P U L S E

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## In Focus

Meningioangiomatosis: A Clinicoradiological and Histopathological Challenge 1

## Case Report

1. The Contribution of the ‘Fourth’ Major Hemoglobin Peak in High Performance Liquid Chromatography in the Diagnosis of qDouble Heterozygotes of Alpha and Beta Globin Chain Variants 5
2. Microfilariae in an Encysted Pleural Haemothorax 7
3. Hepatosplenic T-cell Lymphoma; A Clinical Diagnostic Challenge 9
4. Langerhan’s Cell Histiocytosis of Lymph Node in an Adult Female – A Rare Presentation 11

## Brain Teasers

13

## Some of Our Recent Activities

- Recent Publications from SRL 14
Dear Friends,

“The whole is greater than the sum of its parts.” — Aristotle

With gratification, we put forth this 21st issue of Pulse, our biannual newsletter; an assemblage of the empirical and scientific contribution by the doctors, technical and scientific staff of SRL which gives glimpses of our journey through this second part of the year. Despite a hectic professional life at SRL that we continue to maintain our passion for research and publication, is a testimony to the legacy of this organization.

Dr. Sunita Ahlawat and her colleagues from Fortis Memorial Research Institute, Gurugram in this issue’s In Focus section present an infrequent entity of unclear origin, Meningioangiomatosis (MA), thought to be hamartomatous, maldevelopmental, reactive or neoplastic lesion of meningothelial, fibroblastic, myofibroblastic or pluripotent stem cells. Unless the pathologist is familiar with the histological features of MA, these features may lead to the erroneous diagnosis of malignancy and unnecessary aggressive treatment.

The Medical Case Reports section this time comprises of a wide range of topics including the significance of the ‘fourth’ major hemoglobin peak in high performance liquid chromatography in the diagnosis of double heterozygotes of alpha and beta globin chain variants, microfilariae in an encysted pleural haemothorax, the clinically diagnostic challenge of hepatosplenic t-cell lymphoma and a rare presentation of Langerhan’s cell histiocytosis of lymph node in an adult female.

We also have some Brain Teasers along with the list of the latest Publications in the last 6 months.

Pulse would be incomplete without the contribution of medical case reports, quizzes, and publications shared by our scientific leaders. I take this opportunity to thank each of the thought-leaders who has furnished a piece of their wisdom into the ocean of Pulse that sustains the newsletter. Also, heartfelt thanks to the editorial team and the support staff for continuing to put together one issue after another.

Hope this issue will bring to light some rare accounts that will be useful for the readers. I urge you all to come forward with your suggestions and looking forward to scientific contributions for the various sections of the future issues of Pulse.

Warm regards,

Dr. B. R. Das
Meningioangiomatosis: A Clinico-radiological and Histopathological Challenge

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Case Report
A 9 year old boy presented with chief complaints of intractable seizures for 3 years. There were focal seizures followed by secondary generalisation. He had postictal drowsiness with right hemiparesis. Seizures episode frequency was reduced on antiepileptics Carbamazepine and Sodium Valproate, but not completely controlled. There were no complaints of abnormal behaviour, decreased vision, double vision, decreased hearing, swallowing difficulty or change of voice. There was no weakness or numbness in limbs except postictal phenomenon. Neurological examination was normal with no cranial nerve, sensory or motor deficits. Non-contrast axial CT (Fig 1a) of the brain shows calcified lesion in the left posterior parietal region. Coronal FLAIR (b) MRI showed mixed intensity with perifocal edema lesion in left posterior region which does not show any restricted diffusion on axial diffusion imaging (c) and focal areas of enhancement on post contrast fat suppressed axial T1 weighted image (d). Intraoperatively the lesion was intraaxial with areas of calcifications. Histopathological examination showed extensive areas of nodular calcification in cerebral cortex with proliferating blood vessels (Fig 2a). There was perivascular cuffing of proliferating meningothelial cells and spindled fibroblasts (Fig 2b, 2c). The intervening cerebral cortex showed reactive gliosis with entrapped neurons having neurofibrillary tangles (Fig 2d). No mitosis, necrosis or cellular pleomorphism was noted. On immunohistochemistry, Neurofibrillary tangles were demonstrated by Neurofilament protein (Fig 3a). Proliferating vessels were highlighted by CD34 (Fig 3b), meningeal cells were focally positive for EMA (Fig 3c). The fibroblasts were also seen distinctly with Masson Trichrome stain (Fig 3d). Neurons highlighted by Neu N (Fig 3e) and Ki67 labelling index was <1% (Fig 3f). With morphological, clinico-radiological and immunohistochemical features a diagnosis of Meningioangiomatosis was made.

Fig 1: Radiological findings
Meningioangiomatosis first described in 1915 in association with NF2, was later named as “Meningioangiomatosis” in 1937 by Worster-Drought et al. (5). Although originally described in association with NF2, sporadic occurrence is more common than syndromic Meningioangiomatosis (6). The commonest clinical presentation is intractable seizures for quite some time as seen in our case also (7). Sporadic cases often present with a single clinically symptomatic lesion, while multiple asymptomatic lesions are seen in association with NF which may remain undiagnosed till autopsy (8). This lesion has been reported in all ages ranging from 14 months to 60 years, but the majority of cases are teenagers and young adults (9, 10, 11). MA associated with NF is found at early age than sporadic MA (12). The literature suggests higher occurrence in males and in the right hemisphere (13). Cerebral cortex is the most common affected site (14). Frontal, temporal, or parietal cortex are the common sites with some reports in the third ventricle, cingulate gyrus, and pulvinar (15).

The radiographic findings of MA are often variable. The presence of calcifications on CT and a low-signal intensity rim on T2-weighted MRI images are the most helpful features that suggest the diagnosis of MA (16). Histopathology shows two characteristic patterns - cellular and vascular. In cellular pattern there is proliferation of thin walled small caliber vessels in the cortex with predominant perivascular cuffing of meningotheelial cells and fibroblasts. However predominantly vascular cases show thick-walled, hyalinized and calcified blood vessels with minimal perivascular cell proliferation. The cortex between the vascular and meningotheelial proliferation either remains normal or shows reactive astrocytic changes. Leptomeningeal thickening is due to proliferation of meningeal cells.

The theory of histogenesis of the lesion is disputed. Various hypotheses suggest (i) MA is a cortical vascular malformation induces perivascular meningotheelial proliferation of cells from vessel walls or from pluripotent arachnoid cap cells in Virchow–Robin spaces (ii) MA is a hamartoma that undergoes degenerative changes (iii) MA results from invasion of brain tissue by a leptomeningeal meningioma, though not all cases have a meningeal component and features of malignancy are invariably absent (4, 17, 18). Recent studies show that loss of 22q12 (NF2 gene) and loss of heterozygosity have been found in pure MA and MA associated with meningioma, suggesting that MA may be neoplastic in nature (19).

The occurrence of MA in coexistence with meningioma (20, 21), vascular malformations (22), encephalocele (23), oligodendroglioma (24), and PNET (25) has been described. Among these, meningiomatosis with meningioma is the most frequent combination.

The differential diagnosis include invasive meningioma, intracortical schwannoma with other cortical tumours such as high grade glioma, gangliogioma,
dysembryoplastic neuroepithelial tumour (DNET), vascular tumors and metastasis. Most often confused entity of brain invasive meningioma has a high Ki67 index, mitosis and/or necrosis, nuclear pseudoinclusions which are typically absent in MA. Intracortical schwannoma is a rare lesion with a plexiform growth pattern, and two entities can be easily distinguished on immunohistochemistry. The presence of uniformly distributed small sized vessels with perivascular meningothelial and fibroblastic proliferation and lack of hemorrhage virtually excludes a vascular tumor or malformation. Immunohistochemistry is known to have a limited diagnostic value as staining patterns vary between cases (26). Only vimentin, as a non-specific marker of the mesenchymal cell is known to be consistently positive (27). Nonetheless, immunohistochemistry may aid in the exclusion of other differential diagnoses.

Total surgical removal is the treatment of choice, and after total excision recurrence is not known to occur (4, 21). The seizure-free rates after lesionectomy are variable with improvement in 43-68% of the cases, but almost 70-80% of the patients required continuing antiepileptic therapy (28).

Conclusion
Meningioangiomatosis is an infrequent entity, by large believed to be a benign slow growing lesion. A correct diagnosis may lead to appropriate surgery and a better prognostic reassurance. A clinicoradiological diagnosis is often not possible, and its openly a histopathological diagnosis with little contribution of immunohistochemistry. Unless the pathologist is familiar with the histological features of MA, these features may lead to the erroneous diagnosis of malignancy and unnecessary aggressive treatment.

References


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The Contribution of the ‘Fourth’ Major Hemoglobin Peak in High Performance Liquid Chromatography in the Diagnosis of Double Heterozygotes of Alpha and Beta Globin Chain Variants

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Summary
Diagnosis of hemoglobinopathies by high performance liquid chromatography (HPLC), although widely practiced, can be challenging. Cases of double heterozygosity for an alpha and a beta globin chain variant pose greater challenges in diagnosis under these circumstances. However, the presence of certain clues in the HPLC histogram point towards this possibility. We illustrate this fact by presenting two examples wherein the possibility of this combination was suggested by the presence of a ‘fourth’ peak representing an abnormal Hb produced by an in vivo combination of the abnormal alpha chain with the abnormal beta chain. The presence of this peak should alert the laboratory to investigate the patient for coinheritance of an alpha and a beta globin gene defect.

Background
HPLC is widely used for presumptive diagnosis of hemoglobinopathies. The elution of an abnormal hemoglobin (Hb) in a predefined window of retention time (RT) suggests its possible identity. However, a number of abnormal Hbs elute in the same RT window thereby posing problems in the differential diagnosis of these Hbs. Additional tests such as sickling and solubility test help in the diagnosis of HbS and to distinguish it from the other Hbs eluting in HbS window. In almost all situations, clinical and red blood cell parameters combined with the exact RT of the abnormal peak help in making a likely diagnosis. Finally though, recourse to molecular analysis is the only way to confirm the identity of the abnormal Hb. The HPLC histograms in cases of double heterozygotes for alpha and beta globin chain defects however, have tell-tale features that point towards the possible diagnosis (1). Here we present two such cases seen by us. We will use these cases to highlight the role of the four major Hb peaks, especially the ‘fourth peak’, in the diagnosis of double heterozygotes for alpha and beta globin chains.

Case Reports
Case 1 The patient is an 18 years old Sindhi female from Mumbai who was referred to our laboratory for investigation of anemia. The patient had a thalassemic blood picture - microcytic anemia with high RBC count. The patient’s parents could not be investigated. This case was diagnosed as a double heterozygote for HbQ India and HbD Punjab on HPLC.

Case 2 This is a 24 years old female from Madhya Pradesh who was investigated for the presence of a hemoglobinopathy. Unlike the first case, this patient had a normal CBC and red cell indices. Patient’s child and husband were also investigated by us. However, their findings are not being presented here. Interested readers are referred to reference number 2 of this article for this purpose. On HPLC the preliminary diagnosis in this case was a double heterozygote for an unknown alpha chain variant and HbS. The alpha chain variant was subsequently identified as HbO Indonesia on DNA sequencing.

The hemogram and HPLC findings of both the cases are shown in the table below.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Case 1 (HbD Punjab / HbQ India)</th>
<th>Case 2 (HbS/HbO Indonesia)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin [g/dl]</td>
<td>6.9</td>
<td>12.5</td>
</tr>
<tr>
<td>RBC count [10^6/l]</td>
<td>4.95</td>
<td>4.44</td>
</tr>
<tr>
<td>Hematocrit [%]</td>
<td>25.9</td>
<td>38.7</td>
</tr>
<tr>
<td>MCV [fl]</td>
<td>52.4</td>
<td>87.2</td>
</tr>
<tr>
<td>MCH [pg]</td>
<td>14.0</td>
<td>28.2</td>
</tr>
<tr>
<td>MCHC [g/dl]</td>
<td>26.8</td>
<td>32.3</td>
</tr>
<tr>
<td>RDW (CV)</td>
<td>21.9</td>
<td>11.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HPLC</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA (RT 2.45 mins)</td>
<td>50.3%</td>
<td>76.1%</td>
</tr>
<tr>
<td>HbA2 (RT 3.66 mins)</td>
<td>1%</td>
<td>2.7%</td>
</tr>
<tr>
<td>HbF (RT 1.1 mins)</td>
<td>0.2%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Beta chain variant</td>
<td>23.9% - HbD Punjab (RT 4.1 mins)</td>
<td>33.1% - HbS (RT 4.34 mins)</td>
</tr>
<tr>
<td>Alpha chain variant</td>
<td>10.8% - HbQ India (RT 4.7 mins)</td>
<td>6.6% - HbO Indonesia (RT 4.86 mins)</td>
</tr>
<tr>
<td>Hybrid Hb</td>
<td>5.1% - alpha HbQ/beta HbD hybrid (RT 4.95 mins)</td>
<td>4.6% - alpha HbO Indonesia/beta HbS hybrid (RT 5.15 mins)</td>
</tr>
</tbody>
</table>

Case 1 had anemia (Hb 6.9g/dl) and thalassemic red cell indices. Iron studies could not be done in this patient. The quantity of alpha chain variants in both the cases was low while that of the beta chain variants was in the expected range for heterozygous state. The levels of the hybrid Hbs were similar (5.1% and 4.6%) in the two cases.

Discussion
The HPLC histogram in the first case (Figure 1) highlights the presence of four main Hb peaks representing, HbA, HbD Punjab, HbQ India and a fourth hybrid Hb peak (from
left to right), the fourth peak being made of the abnormal alpha chain of HbQ India and the abnormal beta chain of HbD Punjab. The presence of the last named peak is a ‘give away’ as far as the possible diagnosis of an alpha and beta chain double heterozygous state is concerned since this is a typical finding in such cases. We reported a similar observation in a double heterozygote for HbO Indonesia (a rare alpha chain variant) and HbS in a patient from Madhya Pradesh (case 2; Figure 2) (2). Laboratories performing Hb HPLC can use this information to make a preliminary diagnosis of a double heterozygote for an alpha and a beta globin chain variant.

It is noteworthy that double heterozygotes for alpha and beta globin chain variants such as the ones described here always have a good amount of HbA (Table 1, Figures 1 & 2) produced by two normal alpha globin genes (out of four) and one normal beta globin gene (out of two). In contrast, in double heterozygotes for beta globin chain defects no HbA is produced since both beta globin genes are defective. Therefore, in the former example there are four major Hb peaks in HPLC while only two peaks are seen in the latter. This histographic pattern in HPLC is an important clue for distinguishing between these two groups of conditions.

Unlike the cases of double heterozygotes for HbQ India and HbD Punjab reported earlier (1), our patient (case 1) had a thalassemic red cell profile in CBC along with a low Hb (Table 1). This could be multifactorial in origin such as co-inheritance of a thalassemic globin gene defect such as alpha thalassemia, accompanied by iron deficiency. In the study reported by Harrison et al. (3), a very small number of cases of HbQ India trait had mild anemia and thalassemic red cell indices and these patients were found to have concomitant iron deficiency. Our case was not investigated for iron deficiency. Similarly HbD Punjab trait is not associated with anemia or microcytic red cell indices. However, it is possible that the combined effect of double heterozygocity for HbQ India and HbD Punjab could cause a thalassemic red cell profile when associated with iron deficiency.

References

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Microfilariae in an Encysted Pleural Haemothorax

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Summary
Filarial infection in India is endemic. The parasite has been identified in different kinds of cytologic specimens of which few cases of pleural effusions with microfilariae have been reported. We report a case of a 71-year-old man presenting with chest pain and breathlessness showing an encysted pleural effusion on imaging studies. On aspiration of this effusion was haemorrhagic and the smears studied showed microfilariae. Microfilariae was not found in the peripheral blood. The patient had a mild peripheral eosinophilia and circulating filarial antigen test was positive. Our case shows that filariasis can be seen within a haemothorax even though few cases have been reported.

Keywords
microfilariae, pleural effusion, haemothorax

Background
Filariasis is a common parasitic disease in India. Filariasis is endemic in 17 states and six union territories, with about 553 million people at risk of infection (1). Microfilariae have been detected in many different types of cytology specimens, but its presence in pleural fluid is rare and unusual.

Case Presentation
A 71-year-old male presented in the emergency department with chest pain since 10-15 days, breathlessness, generalized body weakness and burning micturition. He was a known case of type 2 diabetes mellitus, hypertension and chronic renal disease on dialysis.

Investigations
On admission his Hemoglobin was 8.5 g/dl, WBC count 5800 cells/µl, Platelet count 192,000/µl, differential leucocyte count was 69% neutrophils, 8% eosinophils, 17% lymphocytes and 6% monocytes. His creatinine levels were elevated at 4.17 mg/dl, Blood urea nitrogen 49 mg/dl, sodium 131 mmol/l, potassium 5.24 mmol/l, Troponin T-HS 31 pg/ml and CKMB level was 20.1 U/l.

HRCT chest revealed multiple centrilobular nodules in both the lungs with tree in bud appearance at places. Interlobular septal thickening was seen in both the lungs. An encysted pleural collection in left lower zone, posteriorly with heterogenous attenuation and calcific foci was seen. It measured 6.6x12.4x11.9 cm in size. Passive partial collapse of left lower lobe was seen with calcific foci. The overall impression give on CT was that of an encysted pleural collection - chronic haemothorax, hydrostatic edema with active chest infection.

An ultrasound guided aspiration of the encysted pleural effusion was done. 3 ml of haemorrhagic fluid was obtained. Smears were prepared and the remaining fluid was sent for microbiological tests. The sample clotted very quickly and biochemical tests could not be performed. Cytological examination of the smears revealed microfilariae of Wuchereria bancrofti against a hemorrhagic background along with neutrophils and few eosinophils.

Aerobic culture, PCR and culture for Tuberculosis were performed on the remaining fluid which did not show positive results. The patient’s peripheral blood was examined for microfilariae, however, they were not detected.

Rapid Filaria Antigen testing was done which turned out to be positive. Filarial IgG levels were detected but IgM levels were not detected. Bronchoalveolar lavage fluid did not show any microfilariae.
**Treatment and Outcome**

The patient was started on diethyl carbamazine, 100 mg twice a day along with doxycycline 100 mg twice a day. The patient showed improvement with this treatment.

**Discussion**

Filarial parasites are thread like worms which are found mainly in the lymphatic and circulatory systems, but can also be found in muscles, connective tissue and serous cavities (2). Lymphatic filariasis caused by Wuchereria bancrofti and Brugia malayi is an important public health problem in India. The Government of India has accorded a high priority for elimination of this infection through mass chemotherapy programme (annual, single dose of Diethylcarbamazine citrate, i.e. DEC- 6 mg/kg of bodyweight, plus Albendazole repeated four to six times) (1). Apart from peripheral blood, Microfilaria can be found in aspirated material from lymph nodes, breast lump, cutaneous swellings, cervicovaginal smears, effusions, urine, bronchial washings and ovarian cyst fluid (3, 4). Detection of microfilariae in pleural effusions is not a common finding. Jyotima et al (5) detected microfilariae in straw coloured pleural effusion of a case previously treated as tuberculosis. Microfilariae were not detected in the peripheral blood of this patient. Shukla et al detected microfilariae in the pleural fluid of a 58-year-old man who presented with left side chest pain and breathlessness. This patient did not have a peripheral blood eosinophilia (6). A case of metastatic adenocarcinoma in the pleural cavity with coexistent microfilaria in the pleural effusion was reported by SK Singh et al (7).

At present three laboratory methods are used to diagnose active infections with Wuchereria bancrofti. They are detecting microfilariae in night blood specimens, detecting circulating filarial antigens released in the blood by adult worms and detection of filarial DNA in blood by polymerase chain reaction (PCR). Antigen testing is most widely used at this time because it is more sensitive and convenient for detecting infection than microfilaria testing or PCR (8). The circulating filarial antigen (CFA) test is regarded as a “gold standard” by World Health Organization for diagnosis of lymphatic filariasis. In the absence of evidence of presence of microfilariae in the peripheral blood of the patient, the detection of CFA in this case only served to strengthen the diagnosis.

**Learning Points**

- Apart from peripheral blood, Microfilaria can be found in aspirated material from lymph nodes, breast lump, cutaneous swellings, cervicovaginal smears, effusions, urine, bronchial washings and ovarian cyst fluid (3, 4).
- Our case shows that filariasis can be seen within a haemothorax even though few cases have been reported.
- Antigen testing is most widely used at this time because it is more sensitive and convenient for detecting infection than microfilaria testing or PCR (8). The circulating filarial antigen (CFA) test is regarded as a “gold standard” by World Health Organization for diagnosis of lymphatic filariasis.
- In the absence of evidence of presence of microfilariae in the peripheral blood of the patient, the detection of CFA in our case only served to strengthen the diagnosis.

**References**

4. Subrata pal, Sajeeb Mondal, Rajashree Pradhan, et al. Cytological findings of microfilariae in different...


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Hepatosplenic T-cell Lymphoma; A Clinical Diagnostic Challenge

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Department of Gastroenterology, Fortis Escorts Heart Institute, Okhla Road, New Delhi

Abstract
Hepatosplenic T cell lymphoma (HSTCL) is rare variant of T cell lymphoma and comprises less than 5% of all peripheral T cell lymphomas. These lymphomas have an aggressive course and dismal prognosis. We report a case of a 28 year old male who presented with repeated episodes of fever and abdominal pain. USG revealed hepatosplenomegaly. Liver biopsy performed showed sinusoidal lymphoid cell infiltration of T cell immunophenotype with aberrant antigen loss. The case was finally diagnosed as Hepatosplenic T Cell Lymphoma.

Introduction
Hepatosplenic T cell lymphoma is very rare type of T cell Non Hodgkins Lymphoma. These lymphomas are characterized by primarily involving the liver and spleen with relative sparing of lymph nodes. Bone marrow involvement is usually seen. Most of these cases are seen in young and adolescent males usually presenting with fever and abdominal symptoms. Liver or spleen biopsy helps in establishing the diagnosis. We report a case of HSTCL lymphoma in a 28 year old male.

Case Report
We report a case of a 28 year old male software engineer by profession who presented with complaints of fever, abdominal pain, blood in urine for last 6 days and black colored stools. Past history revealed history of high grade fever 2 months back which was managed by supportive therapy. On examination BP 130/80 mm Hg, there was no pallor, icterus, cyanosis, clubbing, pedal edema or lymphadenopathy. Lab investigations revealed hemoglobin of 10.1, WBC 4.2, ESR 06, Platelet 130000, urea 13 (13-43 mg/dl), creatinine 0.7 (0.72-1.18 mg/dl), bilirubin 0.47 (0.0-0.2 mg/dl), SGOT-77 (1-35 IU/l), SGPT-217 (1-45 IU/l), SAP 191 (41-137 IU/l), total protein 5.6 (6.4-8.3 g/dl), albumin 3.3 (3.5-5.2 g/dl), AG ratio 1.4 (1.5-2.5), TSH 1.49, PT 18.4, Ferritin 228.5 (20-250 ng/ml), iron 180, TIBC 215 (250-450 ug/dl). Liver elastography showed increased liver stiffness-16.3 kpa and increased median transmission of wave 2.33m/s (Normal <1.4 m/s) indicative of fibrosis. Ultrasound abdomen showed right UVJ calculus (4.5 mm), massive splenomegaly (18 cm) and mild hepatomegaly (15.6 cm). Patient was managed with antibiotics, IV fluid, antacids, antiemetics, multivitamin. In view of hepatosplenomegaly and increased liver stiffness liver biopsy was performed.

Liver biopsy tissue revealed diffuse sinusoidal infiltration by monotonous round cells having round hyperchromatic nuclei, inconspicuous nucleoli and pale cytoplasm. The infiltrate was predominantly sinusoidal with relative sparing of portal tracts. (Fig 1a, b) IHC performed showed the cells within the sinusoids are diffusely CD 45 and CD 3 positive and negative for CD 20, CD5, CD 4, CD 8, CD 7, CD 56, EBV, tdt and CD 34. (Fig 2a, b) Based on histology and immunohistochemical studies the final diagnosis of HTCL was thus rendered.

Discussion
Peripheral T cell lymphomas are a heterogeneous group of post-thymic, mature lymphoid malignancies, accounting for approximately 10–15% of all non-Hodgkin’s lymphomas (1).

Hepatosplenic T Cell Lymphoma are rare subtypes peripheral of T cell lymphoma comprising less than 5% of all peripheral T-cell and natural killer (NK) cell lymphomas (2).
HTSCL were first identified as a distinct category of T cell lymphoma by Farcet et al in 1990 (3). Since then less than 150 cases have been reported so far.

In normal circumstances, γδ T cells represent only 1% to 3% of the lymphocytes in the peripheral blood and in liver comprise 3–5% of all intrahepatic lymphocytes. These cells develop from CD4/CD8 thymocytes in the bone marrow.

It is believed that HSTL arises usually from peripheral γδ T cells (or less commonly αβ) cytotoxic memory T cells of the innate immune system (4, 5). Hepatosplenic T-cell lymphoma occurs more frequently in immunocompromised patients, especially in those receiving long-term immunosuppressive therapy. Immunomodulation thus may play a role in activation of these cells. However, our patient was immunocompetent.

Hepatosplenic T-cell lymphoma occurs predominantly in adolescents and young adults, with a median age of 35 years (range, 15–65 years) at initial presentation. The male to female ratio is about 9:1. They are characterized by predominantly extranodal disease with preferential involvement of liver and spleen. Anemia and thrombocytopenia in patients with HSTL have largely been attributed to hypersplenism and to infiltration of the bone marrow by neoplastic cells.

Diagnosis is usually established by tissue biopsy. The histology typically shows sinusoidal infiltration by monotonous cells with medium to small round nuclei, inconspicuous nucleoli and pale cytoplasm. Similar histological involvement was noted in our case. The most common immunophenotype in patients with HSTCL is as follows: CD2+, CD3+, CD4–, CD5–, CD7+/–, CD8–, CD16+/–, CD 38+, and CD56+ (6).

Our patient had a common immunophenotypic profile of CD2+, CD3+, CD4–, CD5–, CD7–, CD8–, and CD56–.

Certain cytogenetic and molecular features have been found in patients with HSTCL, most notably, isochromosome 7q and less commonly, trisomy 8 (7).

Despite these advances, HSTCL remains a very aggressive subset of T-cell lymphoma and confers a poor prognosis, with a reported median survival of 6–11 months (8, 9).

References
1. Weidmann E. Hepatosplenic T cell lymphoma. A review on 45 cases since the first report describing the disease as a distinct lymphoma entity in 1990. Leukemia 2000; 14; 991-97

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Langerhan’s Cell Histiocytosis of Lymph Node in an Adult Female – A Rare Presentation

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Summary
A 43-year-old female presented with complaints of bilateral cervical and axillary lymph node enlargement. Lymph node biopsy done was suspicious of NHL. We received block for custom IHC panel. There was no history of fever, night sweats and weight loss. H&E sections were studied which shows lymph node with partially effaced architecture and histiocytic collections showing large cells with irregular convoluted nuclei and abundant cytoplasm. Many eosinophils were present in the background. Relevant IHC markers were performed and strong CD1a and S100 immunoreactivity was noticed and a diagnosis of Langerhan’s cell histiocytosis of lymph node was given after discussion with the consultant oncologist.

Background
LCH is a rare disorder of Langerhan’s cells. Most cases occur during childhood and there is predilection for males. Dominant sites of involvement in the solitary form are bone and adjacent soft tissue. Lymphnodes are less commonly involved.

LCH in adult female with only lymph nodes involvement is rarely encountered and needs to be distinguished from lymphomas to avoid unnecessary intensive chemotherapy and other common non neoplastic causes of lymph node enlargement with histiocytic predominance on histomorphology. IHC is an easily available and important tool for demonstration of LCH cells as compared to ultrastrucural studies.

Case Presentation
This is a case of a 43-year-old female complaining of bilateral cervical and axillary lymphadenopathy for 6-7 months. There was no history of weight loss, fever or night sweats. Blood and bone marrow picture were normal. Biopsy reporting was done outside and suspicion of NHL was raised. Block was sent to SRL, Gurgaon for custom IHC panel.

Investigations
H&E sections were studied and there was partial effacement of lymph node architecture with collection of atypical looking histiocytes in sinus pattern and also involving paracortex. Cells show folded, lobulated nuclei with fine chromatin and moderate to abundant cytoplasm. Many eosinophils, histiocytes, neutrophils and small lymphocytes were present in the background. Few mitosis were observed.

On IHC, atypical histiocytic cells were positive for CD1a, S100, vimentin and CD68. LCA was patchy positive. CD20, PAX5, CD3, CD5 and CD30 were negative. CK was negative. ZN stain for AFB was negative. Ki67 was 10-15%.

Based on clinical picture, histomorphology and IHC, a diagnosis of Langerhan’s cell histiocytosis of lymph node was given.

Differential Diagnosis
1. Sinus histiocytosis with massive lymphadenopathy- emperiploesis present and CD1a negative
2. Hodgkin’s lymphoma- complaints of fever, night sweat and weight loss and CD30 positive RS cells

Discussion
Langerhan’s cell histiocytosis is a clonal neoplastic proliferation of Langerhan’s cells. LCH is more common in children with male predominance and usually seen in white individuals of Northern European ancestry. The disease can be localized to a single site, multiple sites within a single system usually bone, or more disseminated and multisystem. The dominant sites of involvement in the solitary form are bone and adjacent soft tissue and less commonly lymph node, skin and lung. Liver, spleen and
bone marrow are considered “risk organs”, involvement of which by LCH places patients at higher risk of mortality. The key feature is the identification of LCH cells. These are oval, 10-15um with grooved, folded, lobulated nuclei with fine chromatin. Nuclear atypia is minimal with variable mitotic activity. Characteristic milieu includes variable number of eosinophils, histiocytes, neutrophils and small lymphocytes. Involved lymph nodes have a sinus pattern with secondary infiltration of the paracortex. Ultrastructure hallmark is the cytoplasmic Birbeck granules. On IHC, LCH cells consistently express CD1a, langerin and S100.

**Learning Points/ Take Home Message**

Clinical presentation of Langerhan’s cell histiocytosis is highly variable and definitive diagnosis depends on identification of characteristic immunohistochemical or ultrastructural features of the biopsy specimen. Management depends upon the age, clinical presentation and sites involved. Differentiation from other lymphoproliferative diseases is important to avoid unnecessary chemotherapy as watchful waiting may be an effective management strategy in cases of adult isolated lymph node Langerhan’s cell histiocytosis, due to its possible spontaneous regression.

**References**

2. M. Edelweiss et al. Hum Pathol, 2007; Lymph node involvement by langerhans cell histiocytosis; a clinicopathologic and immunohistochemical study of 20 cases.

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Make a Diagnosis

1. History: A 49-year-old male present with fullness in abdomen & deranged KFT. Bilateral nephrectomy done with kidney transplant.

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2. History: 47yrs/F, FNAC left parotid swelling; follow-up case of multiple myeloma

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3. History: 61yrs/M, FNAC left retroperitoneal mass, Radiological diagnosis: Lipoma

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