

Fever of Unknown Origin Due to Left Atrial Myxoma

Lütfü Savaş, MD,*† Yusuf Onlen, MD,*† Tarık Kızıltan, MD,*‡ Ali Pourbagher, MD,*§
Ergun Seyfeli, MD,*|| Tuba Turunc, MD,*¶ and Fatih Yalcin, MD*||

Abstract: Fever of unknown origin may present diagnostic and/or curative difficulties. Myxomas are one of the rare causes of fever of unknown origin. A 67-year-old man with a 4-month history of fever of unknown origin was admitted to our department. Physical examination revealed 38.4°C axillary temperature and accentuated second heart sound in cardiac auscultation. Blood, urinary, and throat cultures were negative. Transesophageal echocardiography showed a left atrial mass partially prolapsing into the left ventricle during diastole. Left atrial mass was excised, and histological examination showed atrial myxoma. Fever resolved within 48 hours after the operation, and the patient was discharged from hospital with complete improvement.

(*Infect Dis Clin Pract* 2006;14:170–172)

Fever of unknown origin (FUO) is defined as body temperature greater than 38.3°C for at least 3 weeks and hospital workup for a week, yielding no cause.¹ FUO may have a complicated clinical course during its diagnosis and treatment. FUO is caused by miscellaneous mechanisms, including infectious diseases (34%), neoplasm (20%), collagen tissue disorders (13%), and others such as alcoholic hepatitis and allergic alveolitis (20%). Some cases with FUO remain etiologically undefined (13%). These proportions may change geographically.²

It has been reported that myxoma may rarely be one of the causes of FUO.³ The most common primary cardiac tumors in adults are myxomas, originated from endocardium, and may present with a wide spectrum of clinical symptoms.^{3–5} Systemic symptoms such as fever, weight loss, sweating, fatigue, myalgia, arthralgia; laboratory test abnormalities such as high sedimentation rate, increased immunoglobulin levels, increased C-reactive protein (CRP)

level, thrombocytopenia, thrombocytosis, erythrocytosis, and abnormal cardiac auscultation findings; and embolic events have been reported.^{6,7}

Myxomas may mimic infective endocarditis, rheumatic fever and miscellaneous infectious diseases, valvular heart diseases, collagen tissue disorders, vasculitis, and cerebrovascular diseases.^{5,8} In this case, we present a case of FUO caused by a left atrial myxoma.

CASE REPORT

A 67-year-old man was admitted to our department because of fever, night sweating, fatigue, arthralgia, palpitations, and coughing over the last 4 months. One month before the admission, he was first admitted to another hospital where he was not diagnosed and therefore transferred to our department. On physical examination, the body temperature was 38.4°C; pulse rate, 88 beats per minute; and blood pressure, 130/85 mm Hg. There was accentuated second heart sound, but no cardiac murmur. Laboratory tests showed hemoglobin, 9.1 g/dL; white blood cells, $7.3 \times 10^9/L$ with a normal differential cell counts; platelet, $441 \times 10^9/L$; increased serum C-reactive protein (44 mg/dL); increased erythrocyte sedimentation rate (75 mm/h); decreased serum iron (14 µg/dL); and normal serum iron-binding capacity (203 µg/dL). Serum ferritin level was also found as 152 ng/mL. The normal value for males: 70–435 ng/mL was the reference range. Throat, urine, blood, and fecal cultures were negative. Workup for infectious, oncological, collagen tissue disorders were negative. Chest x-ray and electrocardiography were interpreted as normal. Chest computed



FIGURE 1. Thoracic tomography: A mass measuring $3 \times 2.5 \times 4.2$ cm in its diameters within the left atrium.

*Department of Infection Disease and Microbiology, Cardiovascular Surgery, Cardiology and Radiology, Hatay-Adana; †Mustafa Kemal University, School of Medicine Department of Infection Disease and Microbiology, Antakya/Hatay; ‡Department of Cardiovascular Surgery and §Department of Radiology, Başkent University, School of Medicine, Adana Medical Center, Adana; ||Mustafa Kemal University, School of Medicine, Department of Cardiology, Antakya-Hatay and ¶Department of Infection Disease and Microbiology, Başkent University, School of Medicine, Adana Medical Center, Adana, Turkey.

Address correspondence and reprint requests to Lütfü Savaş, MD, Mustafa Kemal Üniversitesi, Tıp Fakültesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı, Eski Devlet Hastanesi. Bağrıyanık Mahallesi, 31100, Antakya-Hatay, Turkey. E-mail: lutfu_savas@yahoo.com.

Copyright © 2006 by Lippincott Williams & Wilkins

ISSN: 1056-9103/06/1403-0170

tomography with contrast showed a mass in the left atrium sizing $3 \times 2.5 \times 4.2$ cm (Fig. 1). Transesophageal echocardiography showed left atrial enlargement, left atrial mass originating from interatrial septum prolapsing into the left ventricle during diastole. The patient underwent a cardiac operation using cardiopulmonary bypass, and his left atrial mass was excised (Fig. 2). Histological examination revealed myxoma (Fig. 3). The patient's fever returned to normal level within 48 hours.

DISCUSSION

Although left atrial myxomas are very rare causes of FUO, they may have a complicated clinical course, and therefore, they should be considered in the diagnosis of FUO.

When associated with FUO, the diagnosis of left atrial myxoma may take time; given the facts that cardiac myxomas are rare⁹ and may present poorly with symptoms, therefore, it is one of the last in a clinician's list. The diagnosis of cardiac myxoma presenting with FUO may take years.¹⁰ The time frame between the initiation of symptoms and the diagnosis was 4.5 months in our case.

Echocardiography, which is a widely available clinical facility, can be used diagnostically when left atrial myxoma is considered. Therefore, it is important to consider echocardiography to rule out cardiac myxomas when the diagnosis of FUO is obscured. Echocardiography can also be considered in patients presenting with symptoms such as palpitations and cerebrovascular events. Notably, this approach also helps to identify FUO caused by infective endocarditis. Although transthoracic echocardiography is a less invasive method which has a 95% sensitivity, transesophageal echocardiography has 100% sensitivity and may locate the tumor location more precisely.⁹ Our case had nonspecific symptoms, then the diagnosis was made with the aid of thorax computed tomography and transesophageal echocardiography.

The cause of clinical and laboratory findings such as fever, shivering, sweating, weight loss, increased erythrocyte sedimentation rate, leukocytosis, and increased immunoglobulin levels have not been fully understood. However,

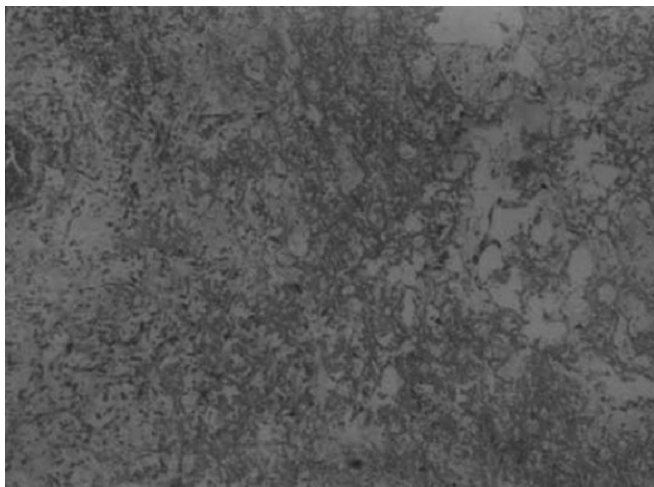


FIGURE 2. Macroscopic morphology of the myxoma that was excised by cardiac surgery.



FIGURE 3. Histological specimen showing primitive mesenchymal cells in myxoid stroma (hematoxylin-eosin, original magnification $\times 100$).

these findings had been linked to necrosis in the myxoma and/or an immune response to tumor antigens.¹¹ Serum protein electrophoresis could be used as a diagnostic test in patients with myxoma,¹² but sensitivity of serum protein electrophoresis may be limited because of other causes of hypergammaglobulinemia. It has been reported that the production and release of a cytokine by the tumor itself may be responsible for constitutional symptoms and laboratory abnormalities. Interleukin 6 has been implicated.⁹ Increased interleukin 6 serum levels in patients with myxoma have been reported. Moreover, a significant correlation between plasma interleukin 6 level and tumor size was demonstrated.^{9,13} In addition, cell cultures stemmed from myxoma tissue have revealed increased interleukin 6 mRNA levels.⁹

Infection of atrial myxoma is rare; overall, 40 cases have been reported in the literature. Microorganisms infecting the myxomas mostly are *Streptococcus viridans* (44%) and *Staphylococcus aureus* (15%).⁹ We did not identify any microorganisms from tissue or hemocultures. We believe that the fever was tumor mediated in our case.⁵

In addition, myxomas may cause embolic complications and sudden death. Therefore, when it is diagnosed, appropriate therapy must be prompted. Surgical excision is exact treatment of myxomas.⁵ The fever of our patient returned to normal level within 48 hours.

In conclusion, although it is a rare clinical association, in cases of FUO, myxoma should be considered, and a full cardiac evaluation, including echocardiographic workup, should be performed.

REFERENCES

1. Arnow PM, Flaherty JP. Fever of unknown origin. *Lancet*. 1997;350:575–580.
2. Duract DT. Fever of unknown origin. In: Mackaviak PA, ed. *Fever: Basic Mechanisms and Management*. 2nd ed. Philadelphia, Pa: Lippincott-Raven; 1997:237–249.

3. Johansson L. Histogenesis of cardiac myxomas. An immunohistochemical study of 19 cases, including one with glandular structures, and review of the literature. *Arch Pathol Lab Med*. 1989;113:735–741.
4. Loire R. Is there a carcinologic malignant potentiality of cardiac myxoma? *Arch Mal Coeur Vaiss*. 1991;84:395–399.
5. Pinede L, Duhaut P, Loire R. Clinical presentation of left atrial cardiac myxoma. A series of 112 consecutive cases. *Medicine (Baltimore)*. 2001;80:159–172.
6. Colucci WS, Braunwald E. Primary tumors of the heart. In: Braunwald E, ed. *Heart Disease: A Textbook of Cardiovascular Medicine*. 4th ed. Volume 1. Philadelphia, Pa: WB Saunders; 1992:1451–1464.
7. Scully RE, Mark EJ, McNeely WF, et al. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 20-1997. A 74-year-old man with progressive cough, dyspnea, and pleural thickening. *N Engl J Med*. 1997;336:1895–1903.
8. Reynen K. Cardiac myxomas. *N Engl J Med*. 1995;333:1610–1617.
9. Revankar SG, Clark RA. Infected cardiac myxoma case report and literature review. *Medicine*. 1998;77:337–344.
10. Larson EB, Featherstone HJ, Petersdorf RG. Fever of undetermined origin: diagnosis and follow-up of 105 cases, 1970–1980. *Medicine (Baltimore)*. 1982;61:269–292.
11. Thomas AC, Mills PG, Gibbs NM, et al. Secondary carcinoma of left atrium simulating myxoma. *Br Heart J*. 1980;44:541–544.
12. Karcher RA, Nuttal KL. Electrophoresis. In: Burtis CA, Ashwood ER, eds. *Tietz Textbook of Clinical Chemistry*. 3rd ed. Philadelphia, PA: WB Saunders Co; 1999:150–163.
13. Hövels-Gürich HH, Seghaye MC, Amo-Takyi BK, et al. Cardiac myxoma in a 6-year-old child—constitutional symptoms mimicking rheumatic disease and the role of interleukin-6. *Acta Paediatr*. 1999;88: 86–788.