DOI: 10.4274/tod.galenos.2022.68926
Turk J Osteoporos 2022;28:169-72

Bilateral Pleural Effusion as the Initial Manifestation of Rheumatoid Arthritis Without Articular İnvolvement: Case Report and Literature Review

Eklem Tutulumu Olmadan Romatoid Artritin Başlangıç Bulgusu Olarak Bilateral Plevral Efüzyon: Olgu Sunumu ve Literatür Taraması

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Abstract

Pulmonary involvement due to rheumatoid arthritis (RA) usually occurs after articular involvement, and pleural involvement is rarely seen before articular involvement. A 62-year-old male patient was complaining of exertional dyspnea. He had bilateral pleural effusion on chest radiograph and high C-reactive protein and erythrocyte sedimentation rate in laboratory tests. As a result of exclusion of other etiologies of bilateral pleural effusion and positive results of rheumatoid factor and anti-cyclic citrullinated peptide antibody in the serum, the patient was diagnosed with RA. This case emphasizes that RA, which is a systemic rheumatic disease, should always be among the preliminary diagnoses in the presence of bilateral pleural effusion, even if there is no known RA diagnosis.
Keywords: Anti-cyclic citrullinated peptide antibody, rheumatoid arthritis, pleural effusion

Öz

Romatoid artrite (RA) bağlı pulmoner tutulum genellikle eklem tutulumundan sonra gözlenirken, plevral tutulum nadiren eklem tutulumundan önce görülür. Altmış iki yaşında erkek hasta efor dispnesi şikayeti ile başvurdu. Akciğer grafisinde bilateral plevral efüzyon, laboratuvar tetkiklerinde yüksek C-reaktif protein ve eritrosit sedimentasyon hızı mevcuttu. Bilateral plevral efüzyon yapabilecek diğer etiyolojilerinin dışlanması ve serumda romatoid faktör ve antisiklik sitrüline peptid antikorunun pozitif çıkması sonucu hastaya RA tanısı konuldu. Bu olgu, bilinen bir RA tanısı olmasa bile bilateral plevral efüzyon varlığında sistemik bir romatizmal hastalık olan RA'nın her zaman ön tanılar arasında olması gerektiğini vurgulamaktadır.
Anahtar kelimeler: Anti-siklik sitrüline peptid antikoru, romatoid artrit, plevral efüzyon

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune systemic disease with a frequency of approximately 1% (1). This disease, the etiology of which is not fully known, primarily affects the small joints of the hands and feet polyarticularly and may also show extra-articular systemic involvement at a rate of 50% (2). Pulmonary involvement is important in terms of systemic involvement, because the most common cause of mortality in RA is pulmonary involvement (1). Symptoms of pulmonary involvement in RA occur after arthritis with a frequency of about 85% (1). As in our case, RA, which was diagnosed with pulmonary involvement before articular involvement, is a rare condition (3-10). Here, a case diagnosed with RA while being examined with bilateral pleural effusion is presented.

Case Report

A 64-year-old male patient was admitted to chest diseases department due to chest pain, fatigue and exertional dyspnea. The patient was diagnosed with bilateral pleural effusion, prominent on the right side. In this state, the patient was consulted to our clinic to be evaluated in terms of rheumatological diseases. Chest pain increased with breathing, was stinging, especially on the

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Received/Geliş Tarihi: 26.11.2021 **Accepted/Kabul Tarihi:** 04.01.2022

right side, and there was dyspnea that increased with exertion. The patient had an intermittent cough for the last 1 year, which did not affect his daily life, but his cough had increased in the last 1 month. Bilateral pleural effusion, more on the right side, was detected in the postero-anterior (P-A) chest X-ray. There was no pleural effusion in the thorax computed tomography (CT) taken 1 year ago with the complaint of cough. The patient applied to an external center with similar complaints; he received moxifloxacin (400 mg/day, 7 days) treatment, but his complaints did not regress. As a result of the evaluations made by the cardiology department, it was determined that there was no congestive heart failure (ejection fraction: 65%). Diuresis was recommended to the patient by the cardiology to remain at 0 to -500 mililiters together with the fluid intake follow-up, but despite the diuretic treatment, the patient's complaints did not improve, and it was found that the pleural effusion increased minimally on the right side in the control X-ray. Thoracentesis was recommended to the patient by chest diseases department, but the patient refused; thereupon, empirical 32 mg/day (for 10 days) methylprednisolone treatment was started, and the patient was informed that thoracentesis would be performed if no response was obtained. After methylprednisolone treatment, the patient's cough, weakness and fatigue decreased, and bilateral significant regression was observed in effusions in the P-A chest X-ray. The C-reactive protein (CRP) value was 72.94 mg/L (0-5 mg/L) in the first outpatient clinic application, it decreased to 7.83 mg/L in the control. Thoracentesis was abandoned due to regression in the patient's imaging, clinical and laboratory findings. Steroid therapy was tapered off. The patient did not have any complaints for 2 months, but he admitted to our hospital when the shortness of breath started again, and the patient was hospitalized for further examination and treatment. The patient had no complaints except exertional dyspnea. He had a history of thyroidectomy and hypertension. He was using levothyroxine sodium 100 mcg/day and verapamil hcl + trandolapril 180/2 mg per day. In the rheumatological evaluation of the patient, there was no significant finding other than pain in the small joints of both hands and short-term morning stiffness that had been intermittent for 3 years, there was no arthritis or arthralgia, and there was no deformity in the hand and foot joints (Figure 1). In respiratory examination, respiratory sounds were decreased in the lung bases and there were crepitant rales. Costodiaphragmatic sinuses were closed and dull on percussion. In laboratory examinations; CRP was 20.8 mg/L (0-5 mg/L), erythrocyte sedimentation rate was 65 mm/h (0-20 mm/h), D-dimer was 3.73 ug/mL (0-0.5 ug/mL). The patient's complete blood count, kidney and liver function tests were normal. On thorax CT, there were lymph nodes in the mediastinum with a short axis not exceeding 1 cm, and pleural effusion reaching a thickness of 18 mm in the widest part on the right and 15 mm in the widest part on the left, and compression atelectasis adjacent to it in both hemithoraces (Figure 2). There was an obstruction pattern in the pulmonary function test [FEV1: 62.3% (3.25L), FVC: 72.4% (4.16L), FEV1/FVC: 67.23]. In the examinations of the patient, anti-nuclear antibody, anti-ds DNA, anti-SSA were detected as negative; rheumatoid factor was 85.4 IU/mL (0-14 IU/mL) and Anti-cyclic citrullinated peptide antibody was 266.8 U/mL (0-17 U/mL) with high positivity for RA. Although the patient's findings did not meet the 2010 ACR/EULAR classification criteria, considering that these criteria are designed for patients presenting with synovitis, the absence of a more appropriate diagnosis to explain bilateral pleural effusion, mild joint complaints and laboratory findings were considered together with RA pulmonary involvement in the patient. Although patient's joint complaints were not severe enough to require treatment, chest pain and pleural effusion completely regressed in the follow-up with hydroxychloroquine sulfate and methylprednisolone treatment for systemic involvement.

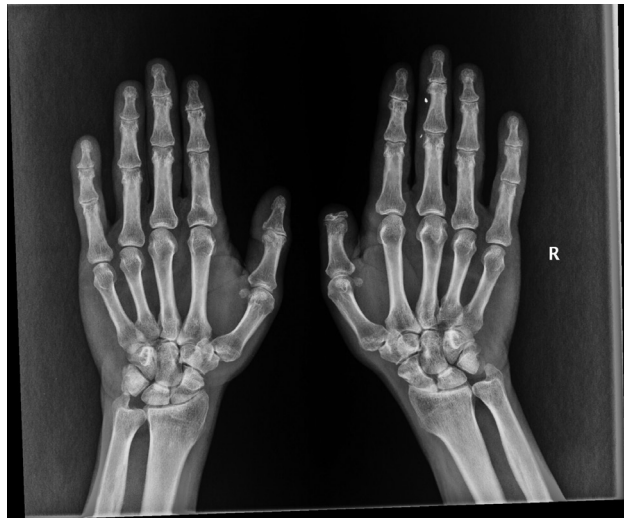

Figure 1. X-rays of both hands of the patient. There was no deformity in the hands

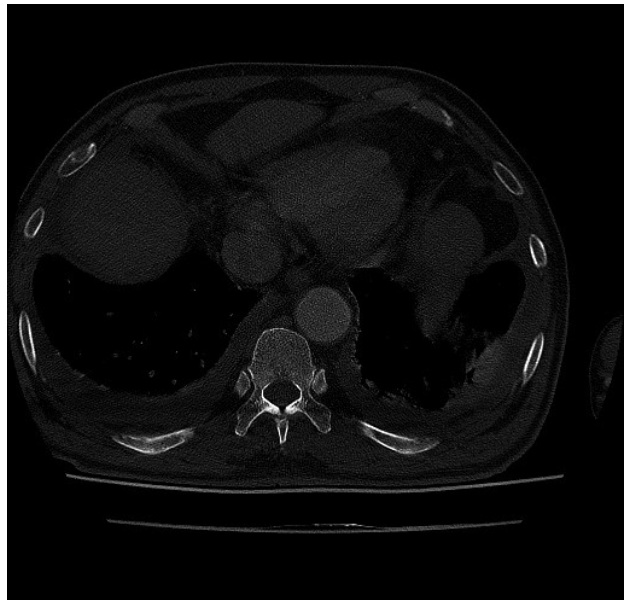

Figure 2. An image from the patient's thorax computed tomography. Areas marked with arrows show bilateral pleural effusion

Informed consent was obtained from the patient regarding the case report. The patient is being followed by physical medicine and rehabilitation and chest diseases departments.

Discussion

Pulmonary involvement of RA is manifested by parenchyma and airway involvement, especially obliterative bronchiolitis, multiple nodules, interstitial pneumonitis, and fibrosis. Pleural involvement can be observed at a rate of 3-5% (2). Different pleura-related lung diseases such as exudative rheumatoid effusion, cholesterol-rich chyliform effusion, drug use (methotrexate and infliximab) related pleuritis, empyema and pyopneumothorax, bronchopleural fistula, pneumothorax or hemopneumothorax can also be observed in RA (11-13). When pleural effusion occurs in the course of RA, 80% is unilateral; It manifests bilaterally at a rate of 20%, as in this case, and its amount is low (1). Pleural involvement in RA is more common in middle-aged men with high RF values, and may be associated with subcutaneous nodules, interstitial lung disease, and pericarditis (1). Although the demographic characteristics of our patient were compatible with literature, no additional findings such as subcutaneous nodules, interstitial lung disease or pericarditis were present in our patient.

In rheumatoid pleuritis, chest pain and/or fever are the most common additional findings. Patients with severe pleural effusions may present with dyspnea. No findings may be seen on physical examination, or decreased breath sounds, pleural rubbing, or unilateral or bilateral dullness to percussion may be detected. The presence of dyspnea that is disproportionate to the size of the effusion may be a clue to any underlying pulmonary or cardiac pathology (14). The approach to pleural effusion in RA is not different from the approach to pleural effusion in general. First of all, it follows the steps such as exclusion of infection and malignancy and alleviation of dyspnea. Ultrasound-guided thoracentesis is an important diagnostic method in patients with RA and pleural effusion. The purpose of pleural fluid analysis is to detect that the pleural fluid is an exudate of rheumatoid effusion and to rule out other etiologies such as infection, malignancy, cholesterol effusion. Therefore, pleural fluid can be sent for glucose, lactic dehydrogenase, cell count, protein, triglycerides, cholesterol, Gram stain, cytology and cultures (11,14). In our case, thoracentesis could not be performed due to the patient's refusal and the rapid regression of the effusion with treatment. The first choice for the diagnosis of pleural effusion is direct radiography, but CT and pulmonary function tests also help in the diagnosis to show the involvement of the pulmonary parenchyma. Because to reveal RA lung involvement, P-A chest X-ray yields approximately 10%, high-resolution CT 70-80% and pulmonary function tests 10-20% (2). Although the pulmonary function tests were expected in a restrictive pattern, our patient's findings were compatible with the obstructive pattern, suggests that our patient's cough that has been going on for the past 1 year may be associated with an undiagnosed obstructive pulmonary disease.

In RA, joint complaints generally occur first and then pulmonary involvement is expected, but rarely pulmonary involvement can be detected before articular involvement (3-10). Thus, the diagnosis of RA can be made after pulmonary involvement. Common features of patients with RA diagnosed with pleural involvement in the literature; pulmonary symptoms are more severe than joint symptoms, other causes of effusion are excluded, a good response to RA treatment and then the diagnosis is clarified, and pleural involvement is accompanied by parenchymal involvement. The general characteristics of the cases diagnosed with RA after pleural effusion are; consists of middle-aged men, musculoskeletal complaints are less than 1 year and lung symptoms are less than 6 months, occur as unilateral effusion, pleural fluid is exudate after thoracentesis, accompanied by parenchymal involvement; in pleural fluid analysis, high adenosine deaminase level, very low glucose level, lymphocyte dominance; and presence of high positive RF, CRP and erythrocyte sedimentation rate in serum (7-10). Since thoracentesis could not be performed in our case, no interpretation of pleural fluid similarities could be made, but other clinical findings were compatible with the literature, except the absence of parenchymal involvement. Pleural effusions due to RA usually do not require specific treatment as they often regress spontaneously or regress 1 to 36 months (mean 14 months) after treatment of articular symptoms of RA, but larger effusions are more likely to be symptomatic and require treatment. When rheumatoid pleuritis is symptomatic and does not improve without treatment, non-steroidal anti-inflammatory drugs (NSAIDs), oral or intrapleural glucocorticoids, and therapeutic thoracentesis for immediate control of dyspnea can be performed (14). In addition, other immunosuppressive drugs can be used in the treatment of RA. If treatment is to be given in the presence of pleuritic chest pain or because of the size of the effusion, NSAIDs are the first choice and recovery is observed in an average of one week with treatment (15). On the other hand, it should not be forgotten that some drugs used in the treatment of RA can cause pulmonary complications. Therefore, more care should be taken in drug selection in patients with pulmonary involvement during the post-diagnosis treatment process. Especially in patients with pulmonary parenchyma involvement, RA and other rheumatological diseases are often questioned, but it should not be forgotten that there may also be extraparenchymal pulmonary findings related to RA.

In conclusion, the possibility of the presence of RA in patients with pulmonary pathology should be kept in mind and the patient should be questioned in terms of RA. In addition, regression of pulmonary signs and symptoms after RA treatment will also make it possible to reach a diagnosis from treatment. In our case, there was a progressive regression of the effusion with glucocorticoid therapy before admission to our clinic, but it later relapsed. Therefore, it was thought that a long-term immunosuppressive or anti-inflammatory treatment should be used in our case. By presenting this case, our aim is to emphasize that although RA is a disease that stands out with its articular

findings, we should not forget that it is a systemic rheumatic disease, and there may be RA patients diagnosed with extra-articular involvements.

Acknowledgement: We would like to thank all of our patient.

Ethics

Informed Consent: Informed consent was obtained from the patient regarding the case report.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: N.Y., H.S.A., Concept: N.Y., H.S.A., Design: N.Y., Data Collection or Processing: H.S.A., Analysis or Interpretation: N.Y., H.S.A., Literature Search: N.Y., H.S.A., Writing: N.Y., H.S.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Özdemir Kumbasar O. Kollajen vaskuler hastalıklara bağlı plevral efüzyonlar. Gözü O, Köktürk O, editör. Plevra hastalıkları. İstanbul: Turgut yayıncılık; 2003. p. 199-206.
2. Sidhu HS, Bhatnagar G, Bhogal P, Riordan R. Imaging features of the pleuropulmonary manifestations of rheumatoid arthritis: pearls and pitfalls. J Clin Imaging Sci 2011;1:32.
3. Pauli G, Pasquali JL, Jory A, Kopferschmitt-Kubler MC, Hauptmann G, Roegel E. Les pleurésies rhumatoïdes inaugurales. Intérêt du dosage du complément dans le liquide pleural. A propos de deux cas [Pleural effusion as the presenting feature of rheumatoid disease. The value of the level of complement in the pleural fluid. A propos of 2 cases]. Poumon Coeur 1981;37:213-7.
4. Fernández-Muixí J, Vidal F, Razquín S, Torre L, Richart C. Derrame pleural como forma de inicio de la artritis reumatoide. Diagnóstico citológico [Pleural effusion as initial presentation of rheumatoid arthritis. Cytological diagnosis]. Arch Bronconeumol 1996;32:427-9.
5. Chou CW, Chang SC. Pleuritis as a presenting manifestation of rheumatoid arthritis: diagnostic clues in pleural fluid cytology. Am J Med Sci 2002;323:158-61.
6. Allan JS, Donahue DM, Garrity JM. Rheumatoid pleural effusion in the absence of arthritic disease. Ann Thorac Surg 2005;80:1519-21.
7. Çimen F, Çiftçi UT, Dursun DG. Romatoid artrite bağlı plöropulmoner tutuluma bir örnek: romatoid plevral efüzyon (Bir Olgu Nedeniyle). Solunum Hastalıkları 2001;12:233-7.
8. Borman P, Ak G, Gökçek YS, Ertürk A, Coşkun S, Bodur H, et al. Romatoid artritin başlangıç bulgusu olarak romatoid akciğer hastalığı (Vaka Sunumu). Turkish J Rheum 2002;17:174-80.
9. Yüksel C, Çelik R, Cangır AK, Sak SD, Kavukçu Ş. Plevral sıvı sitolojisi ve açık akciğer biyopsisi ile tanı konulan bir romatoid artrit olgusu. Ank Üniv T F Mecmuası 2003;56:55-8.
10. Döngel İ, Bayram M, Hayta E, Yıldırım S, İmamoğlu H, Duksal F. Plevral efüzyonla prezente olan romatoid artrit (Olgu sunumu). Cumhuriyet Tıp Derg 2012;34:500-3.
11. Kelly CA. Rheumatoid arthritis: classical rheumatoid lung disease. Baillieres Clin Rheumatol 1993;7:1-16.
12. Basoglu A, Celik B, Yetim TD. Massive spontaneous hemopneumothorax complicating rheumatoid lung disease. Ann Thorac Surg 2007;83:1521-3.
13. Chansakul T, Dellaripa PF, Doyle TJ, Madan R. Intra-thoracic rheumatoid arthritis: Imaging spectrum of typical findings and treatment related complications. Eur J Radiol 2015;84:1981-91.
14. Balbir-Gurman A, Yigla M, Nahir AM, Braun-Moscovici Y. Rheumatoid pleural effusion. Semin Arthritis Rheum 2006;35:368-78.
15. Avnon LS, Abu-Shakra M, Flusser D, Heimer D, Sion-Vardy N. Pleural effusion associated with rheumatoid arthritis: what cell predominance to anticipate? Rheumatol Int 2007;27:919-25.