# Acebutolol-Induced Massive Pleural Thickening

## Acebutolol'e Bağlı Masif Plevral Kalınlaşma

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**ABSTRACT**

Many patients take beta-blockers to control hypertension or angina, and such medication is often continued for years. Drug-induced pulmonary diseases due to beta-blockers have been published previously as pulmonary parenchymal infiltration and pleurisy, but bilateral multifocal and extensive pleural thickening alone has not been mentioned previously. In our case, Naranjo Adverse Drug Reaction probability scale score indicated that massive pleural thickening was a possible adverse reaction associated with long term use of acebutolol.

*(Tur Toraks Der 2010; 11: 90-2*)

**Key words:** Drug, acebutolol, pleural toxicity

*Received: 14. 03. 2008* *Accepted: 23. 05. 2008*

**ÖZET**

Birçok hasta hipertansiyon veya anjina için beta-bloker alır ve bu ilaçları yıllarca kullanır. Daha önceki yıllarda beta-blokerlere bağlı pulmoner hastalık olarak pulmoner parankimal infiltrasyon ve plörezi yayınlaşmışken bilateral multifokal yaygın plevral kalınlaşma bildirilmemiştir. Bizim vakamızda Naranjo ilaç yan etkisi olasılık skala skoruna göre yaygın plevral kalınlaşma uzun dönem acebutolol kullanımının olası bir yan etkisidir.

*(Tur Toraks Der 2010; 11: 90-2*)

**Anahtar sözcükler:** İlaç, acebutolol, plevral toksisite

*Geliş Tarihi: 14. 03. 2008* *Kabul Tarihi: 23. 05. 2008*

### INTRODUCTION

In the medical literature, several articles have been published concerning drug-induced pulmonary parenchymal disorders [1]. However, less attention has been directed to drug-induced pleural diseases [2]. Compared to the number of drugs causing pulmonary parenchymal disease, a relatively small number of drugs can induce pleural disease [2]. Beta-blockers, which have widespread use, can induce both parenchymal and pleural diseases, including interstitial pneumonitis, bronchiolitis obliterans organizing pneumonia, pleuro-pulmonary lupus syndrome and pleurisy. We report herein a case in which treatment with acebutolol was followed by bilateral extensive pleural thickening necessitating withdrawal of the drug.

### CASE

A 50-year-old man, employed in a bank, was referred for evaluation of abnormal shadows found by chance on the chest radiograph. The chest radiograph demonstrated bilateral large pleural opacities and a well-defined opacity in the right middle zone of the lung (Figure 1). The patient denied any history of dyspnea, cough, sputum, chest pain, fever, weight loss, or other constitutional symptoms. The physical examination was entirely within normal limits. He had no history of environmental or occupational exposure to asbestos. The laboratory examination included a normal erythrocyte sedimentation rate, complete blood count and urinalysis. Antinuclear antibody and anti-ds DNA titters were normal, and the rheumatoid factor was negative. Pulmonary function tests (forced vital capacity 4600ml, 97% predicted; forced expiratory volume in one second 3740ml, 98% predicted) and transfer factor for carbon monoxide (32.2ml/mmHg/min, 100% predicted) were normal. PPD was 8 mm with a BCG scar.

He was a former smoker (15 pack years). He had no history of respiratory diseases, including tuberculosis, empyema and chest trauma. His only medication was acebutolol. For the previous nine years, he had regularly taken acebutolol (200mg daily) for systemic hypertension. Two years earlier, he had had a chest radiograph, which was taken as a routine investigation before an operation. The radiograph also revealed the same pleural findings except for a well-defined opacity in the right middle zone of the lung. Opacity in the right middle zone was a new radiological finding. Computerized tomography of the chest revealed bilateral, multi-focal large

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doi:10.5152/ttd.2010.010

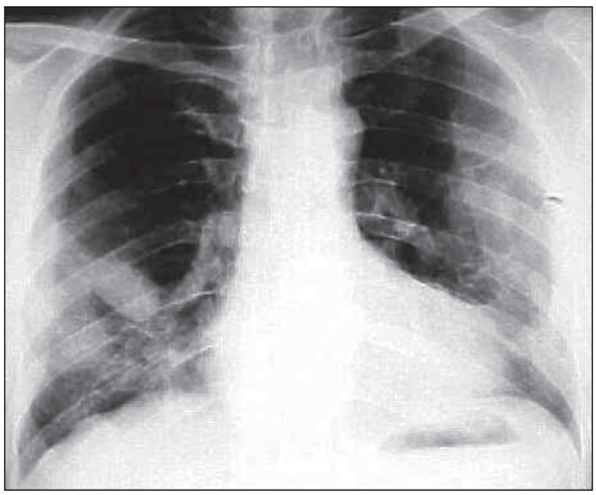

**Figure 1.** The chest radiograph demonstrating bilateral large pleural opacities and a well-defined opacity in the right middle zone of the lung

pleural thickenings and also pleural thickening of the right major fissure appearing as a mass in the parenchyma (Figure 2). True-cut biopsy from the pleural thickening and a transthoracic fine needle aspiration from the mass-like thickening were negative for malignancy and granulomatous lesions. Pleural tissue culture for acid-fast bacilli was negative.

The abnormal chest radiograph was attributed to a drug reaction by exclusion of other causes and acebutolol was withdrawn. During a five year follow up, control chest radiographs revealed the same findings. There was no progression or regression in the pleural lesions.

## DISCUSSION

Many patients take beta-blockers to control hypertension or angina, and such medication is often continued for years. Drug-induced pulmonary diseases due to acebutolol and other beta-blockers have been described briefly as parenchymal infiltration and pleurisy [3-7]. However bilateral, multi-focal and extensive pleural thickening due to beta-blockers has not been reported previously. Up to the present there has been only one case report of an open-lung biopsy showing slight thickening of the visceral pleura that was not apparent on the chest radiography [7].

Asbestos exposure accounts for most cases of bilateral pleural thickening. Our patient lives in an asbestos free area (a city in the north part of Turkey) and also works in an asbestos free job. Additionally pleural biopsy excluded mesothelioma and pleural thickening secondary to asbestos exposure. Other causes of pleural thickening are hemothorax, infectious diseases such as tuberculosis and empyema, collagen vascular diseases and drugs. Pleural thickening secondary to hemothorax, tuberculosis and bacterial empyema is usually unilateral and the calcification is often present. In our case, there was no history of an infective or traumatic cause. Histopathologic examination of the pleura was negative for tuberculosis and other granulomatous lesions. Tissue culture for acid-fast bacilli was negative. Also, the patient

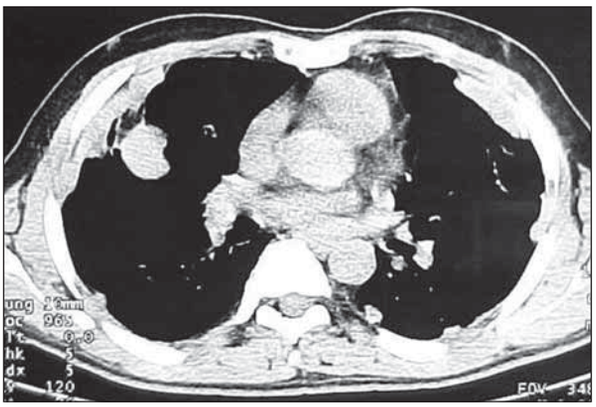

**Figure 2.** Chest CT demonstrating bilateral, extensive and multifocal pleural thickenings. Note that thickening of the right major fissure appears as a mass

had no pulmonary tuberculosis in his past-history. Symptoms, signs and serology were not suggestive of collagen vascular diseases. Among current beta-blockers, acebutolol seems most likely to induce antinuclear antibodies, but in our case, ANA was negative [4].

In the literature, all reported cases with beta-blocker induced pleuropulmonary complications presented with symptoms such as chest pain, cough, and dyspnea since they had pleural effusion and/or parenchymal infiltration [3-7]. In our case, however, there were no pulmonary symptoms since the patient had bilateral pleural thickening without effusion or lung infiltration. Although there was extensive pleural thickening, the patient's lung function test did not reveal restriction. During the five year follow-up period after acebutolol withdrawal, there was no resolution or regression of pleural thickening. Literature reports about practolol induced pleural complications showed that drug withdrawal usually leads to resolution of pleural effusions but no improvement in the pleural thickening [8-10].

In this case, histopathologic examination excluded malignancy and granulomatous diseases. Since drug related pleural toxicity usually has no specific histopathologic findings, open pleural biopsy was not performed.

According to the Naranjo adverse drug reaction probability scale, the final score, which was four, showed a possible relation between acebutolol usage and pleural thickening [11]. There is a case report of an open-lung biopsy showing slight thickening of the visceral pleura related to acebutolol (+1) [7]. We found no other alternative causes except the drug for pleural thickening (+2). The adverse event related to acebutolol was confirmed by objective evidence such as negative histopathologic examination (+1). We consider that the Naranjo scale is not suitable for our case. It is especially valuable for acute drug adverse events. Our case has a chronic pleural thickening. Unfortunately, we have no information about chest radiography before acebutolol usage. However, we know that chest radiography showed progression in the preceding two years while the patient was using acebutolol. However, after withdrawal of acebutolol, chest radiography was neither improved nor progressed during five years follow-up.

The causative role of acebutolol in pleural thickening in this case was made by exclusion of other causes. However, this is often the case with unusual drug complications. History of acebutolol usage for a long time, absence of asbestos exposure, trauma or tuberculosis, normal pathologic, laboratory and physical findings, and no progression during follow-up, all favor an acebutolol-induced pleural thickening. Also the Naranjo adverse drug reaction probability scale indicated a possible relation between pleural thickening and acebutolol usage.

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