Liver transplantation in a patient with Niemann-Pick disease and pulmonary involvement

Transplante hepático em paciente portadora de doença de Niemann-Pick com envolvimento pulmonar

Marina Silveira Mendes, Flaviana Xavier Portela, Ricardo Coelho Reis, José Daniel Vieira de Castro, José Huygens Parente Garcia, Marcelo Alcântara Holanda

To the Editor:

Niemann-Pick disease (NPD) is a rare lysosomal storage disorder that is generalized and severe, as well as being characterized by intracellular sphingomyelin accumulation caused by deficiency of sphingomyelinase activity.[1] From a respiratory standpoint, the various types of NPD, including type B, can cause progressive loss of pulmonary function, with suggestive radiological findings. We report the case of a 27-year-old female patient with type B NPD. The patient was initially referred for outpatient treatment in 2003, presenting with a history of hepatosplenomegaly and delayed psychomotor development since childhood. The diagnosis of NPD was confirmed by measuring peripheral leukocyte sphingomyelinase activity, which was found to be decreased (0.009 nmol . h^{-1} . mg^{-1} of protein; reference value, 0.745 nmol . h^{-1} . mg^{-1} of protein). Serology for HIV, hepatitis B, and hepatitis C was negative, as was serology for syphilis (venereal disease research laboratory test). In addition, ANF was negative. Gaucher's disease was ruled out because beta-glucosidase levels were normal. The patient developed ascites and complained of mild dyspnea, being referred to the pulmonology clinic. She underwent a six-minute walk test (six-minute walk distance [6MWD] = 396 m; predicted 6MWD = 724 m), showing intense dyspnea at the end of the test (modified Borg scale score = 9) but no oxygen desaturation (SpO_2 = 97%). Spirometry results were suggestive of restrictive lung disease (FEV_1 = 1.77 L [61% of predicted]; FVC = 2.07 L [57% of predicted]; and FEV_1/FVC ratio = 85%). A chest X-ray revealed no pulmonary changes. An HRCT scan revealed interlobular septal thickening in the bases and apices, together with right pleural effusion (Figures 1a and 1b).

The patient developed chronic liver failure, having undergone orthotopic liver transplantation with splenectomy in September 2010. Four months later, there was complete resolution of the respiratory symptoms. At the time, a second pulmonary function test revealed improvement in the spirometric parameters (FEV_1 = 2.53 L [80.7% of predicted]; FVC = 2.79 L [77.8% of predicted]; and FEV_1/FVC ratio = 90.8%), and there was improvement in the 6MWD, which increased to 426 m, without desaturation (SpO_2 = 98%). A second HRCT scan revealed resolution of the pleural effusion (Figure 1c) and persistence of the interlobular septal thickening.

A rare entity, NPD is an autosomal recessive disorder characterized by abnormal accumulation of sphingomyelin in the reticuloendothelial system. Type B NPD has heterogeneous clinical manifestations and is mainly characterized by hepatosplenomegaly and progressive hypersplenism. Neurological involvement is rare; when it does occur, it is mild. The diagnosis is made by careful history taking and physical examination, as well as by determination of sphingomyelinase activity (which is decreased in peripheral leukocytes), together with fibroblast cell culture or analysis of bone marrow biopsy specimens revealing characteristic sea-blue histiocytes. There can be respiratory impairment secondary to macrophage and sphingomyelin accumulation in the distal airways and the alveoli, which leads to gradual deterioration of pulmonary function, reducing exercise tolerance. The clinical manifestations are heterogeneous, ranging from absence of symptoms to respiratory failure, and lung disease can progress to hypoxemia requiring oxygen therapy.[2,3]

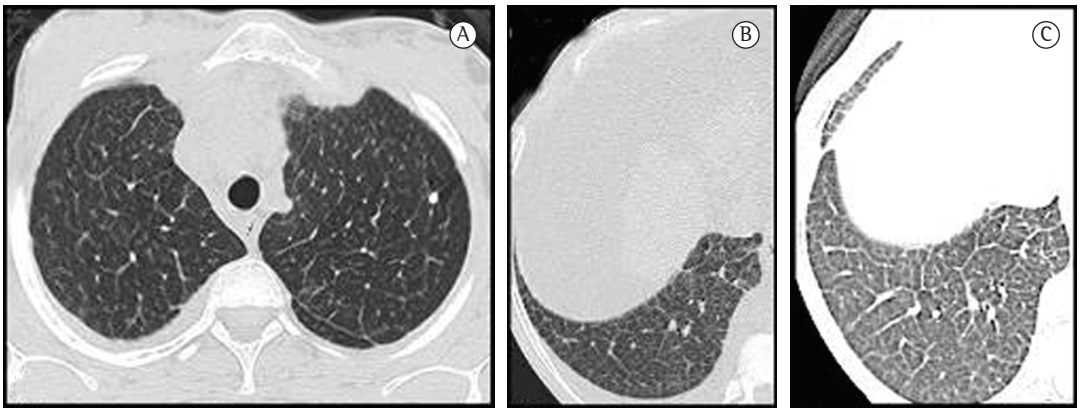

Figure 1 - HRCT scans. In a and b, interlobular septal thickening in the bases and apices, together with right pleural effusion. In c, resolution of the pleural effusion in the right base and persistence of the interlobular septal thickening.

In patients with type B NPD, HRCT findings of NPD are common regardless of the age of the patient. Dissociation among clinical, radiological, and functional findings is common.[3] In type B NPD, there is no correlation between CT findings and the clinical course of the disease.

The morphological changes seen on HRCT include interlobular septal thickening, especially in the lower lobes, and ground-glass opacities, usually in the apical regions. Although they are not predominant, the crazy-paving pattern[2-4] and lung cysts[5] have been described. Over the course of the disease, spirometry can show mild to moderate restrictive lung disease, reduced diffusing capacity of the lung for carbon monoxide, and significant changes in walk test results, such as a reduction in the distance covered and oxygen desaturation.[6,7]

The literature contains few reports of type B NPD patients submitted to liver transplantation, and little is known about the course of the disease after the procedure.[3] In this case report, the patient was asymptomatic after surgery, and it is likely that the respiratory complaints and the initial spirometric findings were related to liver involvement (pleural effusion, ascites, and pancytopenia due to hypersplenism). The CT findings obtained after liver transplantation revealed resolution of the pleural effusion and persistence of the interlobular septal thickening. The six-minute walk test was performed without continuous SpO_2 recording, which could be more appropriate for a better analysis of the patient response to stress, and the diffusing capacity of the lung for carbon monoxide was not measured.[8]

In summary, NPD is a systemic disease that can be diagnosed in childhood, on the basis of delayed development and hepatosplenomegaly. Tomographic findings consistent with NPD, as well as pulmonary function testing, are important tools in the follow-up of patients with NPD and pulmonary involvement.

Marina Silveira Mendes
Medical Student,
Federal University of Ceará,
Fortaleza, Brazil

Flaviana Xavier Portela
Pulmonologist,
Walter Cantídio University Hospital,
Federal University of Ceará,
Fortaleza, Brazil

Ricardo Coelho Reis
Attending Physician,
Walter Cantídio University Hospital,
Federal University of Ceará,
Fortaleza, Brazil

José Daniel Vieira de Castro
Adjunct Professor,
Federal University of Ceará,
Fortaleza, Brazil

José Huygens Parente Garcia
Physician-in-Chief,
Ceará State Liver Transplantation Center,
Fortaleza, Brazil

Marcelo Alcântara Holanda
Adjunct Professor,
Federal University of Ceará,
Fortaleza, Brazil

References

1. Elleder M. Niemann-Pick disease. Pathol Res Pract. 1989;185(3):293-328. http://dx.doi.org/10.1016/S0344-0338(89)80006-8
2. Minai OA, Sullivan EJ, Stoller JK. Pulmonary involvement in Niemann-Pick disease: case report and literature review. Respir Med. 2000;94(12):1241-51. PMid:11192962. http://dx.doi.org/10.1053/rmed.2000.0942
3. Mendelson DS, Wasserstein MP, Desnick RJ, Glass R, Simpson W, Skloot G, et al. Type B Niemann-Pick disease: findings at chest radiography, thin-section CT, and pulmonary function testing. Radiology. 2006;238(1):339-45. PMid:16304086. http://dx.doi.org/10.1148/radiol.2381041696
4. Rodrigues R, Marchiori E, Müller NL. Niemann-Pick disease: high-resolution CT findings in two siblings. J Comput Assist Tomogr. 2004;28(1):52-4. PMid:14716232. http://dx.doi.org/10.1097/00004728-200401000-00008
5. Baldi BG, Santana AN, Takagaki TY, Fujita C, Kairalla RA, Carvalho CR. Lung cyst: an unusual manifestation of Niemann-Pick disease. Respirology. 2009;14(1):134-6. PMid:18699809. http://dx.doi.org/10.1111/j.1440-1843.2008.01352.x
6. Muntaner L, Galmés A, Chabás A, Herrera M. Imaging features of type-B Niemann-Pick disease. Eur Radiol. 1997;7(3):361-4. PMid:9087358. http://dx.doi.org/10.1007/s003300050167
7. Smanik EJ, Tavill AS, Jacobs GH, Schafer IA, Farquhar L, Weber FL Jr, et al. Orthotopic liver transplantation in two adults with Niemann-Pick and Gaucher's diseases: implications for the treatment of inherited metabolic disease. Hepatology. 1993;17(1):42-9. PMid:8423040. http://dx.doi.org/10.1002/hep.1840170109
8. Pimenta SP, Rocha RB, Baldi BG, Kawassaki Ade M, Kairalla RA, Carvalho CR. Desaturation - distance ratio: a new concept for a functional assessment of interstitial lung diseases. Clinics (Sao Paulo). 2010;65(9):841-6. PMid:21049210. PMCid:2954734. http://dx.doi.org/10.1590/S1807-59322010000900005