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Management of thymomatous myasthenia gravis – Case report of a rare Covid19 infection sequelae

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ABSTRACT

INTRODUCTION: SARS CoV19 infection can predispose to many autoimmune and neurological conditions, thymomatous myasthenia gravis being one of them. The rarity of these case poses therapeutic dilemmas about their further management.

PRESENTATION OF CASE: A 61 year old gentleman who had covid19 infection 2 months back, presented with new onset myasthenia gravis and an anterior mediastinal mass. He was diagnosed as a case of anti acetyl choline receptor antibody positive thymomatous myasthenia gravis. The patient was posted for video assisted thoracoscopic excision of thymoma. The procedure was uneventful and patient was discharged with improvement in myasthenic symptoms. Histopathological examination confirmed the diagnosis of WHO Type A Spindle cell thymoma.

DISCUSSION: SARS CoV19 infection is associated with an array of autoimmune disorders due to various proposed phenomenon including molecular mimicry and loss of immune tolerance. Post infectious thymomatous myasthenia gravis is extremely uncommon, and can be managed with open, minimally invasive or robotic approach.

CONCLUSION: This is the first documented case of post covid19 infection thymomatous myasthenia gravis to the best of our knowledge, managed with minimally invasive thoracoscopic surgery. Further research is required for documentation of the natural history of the disease and therapeutic outcomes.

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1. Introduction

The outbreak of SARS CoV19 pandemic has resulted in unmasking and exacerbation of various autoimmune and neurological disorders [1]. There are uncertainties regarding their further management. Our patient presented with a new onset thymoma following covid19 infection with anti acetyl choline receptor (AChR) antibody positive myasthenia gravis. He was managed with minimally invasive surgery and is presently on follow up. This case report has been reported in line with the SCARE Criteria [2].

2. Case report

A 61 year old gentleman, who is a diagnosed case of bronchial asthma and diabetes mellitus had SARS CoV-19 infection in September 2020. He was managed with non-invasive ventilation, corticosteroids and antiviral agents. CT scan of the Thorax was done which revealed a CT Severity Score of 13/25 with no evidence of any

mediastinal mass. The patient recovered and was discharged with the advice to quarantine for 7 days. 2 months later, in November 2020, patient experienced an acute episode of breathlessness, with dysphagia and generalised weakness. He was diagnosed with myasthenia gravis and was given intravenous immunoglobulins, corticosteroids and pyridostigmine. Patient required intermittent non-invasive ventilation for respiratory support. CT Scan of the Thorax was repeated which revealed a new finding of a mass in the anterior mediastinum which was suggestive of thymoma (Fig. 1). The patient was subsequently referred to our setup for surgical management.

The patient was asymptomatic when he presented to us and was maintained on oral Prednisolone 30 mg on once a day dosing. Serum Acetyl Choline Receptor Antibodies were significantly elevated (11.3 nmol/L). Contrast Enhanced CT Scan of the Thorax revealed a mass of 1.7 × 5.5 × 4.5 cm in the prevascular space of the anterior mediastinum abutting the ascending aorta, left and right innominate veins and superior vena cava with maintained fat planes, staged IIB according to Masaoka staging system (Fig. 2). Covid-19 infection sequelae in the form of linear fibrotic subpleural bands were also noted (Fig. 3).

The patient was posted for Video Assisted Thoracoscopic Surgery where excision of Thymoma with thymectomy was done.

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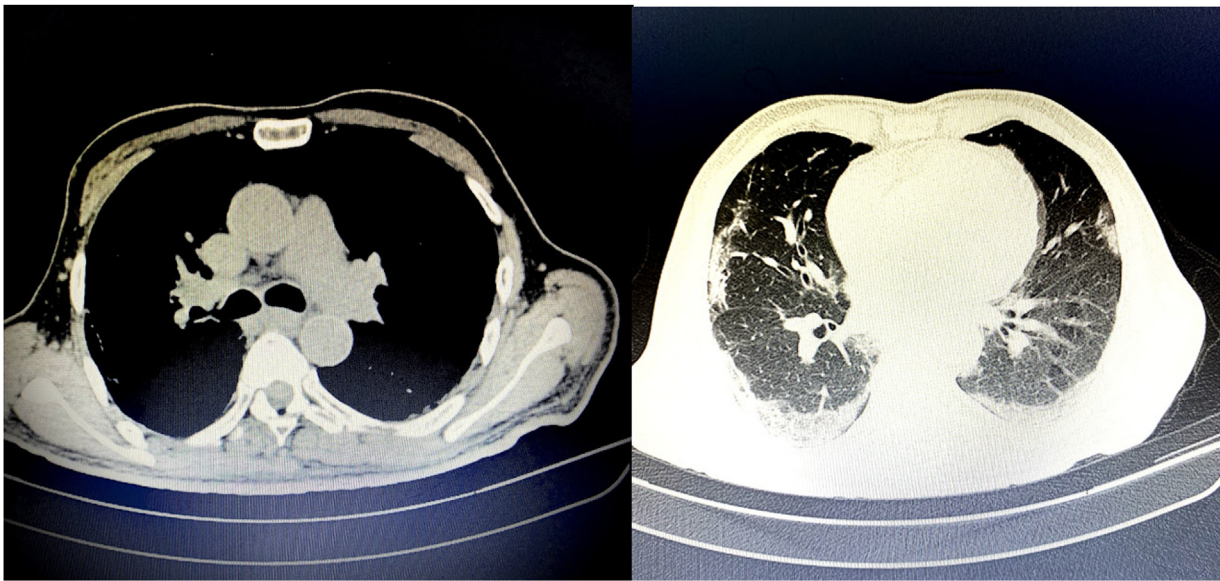


Fig. 1. CT scan of thorax during first admission with covid-19 infection showing absence of mediastinal mass with ground glass opacities occupying the lower lung fields.

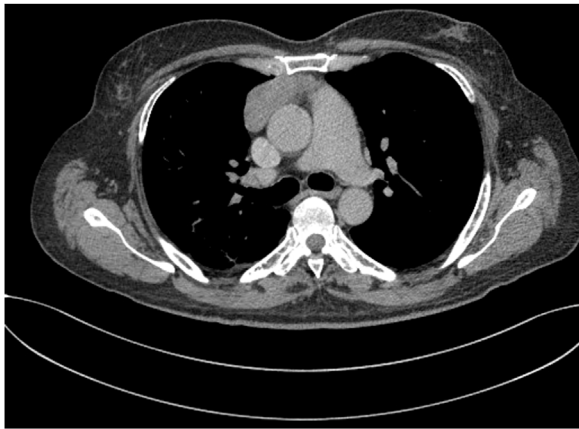


Fig. 2. Contrast enhanced CT of thorax revealing a thymoma in the prevascular space of anterior mediastinum.



Fig. 3. Lung window showing subpleural bands as post covid19 sequelae.

We adopted a right sided approach using single lung ventilation of the left lung. A 10 mm camera port was inserted in the right 5th intercostal space in the anterior axillary line. 5 mm working ports were introduced in the 3rd and 6th intercostal spaces. Dissection was started on the right side anteriorly after identification of the left phrenic nerve (Fig. 4). A large lesion of 6 × 5 × 2 cm was present in the anterior mediastinum with surrounding adhesions to the thymic fat. Using bipolar energy source, dissection was proceeded as medially and as cranially as possible. Administration of Indocyanine Green dye with real time fluorescence angiography further aided in securing a blood less dissection field (Fig. 5). The left and right superior horns of the thymus were dissected out marking the superior extent of our dissection. Remaining mediastinal fat was trimmed off the left innominate vein to the cardiophrenic angle caudally to dissect out the specimen in toto (Fig. 6). The specimen was retrieved in an endobag and chest drain was placed (Fig. 7). The patient was monitored in an intensive care unit for a day and had an uneventful post operative course, he was discharged after 3 days of hospital stay.

Histopathological examination of the specimen revealed a homogenous population of spindle cells showing coarse and evenly distributed chromatin with rare mitosis and sparse lymphocytic infiltrate (Fig. 8). The capsule was intact with no evidence of microscopic capsular invasion. The cells were immunoreactive for pancytokeratin (AE1/AE3/TTF1/CK7/p40 with focal immunoreactivity for CD99). The lymphocytes are immunopositive for TdT (Fig. 9). The final histopathological diagnosis of spindle cell thymoma, WHO type A was made. Recovery was evident on oncological terms with complete excision of thymoma having clear resection margins. Improvement of myasthenic symptoms was noted as a decrease in the dose of prednisolone required for maintenance from 30 mg once daily dosing to 15 mg on alternate days now. A repeat Serum Acetyl Choline Receptor Antibody titre showed a fall from pre-operative values to a marginally elevated value of 0.9 nmol/L. The Quantitative Myasthenia Gravis Score decreased to 3 from an initial pre-operative score of 14. The patient was asymptomatic on 6 weeks of follow up.

3. Discussion

Thymoma associated with myasthenia gravis requires a multi-modality management with surgery lying at its cornerstone. The

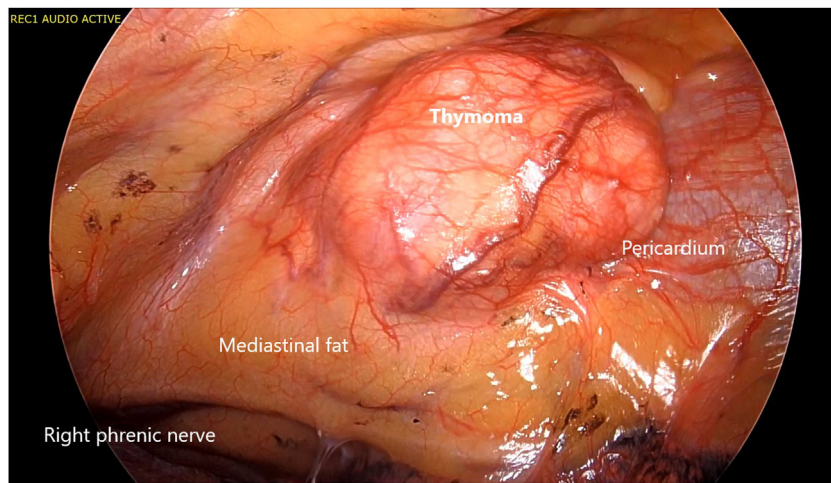


Fig. 4. Thoracoscopic view showing initial survey demonstrating right phrenic nerve, pericardium, mediastinal fat and thymoma.

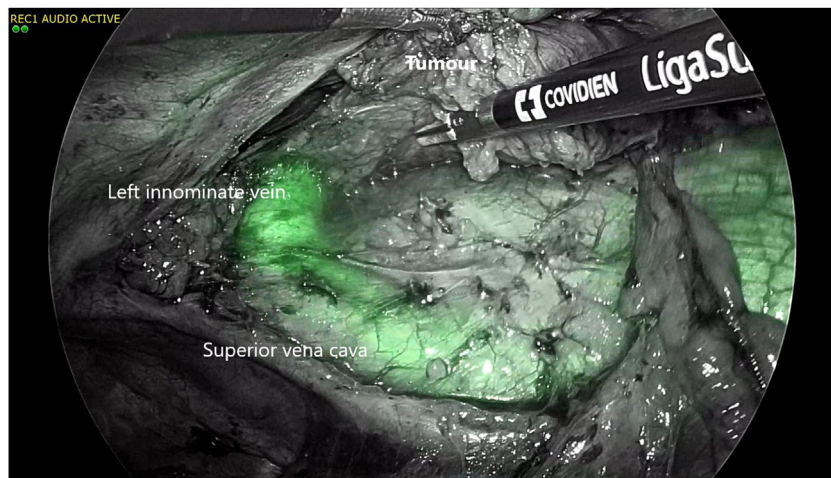


Fig. 5. Use of real time fluorescence with ICG to delineate vascular anatomy.

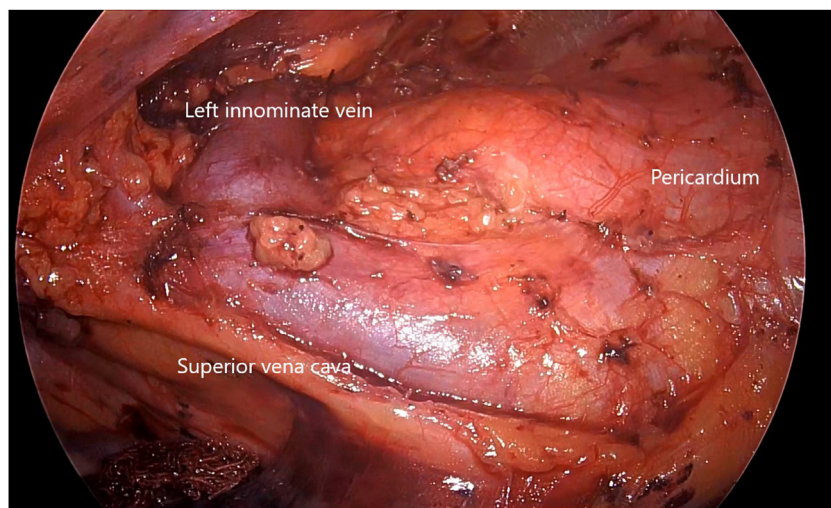


Fig. 6. Thoracoscopic view of anterior mediastinum after resection of thymoma.

surgery is primarily aimed at managing the oncological outcome rather than myasthenia. Equivalent outcomes in terms of disease free survival and recurrence of tumour are observed while comparing radical thymectomy versus a more conservative thymo-

mectomy [3]. Clearance of as much thymic fat as possible however, ensures superior outcomes with respect to myasthenia gravis. Medical management of thymoma involves use pyridostigmine and corticosteroids. Refractory cases are managed with plasma



Fig. 7. Gross picture of the resected thymoma with mediastinal fat.

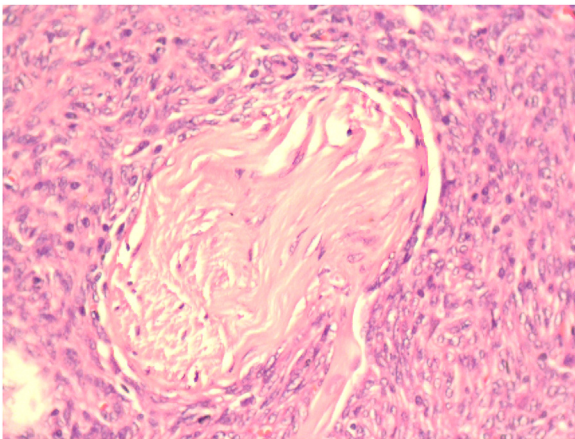


Fig. 8. Spindle cells with Hassall's corpuscles on hematoxylin and eosin staining.

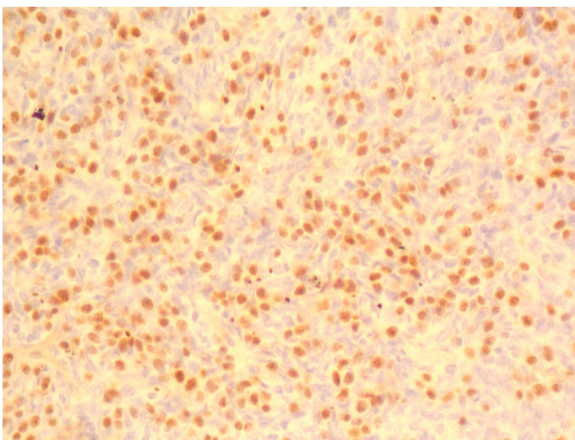


Fig. 9. TdT positive lymphocytes on immunohistochemistry.

exchange and intravenous immunoglobulins [3]. Stabilisation and optimisation of patients prior to the surgery is highly recommended.

Surgical management of thymoma can be done via open approaches, minimally invasive Video Assisted Thoracoscopic Surgery (VATS) approach or robotic approach. A large systematic review conducted recently concluded that the robotic approach and VATS approach had similar rates of complications, mortality, and equivalent oncological outcomes [4]. However, a randomised control trial is required still to make a definitive conclusion. A thoracoscopic approach is ideal in resource limited settings as it combines the advantages of a minimally invasive approach, with better cosmetic outcomes and patient compliance without compromising on oncological and disease outcomes.

Our patient presented with new onset myasthenia gravis and thymoma following SARS CoV19 infection, which to the best of our knowledge is the first reported case of the same. There have been 4 documented cases so far of patients developing myasthenia gravis post covid19 infection, however, none of them were associated with a thymoma [5,6]. The exact pathogenesis of development of autoimmune disorders after infection with SARS CoV19 is not well understood, however various mechanisms have been proposed for the same. It is a well-documented fact that a decrease in AChRs at the post synaptic terminal secondary to autoantibodies or proinflammatory state plays an important role in the development of myasthenia gravis. The cross reactivity between antibodies produced by the host body against covid19 virus and AChR due to molecular mimicry might play a role as well. Activation of proinflammatory cascade, cytokines and chemokines along with B and T cell depletion with increased levels of interleukins and TNF α might result in loss of immunological self-tolerance aiding the disease process. These mechanisms are similar to reported cases of post-infectious myasthenia gravis associated with other viral infections like Varicella zoster, West Nile virus, and Zika virus [7,8]. All the previously documented reports of post covid19 myasthenia gravis were noted in the primary admission, but here it is a delayed presentation after almost 2 months of the initial viral prodrome similar to how it is observed in other post viral prodrome diseases.

Covid-19 infection is known to precede or unmask a latent myasthenia gravis [5,6]. In our patient the onset of symptoms after the primary infection was delayed, which supports the hypothesis that the viral infection might have triggered Myasthenia gravis, however, we cannot rule out the possibility of unmasking of a latent disease with certainty. The absence of any mediastinal pathology on the CT scan of thorax done during the first infection and its appearance after 2 months along with classical symptoms of myasthenia gravis furthers our hypothesis. Timely surgical management of the patient after optimising for elective procedures stands central in the therapeutic game plan for such cases.

4. Conclusion

Covid-19 pandemic has challenged the medical fraternity on various frontiers, not limiting itself to just one broad speciality. To the best of our knowledge this is the first report of a patient developing thymomatous myasthenia gravis following Covid-19 infection. Likely mechanisms behind the pathophysiology include molecular mimicry and loss of immune self-tolerance. Management of this tumour can be done by open, minimally invasive thoracoscopic and robotic approach. Minimally invasive surgery offers superior cosmesis, lesser pain and shorter hospital stay without compromising on oncological outcomes. A prospective follow up on cases is required to document delayed complications and association of covid-19 infection with autoimmune conditions. Further research is also prudent to unravel the underlying natural history of disease as well as efficacy of medical and surgical management.

Declaration of Competing Interest

The authors report no declarations of interest.

Funding

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Ethical approval

Our case report is exempt from ethical approval.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Ajay Bhandarwar – Conceptualising of research, primary surgeon, manuscript review.

Shekhar Jadhav – First assistant during surgery, review of literature.

Amarjeet Tandur – Manuscript preparation, data collection, review of literature.

Nikhil Dhimole – Second assistant during surgery, manuscript preparation, data collection and follow up.

Amol Wagh – Review of literature, complication of images.

Supriya Bhondve – Manuscript review and editing, review of literature.

Registration of research studies

Not applicable.

Guarantor

Ajay Bhandarwar.

Provenance and peer review

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