

Case Report

Pericardial Effusion in a Young Patient with Newly Diagnosed Systemic *Lupus Erythematosus* and a Mediastinal Mass

GEORGE LAZAROS¹, ATHANASSIOS AGGELIS¹, DIMITRIOS TSIACHRIS¹, KOSMAS ILIADIS²,
EVANGELLIA SCARPIDI³, ATHANASIOS BRATSAS⁴, ANASTASIA-ARETI KOMNOU⁴,
CHRISTODOULOS STEFANADIS¹

¹First Department of Cardiology, University of Athens Medical School, Hippokration Hospital, ²Departments of Thoracic Surgery and ³Pathology, Hygeia Diagnostic and Therapeutic Centre of Athens, Athens, Greece, ⁴Department of Cardiology, Elena Venizelou General/Maternity Hospital, Athens, Greece

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We present the case of a 32-year-old-woman who was admitted to the hospital for evaluation of pericardial effusion. The subsequent diagnostic workup revealed the presence of a mediastinal mass along with systemic lupus erythematosus (SLE). The patient underwent thymectomy, and histological evaluation of the resected mass revealed thymic follicular hyperplasia without evidence of malignancy. SLE disease activity was promptly controlled by corticoids. Clinicians should be aware of the occasional association of autoimmune disorders with focal thymic hyperplasia, which might be confused with thymomas or thymocarcinomas.

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Address:
George Lazaros

31 Achilleos St
175 62 P. Faliro
Athens, Greece
e-mail:
glaz35@hotmail.com

Systemic lupus erythematosus (SLE) is an autoimmune disease in which organs, tissues and cells undergo damage mediated by tissue-binding auto-antibodies and immune complexes.¹ Among the cardiac manifestations pericarditis is the most common. In imaging and autopsy series pericardial involvement is demonstrated in approximately 60% of patients; however, clinically significant pericarditis occurs in less than 30%.¹

The thymus gland lies in the upper part of the anterior mediastinum, behind the sternum.² It is a triangular, bi-lobed organ, whose morphology changes with age.² Fatty infiltration of the gland begins in childhood and by the age of 40 the thymus is usually mostly fatty in composition.²⁻⁴ However, under certain circumstances, including autoimmune diseases such as SLE, the thymic gland may retain its normal shape or even enlarge.^{5,6}

We present the case of a 32-year-old-

female patient who was admitted to the hospital for evaluation of pericardial effusion attributed to SLE. It is of interest that a chest computed tomography (CT) scan revealed an anterior mediastinal heterogeneous mass simulating thymoma, whose microscopic analysis, however, revealed benign thymic follicular hyperplasia. The association between the above conditions and their possible pathogenic link is also discussed.

Case presentation

A 32-year-old- female patient was admitted to the hospital because of intermittent retrosternal pain, aggravated by lying supine, shortness of breath, and weakness, all of 2 days' duration, as well as moderate pericardial effusion.

There was a history of hypothyroidism of 10 years' duration under levothyroxine therapy, premature ovarian failure, which

had appeared two years earlier, one year after childbirth, and arthralgias (especially of the knee joints) for the last couple of months. She also reported a cytomegalovirus infection 6 years before, with persisting positivity of the relevant IgM antibodies since then.

On admission, the patient was afebrile, the pulse was 65 beats/min and the blood pressure 115/80 mmHg. On physical examination, cardiac auscultation revealed a grade 1 systolic murmur at the cardiac apex, but not pericardial friction rub, while the rest of the examination was unremarkable.

An electrocardiogram showed sinus rhythm at a rate of 65 beats/min with diffuse but non-specific repolarisation abnormalities. Chest X-ray revealed a slight diffuse enlargement of the cardiac silhouette (Figure 1). An echocardiographic examination was remarkable only for the presence of a moderate amount of pericardial fluid (maximal diameter 10 mm at end-diastole), which was most prominent in the postero-inferior pericardial space, without signs of cardiac tamponade (Figure 2).

Blood chemical analysis showed mild leucopenia ($WBC\ 3.89 \times 10^3/\mu L$), with normal haemoglobin (13.4 g/dL) and platelet count ($257 \times 10^3/\mu L$). Erythrocyte sedimentation rate was 17 mm/h, C-reactive protein was 0.5 mg/L (normal values: 0-5) and cardiac troponin I was 0.00 ng/ml (normal values: 0.00-0.4). Renal, liver and thyroid functional tests (including anti-mitochondrial and anti-thyroglobulin antibodies) as well as C3, C4, rheumatoid factor, anti-neutrophil cytoplasmic antibodies and antibodies to extractable nuclear antigens



Figure 1. Posteroanterior chest X-ray, showing slight diffuse enlargement of the cardiac silhouette.



Figure 2. Echocardiographic parasternal long-axis view, disclosing moderate pericardial effusion (PE), which appears more prominent in the posterior pericardial space (~1 cm in diastole).

(SSA, SSB, Sm, RNP, Scl-70) were within the normal range. Antiacetylcholine receptor antibodies were also not detectable. In contrast, serum antinuclear antibodies (ANA) were positive at a dilution of 1:640 (homogeneous pattern) and anti-double-stranded DNA antibodies (antiDs-DNA) by ELISA were 213 (normal values <30). Accordingly, the diagnosis of SLE was established as the 1982 American College of Rheumatology criteria were fulfilled (serositis, ANA positivity / antiDs-DNA elevation, leucopenia).⁷

Chest CT revealed a $4 \times 4 \times 2.3$ cm mass located in the antero-superior mediastinum, which was non-uniformly engaging the contrast agent and was compatible with either thymoma or thymic lymphoma (Figure 3). For further evaluation of the nature of the mass, chest magnetic resonance imaging with



Figure 3. Chest computed tomography scan, revealing a $4 \times 4 \times 2.3$ cm mass located in the anterior-superior mediastinum, which non-uniformly engages the contrast agent.

gadolinium injection showed neither evidence of pericardial or pleural implants nor involvement of vascular structures or invasion to regional lymph nodes. (Figure 4A) In addition, combined ^{18}F -fluoro deoxy-glucose positron emission tomography (^{18}F -FDG-PET) CT revealed an homogeneous ^{18}F -FDG uptake, slightly elevated for the patient's age, in the region corresponding to the thymus gland (maximum standardised uptake value 2.6) (Figure 4B).

On completion of the diagnostic work-up, surgery was scheduled, the mediastinal tumour was removed, and a pericardial window was performed. Histological examination of the mediastinal mass revealed thymic follicular hyperplasia without evidence of malignancy, nor was evidence of malignancy found on examination of the pericardial specimen (Figure 5).

A week after surgery, the patient experienced high grade fever (38.8°C), chest pain and shortness of breath, and was readmitted to the hospital. A new chest CT scan showed relapse of the pericardial effu-

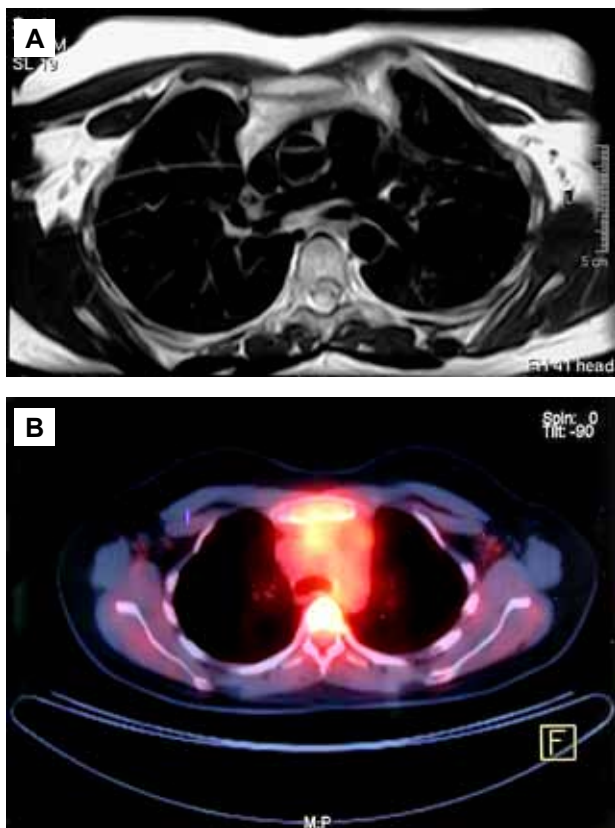


Figure 4. A. Chest magnetic resonance imaging confirming the thymic mass without invasion of the adjacent structures. B. Combined ^{18}F -fluoro deoxy-glucose positron emission tomography / computed tomography revealing a homogeneous ^{18}F -FDG uptake, slightly elevated for the patient's age, in the anatomical region of the thymus gland.

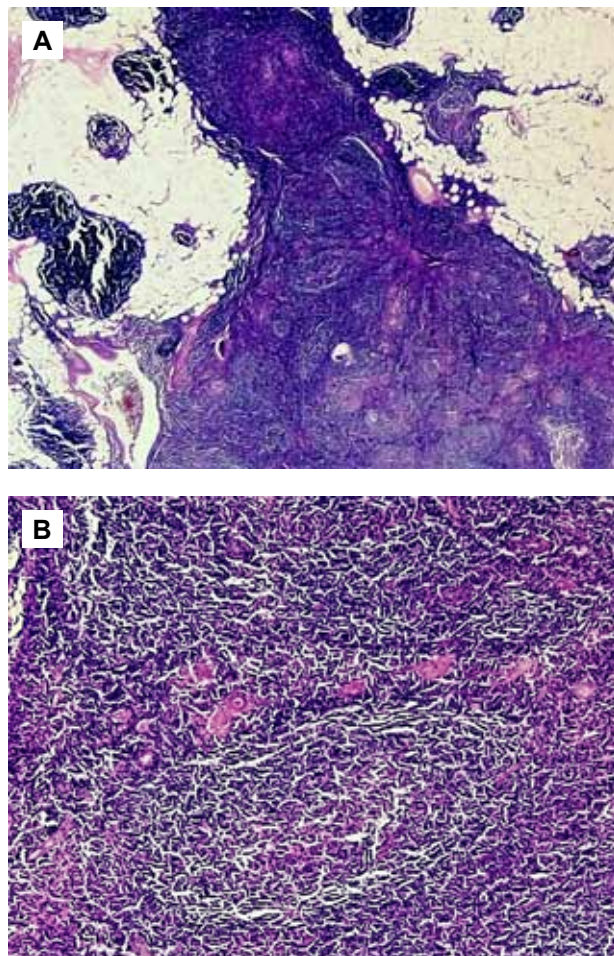


Figure 5. Histological examination following haematoxylin-eosin staining of the resected mass. A. Low power view (20 \times) revealing hyperplastic lymphoid follicles with germinal centres in thymic tissue. B. High power view (100 \times) showing a hyperplastic lymphoid follicle in the lower part of the image.

sion along with left pleural effusion. The patient was treated with methylprednisolone, initially with an intravenous load, and subsequently *per os* at a dosage of 32 mg, and showed significant clinical improvement. Methylprednisolone was progressively tapered to a maintenance dose of 8 mg daily and at this point hydroxychloroquine 250 mg along with azathioprine 100 mg daily were added. Surprisingly, two months later regular menses reappeared. At 1-year follow up the patient is free of symptoms, receiving maintenance doses of methylprednisolone and hydroxychloroquine.

Discussion

SLE is an autoimmune disorder that affects the cardiovascular system with a high prevalence. As men-

tioned above, pericarditis, usually with a mild effusion, constitutes the most frequent cardiac manifestation, reported in 30-50% of cases.^{1,8}

The thymus gland is a small gland residing in the upper anterior mediastinum.² Its shape, size and composition typically change with age and it reaches its peak weight at puberty.²⁻⁴ Thereafter, under the influence of many factors, including adrenal and sex hormones, much of the thymus gland tissue is replaced by fat and connective tissue.²⁻⁴ However, there is a wide variability in the rate of the involution of the thymus.² The thymus is essential for maturation of a variety of immune functions and the association between thymic morphological abnormalities and conditions characterised by disordered immunological function has been steadily growing.^{9,10}

In the case reported here, SLE was recognised on clinical and biochemical grounds as the underlying cause of pericardial effusion in this patient. Moreover, in the setting of the diagnostic pathway, a chest CT scan revealed a mass in the anterior mediastinum with morphological features compatible with thymoma – in the absence, however, of typical FDG-PET findings.

With the suspicion of thymoma, the mass was surgically removed according to current trends, to prevent the eventual malignant degeneration of the tumour.¹¹ Surprisingly, histological examination of the resected mass excluded a neoplastic nature and established the diagnosis of focal lymphoid follicular hyperplasia.

Lymphoid follicular hyperplasia may be associated with autoimmune or endocrine disorders, such as SLE, thyrotoxicosis and Addison's disease, and is also seen in about two thirds of patients with *myasthenia gravis*.^{2,5,6} Lymphoid follicular hyperplasia (also known as autoimmune thymitis) is characterised by normal size, shape and weight of the thymus, with chronic inflammation and proliferation of lymphoid follicles, active germinal centres and increased numbers of lymphocytes and epithelial cells.^{2,5} Occasionally, the thymic gland may be enlarged or, as in this case, there may be a focal mass.^{2,5,6} Regarding the effects of thymectomy in SLE patients the available data are inconclusive, with both exacerbation and improvement having been reported.¹²

Also of interest in the present case is the premature ovarian failure, occurring 3 years before the diagnosis of SLE. Among the various factors that are related to the pathogenesis of ovarian failure, thymic disorders and autoimmunity have been reported, but

the real prevalence of autoimmune premature ovarian failure is unknown.¹³ Interestingly, in this patient, thymectomy and corticosteroid administration resulted in reappearance of regular menses, one month beyond treatment. Contrarily, IgM antibodies against cytomegalovirus continued to be positive at the same time, without any clinical evidence of active infection.

In conclusion, this is an interesting case with co-existence of SLE and focal thymic lymphoid follicular hyperplasia, simultaneously diagnosed in a young female who presented with pericardial effusion. Physicians should interpret thymic masses with caution when they have to deal with a patient who is suffering from an autoimmune disease.

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