a marked polyclonal hypergammaglobulinemia and a moderate hepatosplenomegaly were found. The diagnosis of sinus histiocytosis with massive lymphadenopathy (SHML), also known as Rosai-Dorfman disease was established histologically by lymph node biopsy about 2 years after presentation.

INTRODUCTION
Sinus histiocytosis with massive lymphadenopathy (SHML) known as Rosai-Dorfman disease is a rare pathological entity of unknown aetiology characterised by massive, painless cervical lymph node enlargement. Extranodal involvement occurs in 25% to 43% and affects the skin (12%), paranasal sinuses (11%), soft tissue (9%), bone (9%), salivary gland (5%), oral cavity (3%), kidney (2%), lower respiratory tract (2%), larynx (1%) and but rarely other locations. CNS involvement is extremely rare.

We report here a case of sinus histiocytosis with massive lymphadenopathy that presented initially with paraplegia due to spinal epidural involvement and subsequently with massive swelling of the cervical lymph nodes.

CASE REPORT
A 18-year-old man with weakness of both lower limbs for 2 years and neck swellings for 16 months was admitted for evaluation.

He was apparently well till 2 years back, when he developed back pain followed over the next several months by progressive weakness of both lower limbs, difficulty in micturation and severe constipation. MRI of dorsal spine done four months into his illness showed fairly large extradural lesion at the D6-7 level with secondary canal narrowing and pressure on cord (Fig. 1). He was started on anti-tubercular drugs (ATDs) elsewhere and was admitted in the neurosurgery department as his symptoms worsened, about 8 months into his illness.

Neurological examination revealed normal cranial nerve function, sensory loss below the level of D5-6 dermatome and spastic paraplegia. Other system examinations were normal except for several 2-3 cm lymph nodes on both sides of the neck. A laminectomy carried out from the D5-D7 vertebrae revealed an

![Fig. 1: MRI of dorsal spine four months into his illness showing fairly large extradural lesion at the D6-7 level with secondary canal narrowing and pressure on cord.](image)
epideral, un-encapsulated, posteriorly placed tumor, which was removed.

Histological examination was reported as focal accumulation of lymphocytes, oedema and a large number of foamy histiocytes in broad sheets; no specific granuloma or evidence of malignancy was found.

His postoperative course was uneventful and within a month the patient was walking without support and had regained bladder control. But his neck glands continued to enlarge and ATDs, which were stopped before laminectomy, were restarted.

Over the next year or so the lymph nodes enlarged in size (Fig. 2) causing mechanical problems like difficulty in opening his mouth. He had significant weight loss and episodes of low-grade fever. During this period he underwent 3 cervical lymph node excision biopsies and 2 FNACs - most reported “non specific hyperplasia of lymph node”.

The patient had no history of haemoptysis, chest pain, hoarseness of voice, diabetes mellitus, hypertension, arthritis, skin rash or pruritus. There was no h/o contact with pulmonary tuberculosis or any risk factor for HIV.

Examination revealed pallor, poor nutrition and multiple lymph nodes on both sides of neck, which were firm, non tender, some matted and ranging in size from 1cm to 5-6cms. The liver was enlarged 3 cms in the mid clavicular line and the spleen 5 cm along its axis. Sternal tenderness was absent.

Neurological examination revealed increased tone in both lower limbs with normal power, both knee and ankle jerks were exaggerated and the plantars were extensor. There was no sensory deficit. Other system examinations were normal.

Laboratory investigations showed anemia (Hb: 9.5/dl), leucocytosis (25,000/mm³) with neutrophilia (84%) raised ESR (160mm) and negative HIV serology. Chest radiograph was normal. Ultra-sound examination of abdomen showed hepatosplenomegaly with multiple retroperitoneal lymphadenopathy. CT scan of thorax with contrast showed bilateral para vertebral enhancing of soft tissue masses around D₃-D₄ downwards involving adjacent pleural surface and posterior mediastinum encasing the descending aorta. Bone marrow examination revealed reactive marrow and serum protein electrophoresis showed polyclonal hyper gamma globulinemia (no ‘M’ band).

A cervical lymph node excision biopsy revealed marked dilatation of the sinuses resulting in effacement of nodal architecture. These sinuses were occupied by numerous histiocytes along with lymphocytes, plasma cells and a few polymorphs. Many of the histiocytes showed lymphocyte explain emperipolesis (Fig. 3) which is characteristic of sinus histiocytosis with massive lymphadenopathy, SHML (Rosai-Dorfman’s disease).

He received monthly cycles of chemotherapy consisting of inj vincristine 2mg iv on days 1 and 8 and tab prednisolone 40 mg daily from day 1 to day 15. At the end of the 7th cycle of chemotherapy his lymph nodes showed considerable regression in size (Fig. 4). But he developed peripheral neuropathy and therefore chemotherapy was withheld. He is presently on follow-up.

**DISCUSSION**

Rosai and Dorfman¹ described the triad of massive cervical lymphadenopathy, expanded lymph node sinuses, and characteristic histiocytes showing emperipolesis as a novel entity among the histiocytosis. Lymphocytophagocytosis (emperipolesis) describes the presence of lymphocytes within the histiocytes. The active phagocyte is a histiocyte that is positive for s-100 protein, CD₁₄; and the histiocytic proliferation is polyclonal.²

Sinus histiocytosis with massive lymphadenopathy (SHML) is a rare, self-limiting disorder of unknown

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**Fig. 2 : Massive cervical adenopathy.**

**Fig. 3 : Lymph node biopsy (high power view: magnification 400) showing lymphocyte emperipolesis.**
aetiology more common in children and young adults than in other age groups. Though usually non-progressive, the disease in association with invasion of critical structures can cause significant morbidity and even death.1,3

The typical presentation is with bulky, bilateral, painless, cervical adenopathy either alone or associated with lymphadenopathy elsewhere.2 Extra-nodal disease is present in about 43% of patients3 especially in the head and neck region, involving the skin, soft tissue, orbit, lacrimal glands, paranasal sinuses, thyroid or oral cavity. The respiratory tract, breast, mediastinum, thymus, heart, liver, kidney, testes, synovia, bone meninges and spinal cord may also be involved.3

Patients often have signs of chronic inflammation in the form of anemia, neutrophilia, raised ESR and polyclonal hypergammaglobulinemia2 as in our patient, and marrow is not involved.

Involvement of the CNS is rare with 44-reported cases4 but relapsing/recurring course can become a serious problem.5 In our patient the dominant symptom at presentation was paraplegia. Paraplegia secondary to epidural involvement is a rarity. It has been described in less than 10 of the reported cases of CNS tumors. After laminectomy, bulky cervical lymph nodes became the major presenting complaint, leading to multiple lymph node biopsies (which were inconclusive) followed by ATD course presumably as a therapeutic trial.

As the previous biopsy blocks were not available, the patient was subjected to a fourth biopsy and the problem was discussed with the pathologist.

The histopathologic features showed distention and engorgement of medullary and subcapsular sinusoids by phagocytic histiocytes with lymphophagocytosis and erythrophagocytosis by histiocytes in the lymph node sinus. These are characteristic of RDD.2,3 On review of the histopathologic slide of the laminectomy tissue, identical evidence of lymphophagocytosis was found (Fig. 5).

One of the diagnostic dilemmas of RDD is that the pathologist often mistakes the histopathologic features as atypical/reactive lymph node hyperplasia. Our patient needed 5 biopsies to come to a diagnosis. Immune-staining is helpful as the phagocytic histiocyte is positive for s-100 protein and CD68. The histological picture of extra-nodal biopsies is strikingly similar to that of lymph nodes.

Though in most cases lymph node enlargement may progress for weeks or months and then recede by 9 to 18 months5 with no or little evidence of disease, in our patient the lymph nodes persisted and progressed at 18 months causing difficulty in opening the month and chewing.

Glucocorticoids, cytotoxic agents, radiotherapy do not have consistent effect on the duration of the disease6 so treatment is usually reserved for special circumstances like tracheal or epidural compression. Surgical debulking or radiotherapy can be performed.

Although paraparesis improved with surgical debulking, in view of the patient’s progressive difficulty in opening the mouth and cosmetic disfigurement due to the massive lymphadenopathy, he was considered for chemotherapy. Since the literature shows no single chemotherapy regime to be more beneficial than others, he was put on the above trial regime that showed considerable short-term benefits. He is currently on follow-up after development of chemotherapy induced peripheral neuropathy.

Presentation with paraplegia followed by massive cervical lymphadenopathy is an extremely rare manifestation of this polyclonal non-malignant but...
invasive histiocytic proliferative disorder known as Rosai Dorfman disease.

REFERENCES

Book Review
Management of Acute Pancreatitis
Shirish K Bhansali and Sharad C Shah

There are very few books exclusively dealing with acute pancreatopathies across the globe. Two well known senior consultants Prof S C Shah the gastroenterologist and Shirish K Bhansali the Surgeon combine their lifetime experience with current evidence base from the Indian subcontinent how they dealt with this difficult problem. The book has the whole Jaslok hospital faculty (which has published the book) with some leading Indian luminaries contributing their personal experiences. Its forward is written by one of the global giants in pancreas in the US Prof CS Pitchumoni who is well known to both the editors.

This book is meant to be an advanced referral manual. After a brief introduction of the well-accepted Atlanta Classification, it encompasses the vast personal experience of pancreatologists from Indian with a healthy blend of distillate from world literature. The benign, self-limiting course of Mild Acute Pancreatitis is reiterated. Aggressive ICU treatment of Severe Acute Pancreatitis to resuscitate the patient, minimize organ dysfunction, retard the progression of necrosis and prevention of infection are stressed. Changing trends in the management of the causative biliary lithiasis are dwelt upon. Benefits of delaying surgery for Infected Pancreatic Necrosis (IPN) and the modalities to achieve this are discussed. Current gold standard conventional surgery for IPN and the increasing beneficial role of Minimal Access Surgery as well as its limitations are deliberated. Evolving status of treatment of complications of the disease as well as postoperative complications have been evaluated. The utility of interventional radiology, especially for therapy is highlighted. Finally, based on current scenario, future directions for this multifaceted disease are postulated.

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