Respiratory Failure, Hepatic Failure, and Hemoptysis with Thrombocytopenia in a 79-Year-Old Man

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To the Editor: Langerhans cell histiocytosis (LCH) is a rare disease that usually occurs in the first two decades of life.[1] Multisystem-LCH (MS-LCH) mainly affects youth. Bone, lung, and skin are the most common systems involved.[2] Here, we report a case from China of MS-LCH in a 79-year-old patient with bone marrow, liver, spleen, and lung involvement, but without bone and skin involvement.

A 79-year-old man with a smoking history of 100 pack-years was admitted to our hospital on August 6, 2015. He complained of shortness of breath and exertional palpitations, accompanied by bloody sputum, of 1-month duration. The shortness of breath had worsened recently, associated with lethargy and loss of appetite. Five days before admission, he developed yellowish staining in the skin and sclera with occasional abdominal distension. His past medical history included type 2 diabetes for 5 years, thrombocytopenia (70–80 × 10^9/L) for several years, and idiopathic atrial fibrillation diagnosed 1 month ago. Amiodarone (dosage unknown) was used to control the ventricular rate.

Physical examination revealed normal vital signs. Yellow staining of the skin and sclera, liver palms were noted. Some fine rales were auscultated at the base of posterior lung fields. Abdominal palpation revealed hepatosplenomegaly and shifting dullness. The liver could be felt 3.5 cm below the costal margin on the midclavicular line and 5.5 cm below the xiphoid. The extremities examination revealed bilateral pitting edema below the level of the knees.

Complete blood count revealed a hemoglobin level of 90 g/L, a white blood cell count of 8.3 × 10^9/L, and a platelet count of 27 × 10^9/L. C-reactive protein was 29.28 mg/L. Liver functions were abnormal with alanine aminotransferase 103.5 U/L, aspartate aminotransferase 138.4 U/L, γ-glutamyltransferase 259.9 U/L, alkaline phosphate 567.1 U/L, serum total bilirubin 137.2 μmol/L, conjugated bilirubin 85.9 μmol/L, total bile acid 46.2 μmol/L, albumin 26.4 g/L, prothrombin time 15.6 s, and prothrombin activity 58%. Urinary bilirubin and urobilinogen were positive. Arterial blood PaO_2 was 46 mmHg (1 mmHg = 0.133 kPa, with oxygen supplied at 2 L/min) and SaO_2 was 88%. High-resolution computed tomography (HRCT) [Figure 1a and 1b] revealed bilateral symmetric diffuse ground-glass opacities with interspersed consolidation along the bronchovascular bundles, scattered small emphysema-like spaces, mediastinal lymphadenopathy of maximum diameter 12 mm, and small bilateral pleural effusions. Abdominal magnetic resonance imaging (MRI) revealed mild hepatosplenomegaly [Figure 1d]. Abdominal ultrasound revealed hepatomegaly (maximal oblique diameter of the right lobe of the liver, 19.0 cm; anteroposterior diameter of the left lobe of the liver, 18.0 cm; and diameter of the hepatoportal vein, 1.2 cm) and splenomegaly (length, 11.0 cm; thickness, 5.5 cm) and ascites. Neither cervical, lumbar, abdominal MRI nor chest HRCT revealed bony lesions or other space-occupying lesions. A bone marrow biopsy report revealed diffuse infiltration of Langerhans cells with vesicular nuclear chromatin, irregular nuclear contours, pale cytoplasm with phagocytosed normoblasts, and mature erythrocytes. Many eosinophils were intermixed among Langerhans cells. Blood and bone marrow smear showed very little platelet and thrombacytogenous megakaryocyte, with normal numbers of megakaryocytes. Immunohistochemical and hematoxylin-eosin staining [Figure 1e–1l], produced the following results as follows: CD1a (+); S-100 (+, polyclonal); Kp-1 (+); phosphoglucomutase-1 (+); and Ki-67 (+ <25%). These results suggested the diagnosis of LCH.

The patient underwent inductive-chemotherapy including vincristine (1 mg/m^2, qw), etoposide (50 mg/m^2, qw), and prednisolone (initially 40 mg/m^2, bid) (VEP regimen). At the end of induction chemotherapy, his clinical status improved substantially. His cough and bloody sputum abated, his jaundice subsided, and his lower extremity edema resolved. Chest HRCT [Figure 1c] revealed that ground-glass opacities were absorbed and irregular thin-wall cyst in the right middle lobe. Abdominal ultrasound revealed normal liver and spleen. Bone marrow biopsy and immunohistochemical staining showed the absence of Langerhans cells. Blood and serum indices recovered to near normal values. He transferred to a local hospital for the second-phase of chemotherapy, according to guidelines. As the patient was elderly, with multiple risk organs involved, he failed to complete the whole course of chemotherapy and passed away 1 month later.

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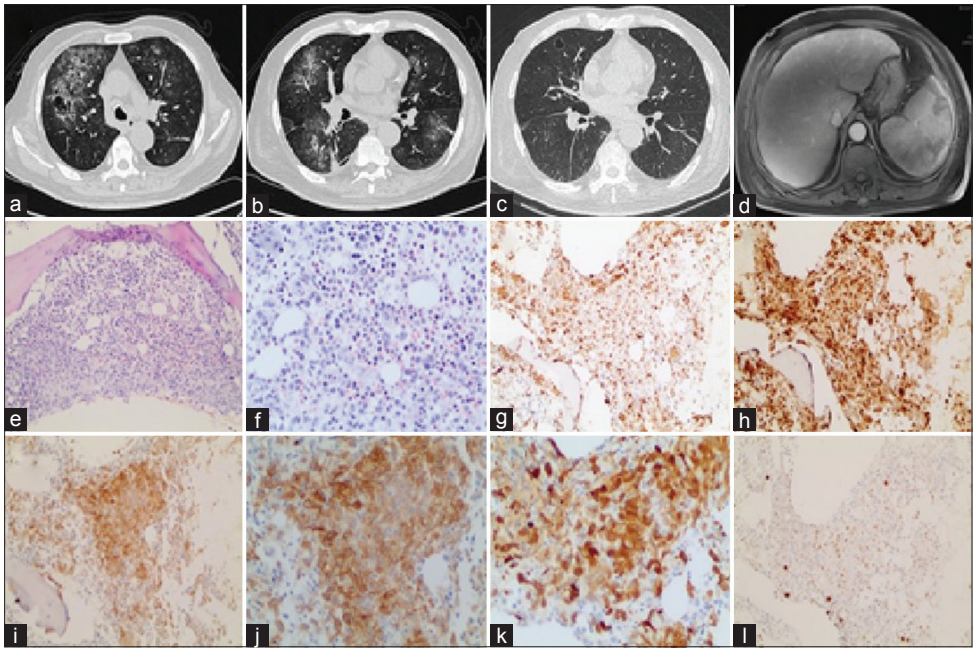

Figure 1: HRCT, MRI results, and bone marrow histopathology images of the patient with Langerhans cell histiocytosis. (a and b) Chest HRCT before the treatment. (c) Chest HRCT after the treatment. (d) Abdominal MRI. (e-l) Bone marrow H&E and IHC staining. (e) H&E staining (×10). (f) H&E staining (×20). (g) phosphoglucomutase-1 IHC staining (×10). (h) KP-1 IHC staining (×10). (i) CD-1a IHC staining (×10). (j) CD-1a IHC staining (×20). (k) S-100 IHC staining (×20). (l) Ki-67 IHC staining (×10). HRCT: High-resolution computed tomography; MRI: Magnetic resonance imaging; H&E: Hematoxylin and eosin; IHC: Immunohistochemistry.

LCH is a rare disease characterized by neoplastic proliferation of Langerhans cells in various organs. The disease can be classified as SS-LCH (one organ/system involved [unifocal or multifocal]) or MS-LCH (two or more organs/systems involved, with or without the involvement of risk organs).[3] Risk organs include liver, lung, spleen, and bone marrow. Diagnosis is based on histological and immunophenotypic examination. Our case here involved a 79-year-old male, who had several years of thrombocytopenia. His condition progressed rapidly for no apparent reason, with respiratory failure, hepatic failure, and hemoptysis with thrombocytopenia. A final diagnosis of LCH was established based on histopathological observations and immunohistochemical staining of the bone marrow with CD1a, S-100, KP-1, and PG-M1 positivity. Re-evaluation of liver, spleen, and bone marrow after the first cycle of chemotherapy revealed remarkable improvement. He was diagnosed with having MS-LCH with the involvement of risk organs and was classified into the high-risk group.

We identified lesions in bone marrow, liver, and spleen; however, whether lungs were involved was doubtful. Pulmonary involvement in LCH mainly presents with nodules (with or without cavitation), favoring centrilobular locations in early stages.[4] In advanced stages, nodules may be absent, and cysts may be the dominant findings. Nodular and cystic changes predominantly involve upper and middle lobes, with relative sparing of lung bases. Ground-glass opacity is relatively rare. Vassallo *et al*.[5] reported a group of LCH cases, only 10.3% of whom showed ground-glass opacities. Our patient's chest images were not typical, primarily revealing ground-glass opacities, interspersed cystic degeneration, and lobular distribution of nodules, even after the ground-glass opacities were absorbed. To the best of our knowledge, our patient was the oldest man in China who has been diagnosed with LCH, presenting as chronic thrombocytopenia, and rapidly progressing to risk organ-involvement (MS-LCH), without bone or skin lesions.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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