British Journal of Medicine & Medical Research
7(5): 425-431, 2015, Article no.BJMMR.2015.349
ISSN: 2231-0614

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Concomitant Onset of Thymoma and Primary Infection with *Toxoplasma gondii*: A Case Report

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2015/8667
Editor(s):
(1) Anonymous.
Reviewers:
(1) Pinar Okyay, Department of Public Health, Adnan Menderes University, Turkey.
(2) Anonymous, Senegal.
(3) Anonymous, Iran.
Complete Peer review History: http://www.sciencedomain.org/review-history.php?iid=945&id=12&aid=8293

Case Study

Received 26th December 2013
Accepted 21st January 2014
Published 27th February 2015

ABSTRACT

Aims: This case reports is about a patient with diagnosis of thymoma with intercurrent infection with *Toxoplasma gondii*. The state of immunosuppression caused by thymoma had probably facilitaded the development of an infection with *Toxoplasma gondii*, that determined lymph nodes involvement and symptoms, appearing like lymphoproliferative disease.
Presentation of the Case: A 57-year-old woman presented with intense night sweats, fatigue, dyspnea on moderate effort, multiple superficial enlarged lymph nodes, and fever with shivering. Blood tests showed marked leukocytosis with lymphocytosis and eosinophilia, normal hemoglobin and platelet counts, increased ESR (40 mm) and LDH (606 U/L). The search for anti-Toxoplasma IgM antibodies was positive and the serum protein electrophoresis showed increased acute phase proteins.
Suspicion of lymphoproliferative disease became stronger after the execution of CT and PET. In agreement with the thoracic surgeon, we decided to perform biopsy of the mediastinal mass in order to confirm diagnosis. The histological examination showed the presence of a thymoma.

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Discussion: When the patient first came to our department, given the physical examination and the reported symptoms, the case seemed easy to solve. Suspicion of lymphoproliferative disease became stronger after the execution of CT and PET. Nevertheless, the diagnostic process was complicated and required two surgical procedures over a short period time, before the thymectomy itself.

Conclusion: This patient was affected by two rare medical conditions involving the lymph node system. The collaboration between the various specialists allowed us to exclude the hypothesis of lymphoproliferative disorder and to reach the correct diagnostic conclusions. The correct diagnosis has allowed appropriate treatment for resolution of thymoma.

Keywords: Thymoma; Toxoplasma gondii; lymphoproliferative disorder; infection; thymus; immune disorder.

1. INTRODUCTION

Thymomas are tumors derived from the epithelial cells of the thymus. These pathologies are associated with several immune disorders [1,2] which may precede or follow thymoma resection including myasthenia gravis, hyperthyroidism, Addison disease, rheumatoid arthritis and dermatomyositis. In patients with thymoma both opportunistic and nonopportunistic infections [1] are reported. In a search of the literature we found only one case description [3] of an association of ocular toxoplasmosis and thymoma.

In this article we describe the rare clinical case of a patient with thymoma and toxoplasmosis at the same time. Clinical symptoms led to assume a lymphoproliferative disorder, like the large lymph nodes involvement confirmed by CT scan and a PET/CT scan. But serology and histological investigations disproved this hypothesis, confirmed that this symptoms was caused by *Toxoplasma gondii* infection.

2. PRESENTATION OF THE CASE

A 57-year-old woman was referred to our Hematology department due to the onset of intense night sweats, fatigue, dyspnea on moderate effort, multiple enlarged lymph nodes, and fever with shivering.

Her family history was positive for malignancy (her father had died of lung cancer, her mother had died of HCC on a previous HCV-related cirrhosis, her maternal grandmother had died of leukemia and her paternal grandmother of gastric adenocarcinoma).

On physical examination, multiple superficial enlarged lymph nodes were present, with a maximum diameter of 2 cm, mobile at underlying levels, and slightly painful on palpation.

Blood tests showed marked leukocytosis with lymphocytosis and eosinophilia, normal hemoglobin and platelet counts, increased ESR (40 mm) and LDH (606 U/L). The search for anti-Toxoplasma IgM antibodies was positive, while anti-Toxoplasma IgG antibodies were low and the serum protein electrophoresis showed increased acute phase proteins. After one week, blood test showed anti-Toxoplasma IgM and anti-Toxoplasma IgG antibodies both elevated, CRP was normal. After one month anti-Toxoplasma IgM antibodies decreased, while IgG increased.

An ultrasound scan of the neck and armpits confirmed the presence of multiple enlarged lymph nodes. Furthermore, in the site where the patient reported pain and heaviness (front left hemithorax) there was a very uneven and richly vascularized bulk with a diameter of about 7 cm. An abdominal ultrasound was normal.

Given these findings, we considered it unlikely that all the reported symptoms and objective findings were due only to a primary infection with *Toxoplasma gondii*; the hypothesis of two comorbidities seemed more likely. The patient underwent a total body CT scan Fig. 1 and a PET/CT scan Fig. 2.

The former showed multiple enlarged lymph nodes in the neck, with a maximum diameter of 3 x 2 cm. The presence of a bulky mass in the mediastinum was confirmed, with overall size of 10.3 x 7.3 x 6.5 cm, closely adherent to left brachiocephalic vein, to the ascending portion of the thoracic aorta, and to the common pulmonary trunk, which were slightly displaced posteriorly and to the right. Other enlarged lymph nodes were visible in the right hilum and in the paratracheal level, with a maximum diameter of 2 x 1.6 cm. A pericardial effusion was evident, with a thickness of about 18 mm. In the abdomen, the only significant finding was enlarged spleen, at

the upper limits of normal (anteroposterior diameter of 12.6 cm).

PET/CT scan showed numerous areas of moderate hypermetabolism, with a maximum SUV of 4.7, both above and below the diaphragm. The scintigraphic findings were compatible with lymphoma.

To come to a diagnostic conclusion, a histological finding was essential. On the suspicion that the superficial lymphadenopathy was secondary to primary infection with *Toxoplasma gondii*, we performed transthoracic biopsy of the bulky mediastinal mass and a bone marrow biopsy. The latter was negative, while the former showed fragments of thymoma. In the material under examination, the tumor showed the features of the type AB thymoma according to the WHO, being composed of a mixture of a lymphocyte poor type A component with elongated spindle cells and a more lymphocyte rich type B-like component. Immunohistochemistry for cytocheratin, CD5, TdT, CD117 and Ki67/MIB1 were performed Fig. 3.

About 3 weeks after surgery, the patient continued to present low-grade fever and night sweats, and superficial lymphadenopathy were increased in size. Further, as the presence of enlarged lymph nodes above and below the diaphragm is not typical of an infection with *Toxoplasma gondii,* we suspected concomitant presence of a lymphoproliferative disease. We therefore performed a biopsy of a right paratracheal lymph node in mediastinoscopy. Histologically the lymph node showed follicular hyperplasia and small clusters of epithelioid hystiocytes: these features, in the correct clinical setting, were in keeping with *Toxoplasma gondii* infection Fig. 4.

Fifteen days later, the patient underwent median sternotomy to remove the thymoma; histological examination confirmed the presence of AB thymoma, stage pT2 N0 according to WHO, stage 2 in Masaoka. The tumor focally exceeded the capsule, with extension to the pericapsular soft tissues; the patient underwent adjuvant radiotherapy about one month later.

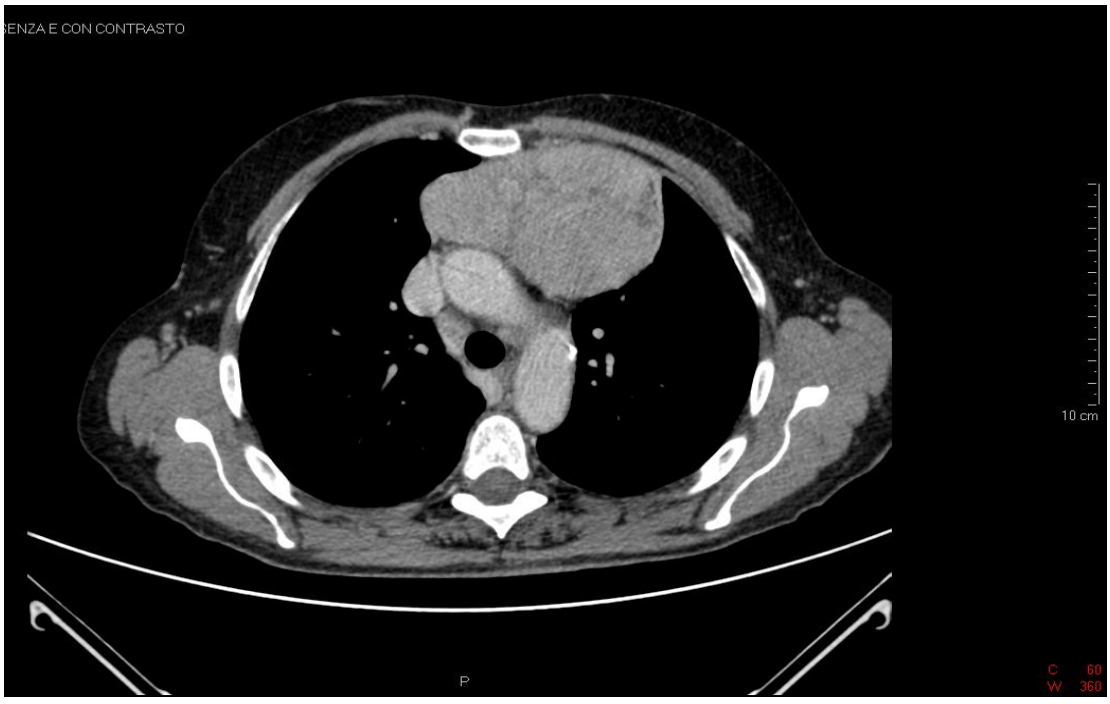

Fig. 1. CT scan of the thorax showing the presence of a bulky mass with overall size of 10.3 x 7.3 x 6.5 cm, enlarged lymph nodes in the right hilum and in the paratracheal level, with a maximum diameter of 2 x 1.6 cm

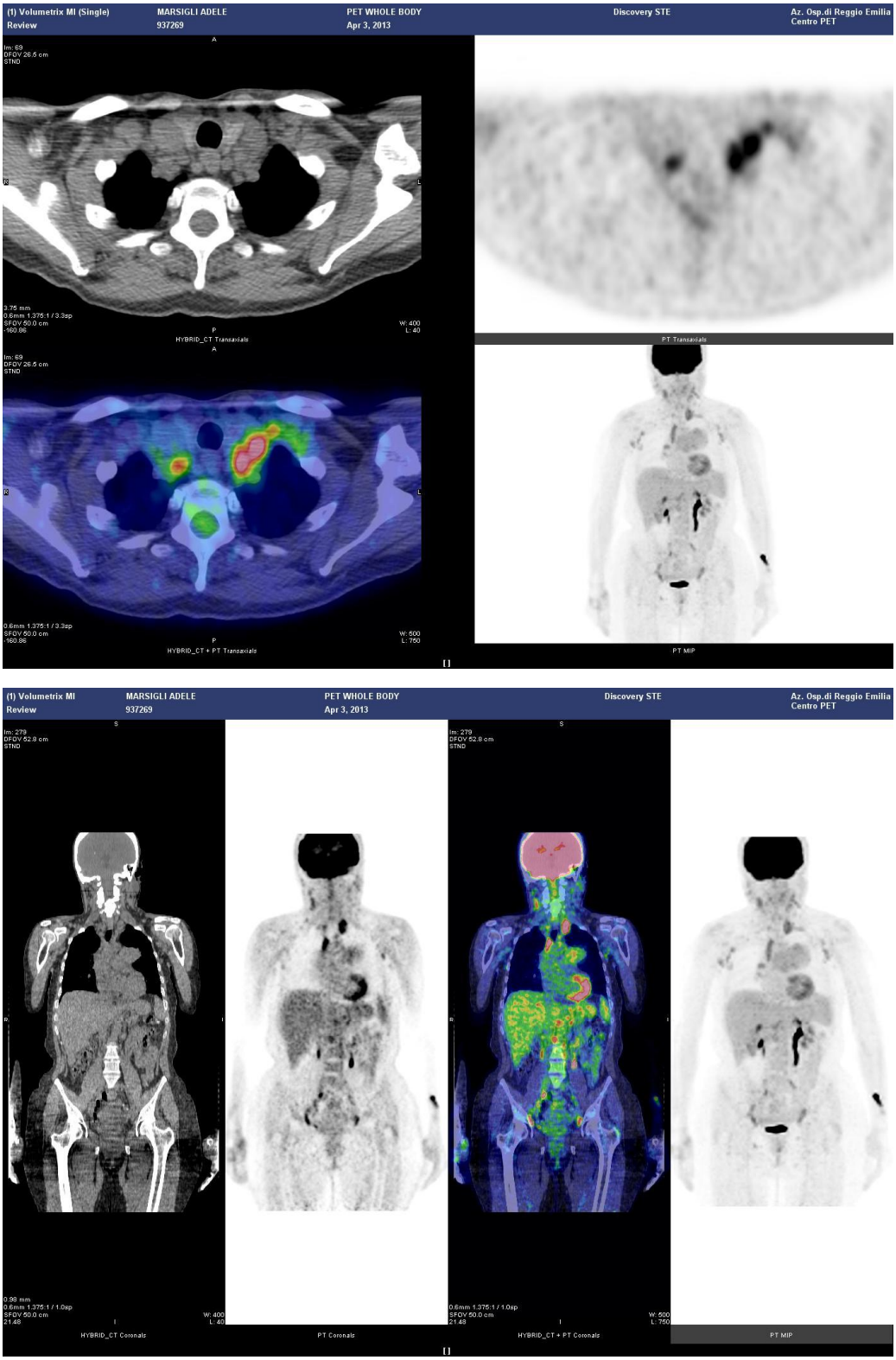

Fig. 2. PET/CT scan showing numerous areas of moderate hypermetabolism, with a maximum SUV of 4.7, both above and below the diaphragm, compatible with lymphoma

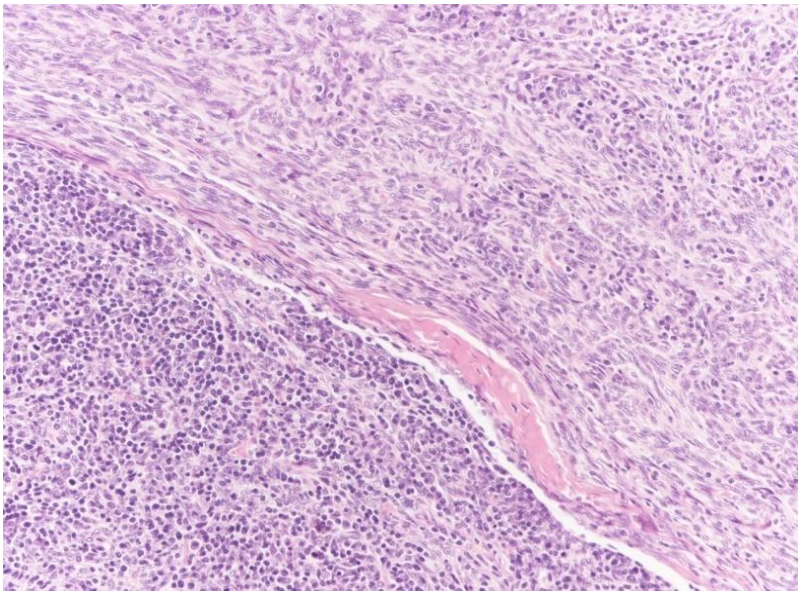

Fig. 3. Histological features of the thoracic mass: type AB thymoma. The type A component with elongated spindle cells is poor in lymphocytes (right); the type B component is lymphocyte rich (left)

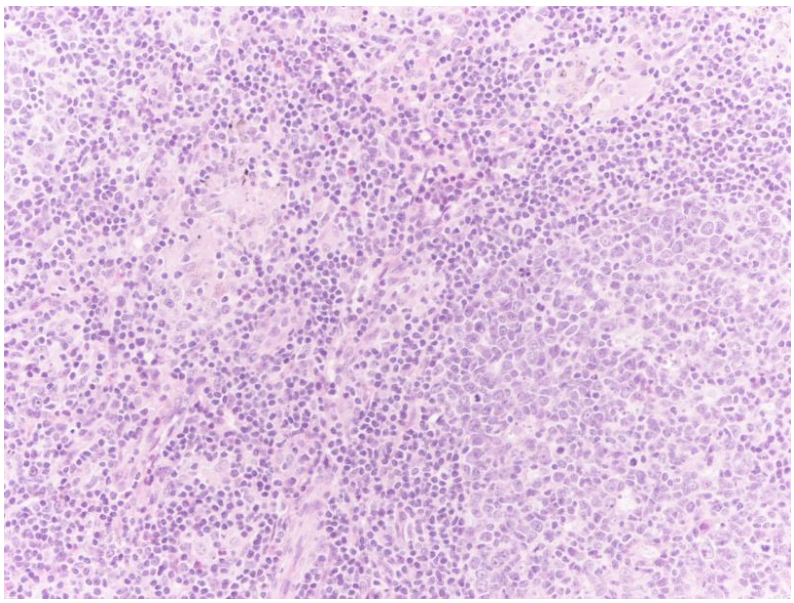

Fig. 4. Histological examination of a right paratracheal lymph node showing follicular hyperplasia and tiny clusters of epithelioid hystiocytes

The dosage of the anti-acetylcholine receptor antibodies before surgery was markedly elevated (> 100 pmol/ml); one month after thymectomy, the patient developed ocular myasthenia with diplopia, for which she started therapy with anticholinesterase. On the other hand, night sweats, asthenia, and fever did disappear, as did superficial adenopathies.

Serology confirmed the gradual disappearance of anti-Toxoplasma IgM antibodies and appearance of IgG antibodies.

The conclusive diagnosis was therefore thymoma with intercurrent infection with *Toxoplasma gondii.* Patient did not receive treatment for this infection because at the time of diagnosis the symptoms had reduced.

3. DISCUSSION

When the patient first came to our department, given the physical examination and the reported symptoms, the case seemed easy to solve. Suspicion of lymphoproliferative disease became stronger after the execution of CT and PET. Nevertheless, the diagnostic process was complicated and required two surgical procedures over a short period time, before the thymectomy itself.

The diagnosis of Toxoplasmosis was the first to be highlighted through serology. However, the clinical presentation and radiological images were not convincing and a histological diagnosis was essential.

In agreement with the thoracic surgeon, to avoid the removal of a superficial lymph node possibly reactive to the presence of toxoplasmosis, we decided to first perform biopsy of the mediastinal mass; the histological examination showed the presence of a thymoma.

However, the systemic symptoms and the presence of enlarged lymph nodes both above and below the diaphragm did not seem to be justified by Toxoplasma infection alone. Thus, again in accordance with the thoracic surgeon, we decided to remove the lymph node with the maximum radioactive glucose uptake on PET scans; the histological examination showed reactive follicular hyperplasia. Bone marrow biopsy was also normal.

Therefore, the conclusive diagnosis was thymoma with intercurrent infection with *Toxoplasma gondii*.

In our case the thymoma had probably caused a state of immunosuppression that facilitated the development of an infection with Toxoplasma with emphasized symptoms and diffuse adenopathies.

Although the clinical and instrumental examinations in this patient were highly suggestive of lymphoproliferative disease, serology and histological investigations disproved this hypothesis. We were thus able to establish the correct treatment, which led to the resolution of the symptoms. In this case, toxoplasmosis did not require any specific treatment because at the time of specific diagnosis, lymphoadenopathies had disappeared and symptoms were resolved; for the thymoma, we performed thymectomy followed by mediastinal radiotherapy.

4. CONCLUSION

In the diagnosis of lymphoproliferative disorders, the hematologist, the surgeon, the laboratory technician, and the pathologist must all collaborate closely.

This case report describes the simultaneous presence of two rare but not exceptional medical conditions involving the lymph node system. The association of the two diseases, which so far has been reported [2] very rarely, made diagnosis difficult.

The collaboration between the various specialists allowed us to reach the correct diagnostic conclusions and to avoid inappropriate treatment with possible severe complications.

CONSENT

All authors declare that written informed consent was obtained from the patient for publication of this case report and accompanying images.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid=945&id=12&aid=8293