Langerhans Cell Histiocytosis, presenting as Central Diabetes Insipidus and Pneumothorax a Case Report

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Abstract

Langerhans cell histiocytosis (LCH) is a proliferative disorder where pathologic Langerhans cell accumulate in a various organ. We report a case of 28 years’ male who was admitted in medical ward for initial evaluation of pneumothorax and increased thirst. Laboratory workup revealed central diabetes insipidus. After careful examination, a skin lesion was found from which biopsy and immunophenotyping was performed that lead to the diagnosis of Langerhans cell histiocytosis with multisystem involvement. Patient was managed as per LCH protocol and intranasal desmopressin was prescribed for Diabetes Insipidus.

Key Words: Langerhans cell histiocytosis (LCH), Diabetes Insipidus, Pneumothorax

Case presentation

On 8th December 2016, a 28 years’ male presented to the emergency department of Institute of Medicine with history of sudden onset of right sided chest pain and difficulty in breathing for few hours. On presentation, he was hypoxemic (SPO2 50%) and was diagnosed with right pneumothorax. He was immediately managed with chest tube drainage after which his symptoms subsided.

His symptoms started 11 month back when he had cough and slight difficulty in breathing for which he took some drugs from local medical shop, after which cough subsided. Four months later he again developed difficulty in breathing, for which he was evaluated and on chest x-ray a bullous lesion was seen. He was empirically started ATT (anti tubercular treatment) for 6 months. But his symptoms did not improve. He also has history of electrocution 2 months back for which left index finger amputation was done. During all this time, he persistently had increased thirst and frequency of urination however he never mentioned it to his physicians. He gives history of smoking 10 sticks per day for 2 years which he left 7 months back. He does not consume alcohol. His past, surgical, family, and social history were otherwise non-contributory.

On examination (at time of admission)

Moderately built, fair general condition, Vitals: BP 110/70mmHg, Pulse 82 per minute and regular, Respiratory rate 22/min Spo2 50% at room air and 90% via face mask. Chest: Decreased movement and expansion of right side of chest, decreased air entry on right side. No abnormality in Cardiovascular, Gastrointestinal and Central nervous system.

Investigations

Plain CT Scan of Chest demonstrated multiple subcentimetric small cystic lesions having irregular margins in both lungs diffusely scattered involving all the segment of both lobes with relative sparing of bilateral basal segments of lower lobes. CT scan suggested possibility of Pulmonary Langerhans cells histiocytosis.

Abdominal and Pelvic Scan and Echocardiography was normal.
Water deprivation test

Urine osmolality     Serum osmolality
Normal (300-900 mOsm/kg of water) Normal (275 to 295 mOsm/kg of water)

| Before deprivation | 158.3 | 291.8 |
| 1 hr after deprivation | 91.74 | 298.0 |
| 2 hr after deprivation | 74.7 | 300.0 |
| 3 hr after deprivation | 100.0 | 315.0 |

After water deprivation urine osmolality was found less than serum osmolality and since two sequential urine osmolality’s varied by less than 30 mOsm/kg of water, desmopressin challenge test was performed.

**Desmopressin Challenge test**

After desmopressin, nasal spray 10 micrograms in each nostril

Urine osmolality was measured in random urine sample

<table>
<thead>
<tr>
<th>Before spray</th>
<th>After spray</th>
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<tr>
<td>78.3 mOsm/kg of water</td>
<td>297.1 mOsm/kg of water (Normal: 300-900 mOsm/kg)</td>
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Urine osmolality increased after desmopressin challenge test suggesting central cause of Diabetes Insipidus.

MRI brain and CT scan of Abdomen was Normal

**Other tests**

ANA- negative
RA factor-negative
Sputum culture- no growth
Sputum for AFB- not seen
Anti-ds DNA (ELISA) – 7.5 IU/ml (negative if below 30)
Anti CCP (ELISA) – 10 IU/ml (negative if below 25)
HIV/HBs/HCV (Serology)- Negative
LFT/CBC/LDH/TFT- within normal limit

Considering CT finding suggestive of LCH and desmopressin challenge test suggestive of central diabetes insipidus, bone marrow biopsy and skeletal radiographs were taken.

Skeletal survey from head to toe was normal.

Bone marrow biopsy demonstrated cellular bone marrow which was negative for malignancy.

Patient was reexamined for presence of any skin lesion or enlarged lymph node. On careful examination, multiple discrete erythematous papules 1-2mm size over right lower leg and back was found. (Figure 1) Skin biopsy was performed from the lesion.

![Skin lesion seen over back. Skin biopsy was taken from same lesion](image)

Skin Biopsy

Consistent with LCH. CD1a, S100 and Langerin were positive.

**Discussion**

Langerhans’ cell histiocytosis (LCH) is an uncommon cause of interstitial disease characterized by uncontrolled proliferation and infiltration of various organs by Langerhans’ cells. It affects lung predominantly in adult smokers like in this case. 

Signs of LCH depends on the localization and extent of the disease. Clinical spectrum is wide and individual can present with different features than those typically described in medical books. In adults with LCH, pulmonary system is the most frequently involved system and typical features can be dyspnea, chest pain, cough and recurrent pneumothorax. In our case patient has primary complains of dyspnea and was managed for pneumothorax. His CT scan of chest revealed multiple subcentimetric small cystic lesions having irregular margins in both lungs that were diffusely scattered strongly suggesting LCH radiologically.

The classic multifocal form of LCH includes diabetes insipidus, exophthalmos and bony defects of skull which is collectively designed as Hand-Schuller-Christian disease. Our patient did not have abnormal finding in
skeletal survey and exophthalmos was ruled out. When patient complained of increased thirst and increased frequency of micturition, he was investigated for the same. Initially his serum sodium was high (148 mEq/L). His serum osmolality was normal and that of urine was decreased. So, he was considered for water deprivation test and after deprivation of free water intake for 8 hours, his serum and urine osmolality was measured. This time his serum osmolality increased and that of urine osmolality decreased. So, he was considered for desmopressin challenge test. After nasal spray of desmopressin 10 micrograms in each nostril, patient’s urine osmolality increased thus making diagnosis of central diabetes insipidus. Patients with multisystem disease, craniofacial involvement, longstanding disease may be at increased risk of developing diabetes insipidus. In our case, patient has long standing disease that might explain occurrence of diabetes insipidus. No neurological abnormality was found in patient and MRI brain was also normal suggesting absence of cranial lesion.

When skin is involved various types of lesion are seen like noduloulcerative lesions in oral, perineal, peri vulvar or retro auricular region. Since, CT scan of chest reported and suggested further work out on cystic lung disease, patient was reexamined for presence of any skin lesion. Multiple discrete erythematosus papules 1-2mm size over right lower leg and back was found. Positive immunophenotyping for major histocompatibility (MHC) class II and CD1a, along with expression of langerin (CD207) which induces formation of Birbeck granules is highly specific marker of Langerhans cells. Skin biopsy was done in this case and Immunophenotyping was positive for CD1a, langerin and S100. Patient was managed with desmopressin nasal spray for diabetes insipidus. LCH is being managed with vinblasting 6 mg/m2 and prednisolone 1 mg/m2 in course 1 and course 2 and addition of 6- Mercaptopurine in continuous therapy as per guideline. Total duration of treatment will be 12 months. After course 1 patient is symptomatically better and his serum electrolyte and osmolality are within normal range.

Conclusion
LCH should be considered as a differential diagnosis in patients presenting with multi system complaints related to pulmonary, central nervous system and skin lesion.

Conflict of interest: None declared.

References