

Multisystem Involvement of Langerhans Cell Histiocytosis

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Abstract

Langerhans cell histiocytosis presents with involvement of skin, bone and lungs. We discuss this case of breast LCH who developed pulmonary cystic lesions leading to bilateral pneumothoraces. PET scan showed involvement of thyroid and marrow involvement. A new nodule developed at ICD site after 9 months and was diagnosed as LCH nodule. This could be because of seeding of LCH cells at ICD site. We review LCH with involvement of multiple systems.

Introduction

Langerhan's histiocytosis was formerly known as histiocytosis X and refers to a group of conditions characterized by the uncontrolled stimulation and proliferation of a normal antigen-processing cell, the Langerhan's cell

LCH is a disease of abnormal clonal proliferation of a unique type of cell in the monocyte-macrophage cell line known as the Langerhans cell. LCH is known to involve skin (39%), bone (77%), lymph node (19%), bone marrow, liver, spleen, lung, endocrine and CNS.¹ Cytokines, soluble secondary products of lymphocytes and monocytes regulate cell growth and differentiation of hemopoietic stem cells by binding to specific receptors to target cells. Langerhans cells are subject to be regulated by cytokines. The morphology of LCH cells and the clinical signs and symptoms suggests that cytokines maybe important in



Fig. 1: Chest X-ray showing right sided pneumothorax with bilateral large thin walled cystic lesions

the pathogenesis of this disorder. Most of the cytokines were of T cell origin and they directly contributed to pathologic sequelae of LCH including fibrosis, bone resorption and necrosis. The term histiocyte refers to large white blood cells resident in tissues, including Langerhans cells, monocytes/macrophages and dermal/interstitial dendritic cells.² The WHO classification of haematopoietic and lymphoid tumours divides disorders of these cells into the following three categories:³

1. Dendritic cell disorders – includes Langerhans cell histiocytosis, secondary dendritic cell processes, juvenile xanthogranuloma, solitary histiocytomas with a dendritic phenotype and Erdheim-Chester Disease.

2. Macrophage related disorders – includes primary and secondary hemophagocytic syndromes, sinus histiocytosis with massive lymphadenopathy and solitary histiocytoma

3. Malignant histiocytic disorders – includes monocyte related leukemias, extramedullary monocytic tumor and dendritic cell

Case report

A 35 year old lady, non smoker, diabetic on insulin since 3 years, came to us with complaints of breathlessness, mMRC grade 4 since 4 days which was of sudden onset and right sided chest pain since 4 days.

She had history of left breast mass

in 2008, cut section was creamish white firm consistency with multiple tiny cystic spaces and on microscopy proliferating ductotubular units embedded in stroma suggestive of benign fibrocystic mastopathy. Her chest radiograph showed bilateral small thin walled cavities. It was diagnosed clinically as left TB mastitis by surgeon, for which he patient was treated with anti tuberculous chemotherapy for 18 months.

In 2010 she underwent an excision biopsy of the persistent breast mass and the biopsy report showed the fibro-fatty and fibro-muscular stroma showing scattered nodules with sheets of round to oval cells with abundant eosinophilic cytoplasm and vesicular folded and grooved nucleus, morphology suggestive of Langerhan's cell histiocytosis of breast. CD1a of the sample was positive. However patient gave no history of any treatment at that time.

The patient underwent a bronchoscopy with TransBronchial Lung Biopsy, in 2012 due to symptoms of breathlessness for 1 month. The histopathology of the lung biopsy sample was features suggestive of pulmonary Langerhan's cell histiocytosis. The IHC report showed the sample cores containing an almost exclusive population of mononuclear cells with an abundant eosinophilic cytoplasm. The mononuclear cells display an immunopositivity for CD1/S100 protein and focal immunoreactivity for CD68.

The patient was lost to follow up and came back in 2014 with acute onset breathlessness.

On examination, the breath sounds were decreased on the right side.

Chest radiograph revealed right sided pneumothorax, with multiple bilateral thin walled large bullae, Right sided ICD insertion was done. Column movement and Bronchopleural

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Received: 16.05.2016; Revised: 24.10.2016; Accepted: 21.12.2017



Fig. 2: PET scan showing active uptake of FDG in pre and parasternal soft tissue, cervical and mediastinal nodes. There were pulmonary lesions, infiltrative lesions in thyroid and marrow

fistula was present, post ICD insertion (Figure 1).

A PET scan was advised by the oncologist which showed active uptake of FDG in pre and parasternal soft tissue, cervical and mediastinal nodes. There were pulmonary lesions, infiltrative lesions in thyroid and marrow lesions which were suggestive of histiocytosis involvement. No active disease in the left breast or elsewhere in the body (Figure 2).

The patient was started on chemotherapy with vinblastine + oral steroids as per oncologist opinion. During the course of hospitalization serial chest radiographs revealed a loculated pneumothorax on the left side for which a USG guided Pig-tail catheter was inserted. The patient was discharged with both catheters in-situ (Figure 3).

The ICDs were removed after a month and the patient still comes for regular follow-up after 6 months. She received 5 courses of vinblastine.

After 6 months she presented with a small nodule at the site of right ICD scar. FNAC and excision biopsy of the right nodule suggested histiocytosis subcutaneous nodule (Figure 4).

Repeat CT scan showed expanded right lung with few bullae and few cysts in the left lung.

Discussion

Our patient has a history of a left breast mass diagnosed as LCH of the breast on excision biopsy 4 years back. She presented with bilateral pneumothoraces and underlying multiple large lung cysts. Bilateral ICDs was inserted and patient was sent



Fig. 3: X-ray on discharge in January 2014 - right sided ICD and left sided pigtail catheter in situ with bilateral expanded lungs

home with bilateral ICDs as bilateral BPF was present. She was prescribed chemotherapy with vinblastin by the oncologist and she completed 5 cycles out of the 6 cycles advised. Her general condition improved as well as closure of the BPF within a month, so ICDs were removed. On presentation after nearly 1 year, the lung cysts had reduced considerably in size and bilateral atelectactic lower lobes had re expanded. Incidentally noted the patient had a subcutaneous nodule at the scar site. On biopsy this nodule showed cellular features of LCH.

The subcutaneous nodule of histiocytosis developed at right ICD scar, perhaps as a result of seeding of the LCH cells. It has not been previously reported of LCH cells seeding unlike other malignant cells.

Our patient initially had breast involvement later on lung was involved. Lung involvement is seen in approximately 10% of cases¹. It is less frequent in children than in adults, in whom smoking is a key etiologic factor.⁴ Although the lung has been considered a "risk organ", more recent studies have suggested that it has less of an effect on prognosis.^{5,6} In adults, pulmonary involvement with Langerhans' cell histiocytosis usually occurs as a single-system disease and is characterised by focal Langerhans' cell granulomas infiltrating and destroying distal bronchioles. High-resolution computed tomography (HRCT) of the chest is essential to the diagnosis, typically showing a combination of nodules, cavitated nodules, and thick- and thin-walled cysts. A high macrophage count in bronchoalveolar lavage (BAL) fluid is a common but nonspecific finding that merely reflects exposure to tobacco smoke. BAL is useful for eliminating infections and the other infiltrating lung disorders that can be seen in young adults. Langerhans' cells can be identified in



Fig. 4: Nodule at ICD insertion site

BAL fluid, but, in contrast to what was initially hoped, this test shows a very low sensitivity and is rarely useful in the diagnosis of the disease.

The definite diagnosis of pulmonary Langerhans' cell histiocytosis requires identification of Langerhans' cell granulomas, which is usually achieved by surgical lung biopsy at a site selected by chest HRCT. In practice, however, lung biopsy is performed on a case-by-case basis.

Breast involvement with LCH has not been described in literature. Our patient first presented with a breast mass which was diagnosed with a LCH mass, later after 2 years came with lung lesions which were diagnosed as pulmonary LCH. She does not have any bone or skin lesions which are commonly associated with LCH. The left breast excision scar is healthy. But the right ICD scar developed a nodule which on biopsy came out to be CD1a positive suggestive of LCH nodule.

In view of a new nodule at ICD site, it is concluded that this is due to seeding of LCH cells at the ICD site. There have been no descriptions of seeding of LCH cells as also breast LCH. Hence this is a rare presentation indeed of LCH.

Conclusion

Thus we present this rare case of a Pulmonary LCH with history of breast LCH and coming with seeding subcutaneous LCH nodules at the site of intercostal tube drain.

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