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Integrating multi-disciplinary discussion in clinical practice

Case presentation

A 68 year-old male was referred to our clinic in order to investigate an abnormal chest radiography that was performed during work-up of an anemia with unknown onset. The patient reported shortness of breath over the last 4 months (MMRC scale 2), dry cough, fatigue and an irregular fever up to 38°C two times/week. He is a former smoker (80 pack years) with no prior illnesses and without environmental or occupational hazards.

On physical examination, the patient had conjunctival paleness, diffuse crackles on auscultation of the lower lung fields bilaterally and palpable inguinal lymph nodes. Pulmonary function testing showed a mixed obstructive-restrictive defect and a moderately compromised diffusing capacity (FEV_1 72%, FVC 81%, FEV_1/FVC 0.74, TLC 71%, DLCO 52%). Blood tests showed hematocrit 37%, hemoglobin 12.3 g/dL, an erythrocyte sedimentation rate of 40 mm, and a C-reactive protein value of 6 mg/dL. An auto-immunity panel was normal. A High-Resolution Computed Tomography (HRCT) scan showed a probable usual interstitial pneumonia (UIP) pattern with subpleural distribution consisting of reticulation and traction bronchiectasis, minimal ground-glass opacities, para-septal emphysema and one middle lobe nodule (Figure 1). A positron emission tomography (PET)-CT scan was performed to evaluate the nodule and to investigate enlarged lymph nodes in the abdomen. It demonstrated uptake in bones (spine, ribs, scapula), mediastinum, a pulmonary nodule, liver, spleen, iliac and inguinal lymph nodes (Figure 1). Bronchoalveolar lavage was then performed and it showed increased cellularity (28×10^6 cells) with lymphocyte predominance (neutrophils 5%, lymphocytes 27%, eosinophils 1%, macrophages 67%). Perls' and CD1a stains were negative.

Multi-disciplinary discussion (MDD) consisted of consultation between a radiologist, a pulmonologist, a pathologist and a hematologist. Together, they recognized a case of probable UIP with a non-diagnostic BAL demonstrating lym-

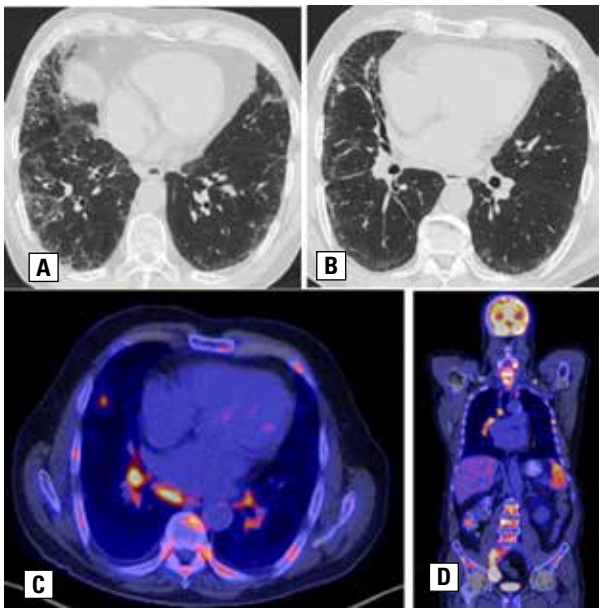

Figure 1. A. High resolution computed tomography scan of the lungs showing subpleural lower lobes reticulation, ground-glass opacities and bronciolectasis; **B.** Reticulation and a middle lobe nodule; **C.** Positron emission tomography-computed tomography scan showing pulmonary nodule and lymph nodes uptake as well as **D.** diffuse uptake in skeleton, spleen and lymph nodes

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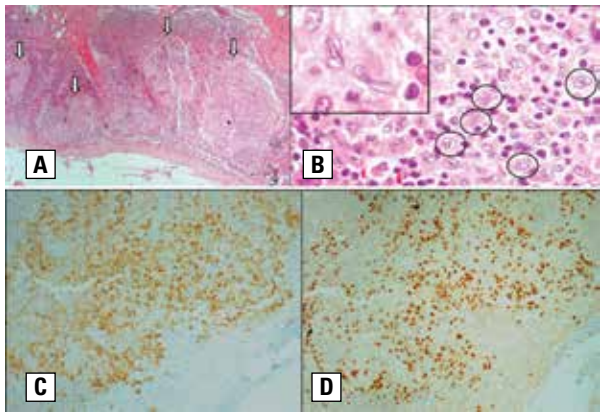

Figure 2. A. Lymph node involved in Langerhans cell histiocytosis exhibited partial effacement of normal nodal architecture (H&E, magnificationX40); **B.** Lymph node biopsy showed the presence of numerous Langerhans cells with the characteristic grooved nuclei (H&E, magnificationX400), (inset: magnificationX600). No nuclear atypia, necrosis or increased number of mitotic figures were noted; **C.** Langerhans cells stained immunohistochemically positive for CD1a and **D.** langerin (CD207) (DAB, magnificationX100)

phocytosis in a clinical context not typical for idiopathic pulmonary fibrosis (IPF). In addition, there were many systemic symptoms and findings suggestive of possible alternative diagnoses. Histological diagnosis was deemed necessary; a decision was made to pursue a surgical biopsy from the most easily assessible site. Inguinal lymph node pathology demonstrated numerous Langerhans cells with characteristic grooved nuclei which stained immunohistochemically positive for langerin and CD1a (Figure 2). MDD considered the findings and a diagnosis of multisystemic Langerhans cell histiocytosis (LCH) was established.

Discussion

Our patient's HRCT pattern was classified as having a probable UIP pattern (reticulation, subpleural distribution, without honeycombing) based on the latest ATS/ERS/JRS/ALAT guidelines for the diagnosis of IPF [1]. Although Langerhans cell histiocytosis is considered among the etiologies of the alternative diagnosis HRCT pattern, this patient's scan had no cysts, no profound ground-glass opacities and only one nodule. The probable UIP pattern, however, needs to be investigated further. The same guidelines provide conditional recommendation for an MDD procedure in order to select further diagnostic procedures in the case of a probable UIP pattern, indicating BAL cellular analysis and surgical lung biopsy as potential next steps.

Fleishner's society white paper on IPF diagnostic criteria identifies the presence of systemic features (like in this case) as a key checklist component for a diagnosis alternative to IPF [2]. Moreover, the authors conclude that MDD is necessary when the clinical context or the HRCT pattern is/are indeterminate for IPF. The clinical context in the case we present was clearly indeterminate considering the systemic features and multi-organ involvement. According to the authors, the outcome of the MDD will lead to a decision on whether to perform additional investigations, BAL or surgical lung biopsy and to integrate, after a biopsy is performed, the clinical, imaging and pathological features. Based on these conclusions, MDD may provide guidance as to what is the most suitable procedure.

A clinical practice guideline by the American Thoracic Society recommends performing BAL in patients that lack a confident UIP pattern on HRCT and who can tolerate the procedure [3]. BAL may be diagnostic in rare diseases and may narrow the differential diagnosis by the respective cellular profile (lymphocytic, neutrophilic or eosinophilic). In our case, BAL was CD1a negative and demonstrated lymphocytosis. Therefore, the need for a surgical diagnosis was not obviated. BAL may precede surgical lung biopsy as a less interventional procedure when the differential diagnosis includes rare diseases or diseases with a predominant lymphocytic or eosinophilic cellular profile as an adjunct to diagnosis.

Langerhans cell histiocytosis (LCH), as classified by the World Health Organization, is a rare dendritic cell disorder [4]. Acute disseminated multisystem disease is commonly seen in children less than three years old [5]. Our patient was started on prednisolone plus vinblastine, with partial response. Of note, the pulmonary nodule completely disappeared after the initial regimen and did not re-appear. The prognosis was poor and our patient passed away 13 months after initial diagnosis.

In the era of modern anti-fibrotic medications approved for use in IPF, we present a case of probable UIP other than IPF. We would like to point out that the pulmonologist should always rigorously investigate extra-pulmonary signs and symptoms when present, and not restrict his differential diagnosis to solely lung-oriented diffuse pulmonary diseases. Provisional IPF diagnosis that allows to avoid invasive procedures like surgical lung biopsy is useful but only when used in the appropriate clinical setting.

Conflict of interest

None declared.

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