Case Report

Thymoma diagnosis in a 37-year old woman hospitalized for SARS-CoV-2 infection

A case report

Maria Giannaki,
Rouzana Pechlivanidou,
Vasiliki Drampa,
Dimitrios Mpompotas,
Aikaterini Mitka,
Antonis Antoniadis

Pneumonology Department of General Hospital of Serres, Greece

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Correspondence:
Dr Antonis Antoniadis,
Director of Pneumonology Clinic,
General Hospital of Serres, Greece,
Tel.: +30 23210-94607,
Fax: +30 23210-94624,
E-mail: antonisant100@gmail.com

ABSTRACT

A 37-year-old woman with recent travel history from the UK presented to the emergency department with high fever, dry cough and weakness. Due to the COVID-19 pandemic she was admitted to the isolated COVID-19 unit and tested positive for SARS-CoV-2 through pharyngeal swab PCR. Chest x-ray revealed no lung opacities rather than mediastinum enlargement. CT scan showed a mediastinum mass and small subpleural lung opacities bilaterally. PET SCAN was performed followed by radical excision of the mass through VATS. The histologic analysis revealed type B2 Thymoma with partial invasion of the capsule, thus the patient underwent postoperative radiotherapy. This case report could be the principle for further investigation in the field of association between thymous gland and SARS-COV-2 infection through immunity pathway disorders.
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BACKGROUND

The thymus gland is located in anterior mediastinum and is responsible for producing immune cells in early life. It is predominantly consisted of epithelial cells and lymphocytes. Thymomas are morphologically heterogeneous tumors originating from cortical and medullary thymic epithelial cells (TECs). Different types of thymomas have been reported. Type A thymomas have neoplastic cells with spindle- or oval-shaped nuclei and are uniformly bland. Type B thymomas resemble the thymic cortex with the presence of immature lymphocytes. Type AB thymoma combines the features of both A and B thymoma. Thymomas are in most cases benign, but they can also become malignant and invade surrounding tissues in the mediastinum or spread to other organs such as the lungs. Their etiology remains not clear but they seem to be associated with various systemic syndromes such as MG (30-40% of patients with thymoma), red cell aplasia, dermatomyositis,

systemic lupus erythematosus (SLE), Cushing syndrome, and syndrome of inappropriate antidiuretic hormone secretion (SIADH), suggesting a strong link between thymomas and autoreactivity.[1] Several abnormalities have been reported in thymomas that affect T-cell development. Once identified by imaging studies or biopsy, treatment usually involves surgery and may also involve radiation therapy to reduce the likelihood of tumor recurrence.

CASE PRESENTATION

A 37-year-old woman with no medical history presented to the emergency department with high fever since 4 days, dry cough and weakness. She had recent travel historyt from London 10 days prior to her presentation.

In the ED she was normotensive, with oxygen saturation 96% on room air. On physical examination she had normal lung sounds without any other remarkable finding.

Laboratory workup revealed haemoglobin 14.9 g/dL, slightly elevated white cell count of 12.20 K/μL with absolute lymphocyte count of 1.18K/μL, D-dimer 200 ng/mL (normal ≤278 ng/mL), C-reactive protein (CRP) 4.05 mg/dL (normal ≤0.50 mg/dL), with otherwise unremarkable liver function tests and a normal renal function panel. A 12-lead ECG showed sinus rhythm without specific changes. Chest radiograph revealed no lung opacities rather than a significant dilatation of the mediastinum.

Due to the COVID-19 pandemic and the travel history of the patient, she was admitted to the isolated COVID-19 medical service for further workup isolation. Pharyngeal swab for SARS-CoV-2 PCR was obtained, which returned positive.

She was treated with hydroxychloroquine 400mg BID on day 1, followed by 200mg BID and azythromycin 250mg BID for 3 days according to the latest guidelines.

A chest CT scan was obtained and revealed subpleural lung opacities in the right lower lobe and smaller in the right middle lobe and left lower lobe. In the upper anterior mediastinum there was reported a well defined mass of 58x34x40mm. No lymph node enlargement was observed (Figures 1–3).

The differential diagnosis based on these findings included thymoma, lymphoma and teratoma. Due to the SARS-CoV-2 concurrent infection we wondered whether an unknown-not yet reported reactive enlargement of the thymus could also be a scenario.

After 14 days of hospitalization followed by two negative SARS-CoV-2 PCR tests she was discharged from

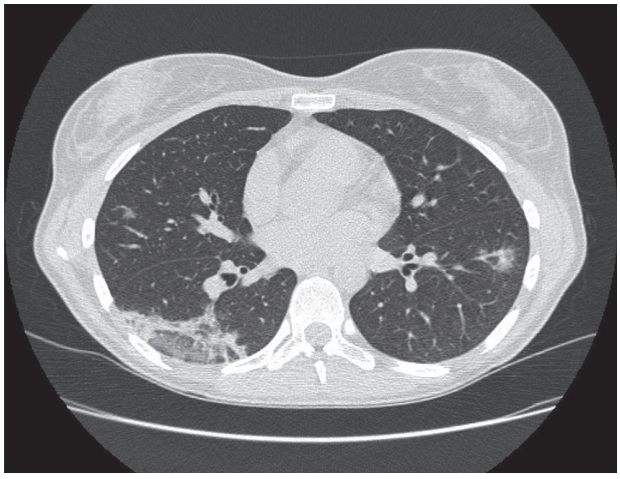

FIGURE 1. Lung infiltrations in RLL and LLL.

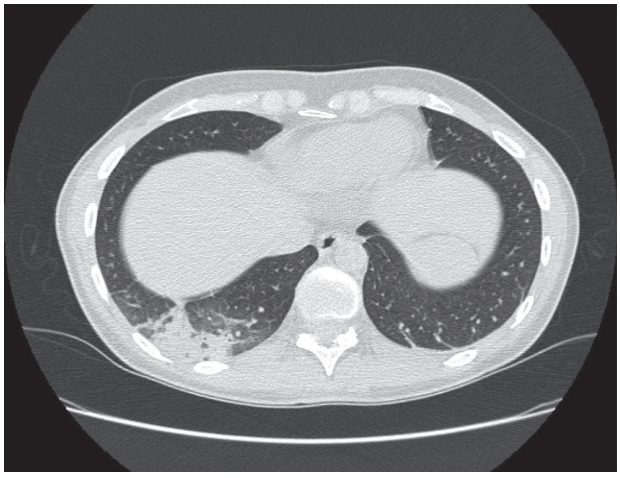

FIGURE 2. Lung infiltrations in RLL.

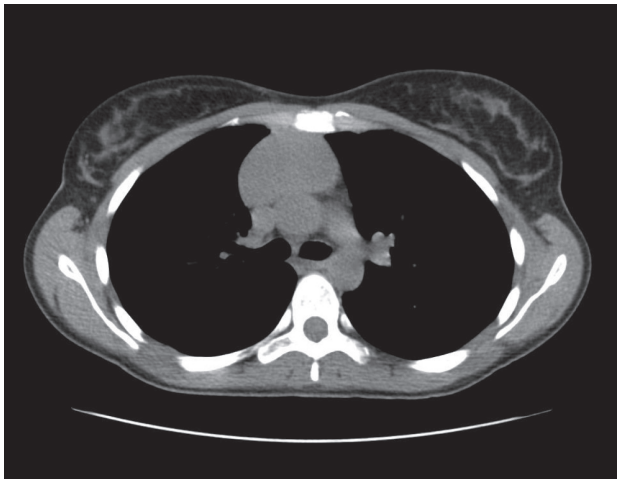

FIGURE 3. Mass in anterior mediastinum.

hospital to initiate the investigation of the mediastinum mass as an outpatient.

PET scan was obtained, which revealed moderate-high metabolic activity of the mediastinal mass suggesting low grade infiltration such as thymoma and excluding high grade lymphoma.

A week after, she undergone Video-assisted thoracoscopic surgery (VATS) to remove the mass. The fast-track biopsy revealed thymoma, so the whole tumor was removed and sent to further histologic analysis. According to the results, the tissue blocks removed revealed type B2 thymoma with invasion of the capsule at one side and thus classifying the tumor as pT2 (direct invasion of the pericardiumeither partial or full thickness) according to the TNM Classification of Malignant Epithelial Tumours 2015. The patient underwent postoperative radiotherapy (Figure 4).

Tissue blocks were also sent to University of Athens for further histologic analysis in order to investigate the possible correlation between SARS-COV-2 and thymous gland. Unfortunately, due to technical issues the procedure couldn't get accomplished.

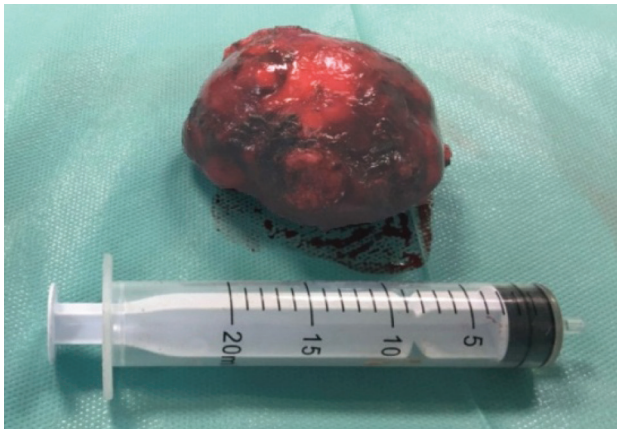

FIGURE 4. The mass as removed through VATS.

DISCUSSION

During the Covid-19 pandemic, an increasing number of studies have increased our knowledge on its epidemiology, pathophysiology and clinical consequences of the infection. In this case report we tried to correlate Covid-19 infection and thymic function, as it has already been established in series of viral infections so far.

According to up-to-date bibliography there are few data to establish the affect of infections on the thymic function due to the difficult access to the gland through biopsy. Most of them origin from HIV infected humans and animal models. Pathogens seem to disrupt thymic structure and function and thus alter T cell selection and export. This procedure takes place through local or systemic ways. Local refers to the direct presence of the pathogen in the thymus and systemic to the effects of the pathways involving glucocorticoids and other pro-inflammatory mediators that are released into the blood stream.[2,3]

In viral infections atrophy of the thymus is most commonly observed, regarding both lymphoid and microenvironmental compartments. It particularly concerns cortical lymphocyte, as it has been shown in AIDS.[4,] There is evidence that thymus cells are phagocyted by intrathymic macrophages through pathways that are related with the involvement of glucocorticoid hormone levels in the blood and TNF-α.[5,6]

The question is, could Covid-19 cause thymus enlargement rather than atrophy as it was a possible scenario at the beginning of our patient's investigation?

Enlargement of the thymus region is mostly observed in autoimmune conditions and tumours. In lymphopenic HIV-infected patients with maintained T-cells, reactive thymus hypertrophy has been also established and is associated with response to profound lymphopenia,[7] which is also common in patients with severe COVID-19 infection.

A significant observational study that was conducted in the Intensive Care Unit of the Clinique Ambroise Paré (Neuilly, France) comes to reinforce this hypothesis by noticing thymus enlargement at CT-scan in adult patients admitted for COVID-19 associated SARS. Thymus enlargement was more frequent in the COVID-19 group than in control, except the elderly, and was associated with more severe pulmonary involvement but lower mortality. They also concluded that it is related to enhanced thymic function that is beneficial to COVID-19 induced lymphopenia through increased production of T-cell precursors as was quantified through PCR TRECS.

In our patient's case seems that thymoma was an incidental finding, even if the correlation with SARS-COV-2 has not been excluded yet. The infection was in total beneficial, since it was the reason for detecting the mass which had already started to become invasive.

Probably in the era of Covid-19 pandemic, practice-based evidence through case reports could help us collect some data on those fields and add valuable information to our medical knowledge.

ΠΕΡΙΛΗΨΗ

Διάγνωση θυμώματος σε 37χρονη ασθενή νοσηλευόμενη για SARS-COV-2 λοίμωξη: Παρουσίαση Περιστατικού

Μαρία Γιαννάκη, Ρουζάνα Πεχλιβανίδου, Βασιλική Δράμπα, Δημήτριος Μπομπότας, Αικατερίνη Μήτκα, Αντώνιος Αντωνιάδης

Πνευμονολογικό Τμήμα, Γενικό Νοσοκομείο Σερρών

Μια 37χρονη γυναίκα με ιστορικό πρόσφατου ταξιδιού στο Ηνωμένο Βασίλειο, προσήλθε στο Τμήμα Επειγόντων Περιστατικών αιτιώμενη εμπύρετο, μη παραγωγικό βήχα και καταβολή. Από τον μοριακό έλεγχο ρινοφαρυγγικού επιχρίσματος προέκυψε θετική σε SARS-COV-2 λοίμωξη. Ο ακτινολογικός έλεγχος ρουτίνας αποκάλυψε διόγκωση του μεσοθωρακίου , χωρίς σαφείς πνευμονικές διηθήσεις. Επί περαιτέρω διερεύνησης διενεργήθη Αξονική Τομογραφία θώρακος με ευρήματα μικρών πνευμονικών διηθήσεων αμφοτερόπλευρα καθώς και περιγεγραμμένη ευμεγέθη, μάζα μεσοθωρακίου, η οποία στη συνέχεια επανελέγχθηκε με PET SCAN και αφαιρέθηκε θωρακοσκοπικά(VATS). Από την ιστολογική εξέταση του παρασκευάσματος προέκυψε θύμωμα τύπου Β2 με μερική διήθηση της κάψας, οπότε η ασθενής, βάσει οδηγιών, υπεβλήθη σε συμπληρωματική ακτινοθεραπεία. Το συγκεκριμένο περιστατικό θα μπορούσε να δώσει το έναυσμα για την περαιτέρω διερεύνηση της παθοφυσιολογικής συσχέτισης SARS-COV-2 λοίμωξης και θύμου αδένα μέσω ανοσολογικών μηχανισμών που δεν έχουν ακόμη κατανοηθεί επαρκώς από την επιστημονική κοινότητα.

Πνεύμων 2020, 33(4):1-4.

Λέξεις - Κλειδιά: *SARS-COV-2, θύμος αδένας, μεσοθωράκιο, θύμωμα*

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