115 年奇美醫院胸腔內科臨床病例討論會

1 時間：115年 06月 02日 PM: 4:00-5:00
2 課程活動題目:Gaucher’s disease in CXR
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6 摘要：

Gaucher’s disease with intrinsic pulmonary involvement appeared significantly more frequent in subjects homoallelic for the L444P mutation than in patients with other genotypes. The foremost feature of lung disease was the involvement of the lung interstitium, as shown on CXR and/or HRCT scans. One subject with hepatomegaly and kyphosis showed minimal functional impairment consisting of mild reduction of FVC in the absence of other signs of primary lung disease.

Gaucher patients with genotypes other than L444P/L444P did not show CXR and/or HRCT evidence of lung damage. Clinical symptoms and/or functional abnormalities were not detected in all cases but one. This subject had massive hepatomegaly and was a current smoker; he had had atopic asthma and mild dyspnea on exertion. With the exception of slight small airways functional abnormalities, no additional signs of lung parenchymal and/or vascular disease could be demonstrated in this patient.

In this study the age of the patients could be regarded as a bias factor for the presence of pulmonary disease because the two groups were not age-matched. However, in the group of homozygotes for the L444P mutation we found pulmonary signs or symptoms at a median age of 6 yr, even in subjects with no overt neurological disease. By contrast, GD patients with other genotypes did not show even minimal signs of lung involvement at a median age of 24 yr. In addition to this, the duration of the enzymatic treatment did not appear significantly different in the two groups. Finally, the patients homozygous for the L444P mutation appeared to have more severe disease, as shown by both higher severity score indices and pulmonary scores.

Clinical signs and symptoms of pulmonary disease have been reported in Gaucher patients. Most of the described cases with severe lung disease, characterized by recurrent pulmonary infections and progressive dyspnea culminating in fatal respiratory insufficiency, were children. Abnormalities on chest radiographs or CT scans have been described also in adults with type I disease. Kerem and coworkers have recently demonstrated that type I patients with pulmonary function abnormalities have significantly more severe disease than those with normal pulmonary function. This study included mostly subjects with the common "mild" genotype N370S. Younger subjects with different genotypes, more severe disease, and possibly, more serious respiratory manifestations were not included in this analysis. Hence the authors could not come to the conclusion that a genotype-phenotype correlation with regard to lung disease exists in GD.

Lung involvement in GD is multifaceted, and several possible pathophysiological mechanisms account for it. Gaucher cells can fill the alveolar spaces and/or the inter- and intralobular septa, leading to air space and/or interstitial disease, respectively. Pulmonary vascular disease seems to be more common than suspected: pulmonary hypertension even in the absence of vascular plugging by Gaucher cells, and intrapulmonary shunts related to the hepatopulmonary syndrome have been reported. Finally, hepatosplenomegaly and spinal deformities can progressively lead to small lung volumes and to changes of the pulmonary vascular bed, and secondary hypoventilation can eventually occur.

In this survey the functional impairment shown in three individuals from both subgroups consisted of mild obstructive and/or restrictive defects. Finally, pulmonary hypertension was ruled out in three cases with respiratory symptoms, while intrapulmonary shunts were excluded only in one of them. However, because the remaining patients did not have either hypoxemia or additional features including finger clubbing, orthodeoxia, and platypnea, we exclude that the other patients reporting respiratory symptoms had intrapulmonary shunts.

Data from the questionnaire showed that the prevalence of a family history of asthma in GD patients is not different from the prevalence recently seen in a population of school children in central Italy (8% versus 8.3%, respectively), whereas the prevalence of asthma is higher in GD subjects than in the normal population (23% versus 15%, respectively). All patients with GD and previous episodes of asthma were clinically stable at the time of the study and had no symptoms of acute respiratory tract disease. Therefore, on the basis of the results of the questionnaire, we conclude that the radiological signs of lung disease in our patients with L444P genotype are primarily due to GD.

In summary, in view of the large proportion in our study of GD patients homoallelic for the L444P mutation with demonstrated lung damage, and even though no clear evidence of a genotype-phenotype relationship can be demonstrated, we hypothesize that homozygosity for the mutation L444P is associated with a major risk of developing intrinsic pulmonary involvement. In these patients primary lung disease is also likely to occur at early ages and does not seem related to the duration of the enzymatic therapy.

We recommend that in GD a comprehensive evaluation of pulmonary disease is made as soon as possible even in the absence of clinical symptoms. It should primarily include imaging studies of the lung to diagnose air space and/or interstitial disease, and PFT to detect functional impairment. Finally, GD patients should be examined for pulmonary vascular disorders through noninvasive tests such as echocardiography to evaluate pulmonary hypertension and the administration of 100% oxygen to reveal even small amounts of intrapulmonary shunts.