Case Report

Implications of COVID-19 On A Rapidly Growing Thymoma Case

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Abstract

Introduction
Thymomas are a rare form of slow-growing malignancy that originate from thymic epithelial cells presenting as an anterior mediastinal mass. Although most are asymptomatic, they can have a variety of presentations, such as local thoracic symptoms, superior vena cava syndrome, or paraneoplastic syndromes. Local compressive thoracic symptoms include shortness of breath, chest pain, and cough. Superior vena cava syndrome presents with respiratory, vascular, or neurologic symptoms. Paraneoplastic syndromes, such as myasthenia gravis, are due to abnormal T-cell maturation leading to an increased risk of autoimmune conditions.

Case Presentation
We report a case of a 71-year-old White male with multiple comorbidities presenting to the emergency room after a mechanical fall with an incidental finding of a 3.8 cm x 6.0 cm anterior mediastinal mass. The patient had no local compressive symptoms or paraneoplastic syndromes. Due to the coronavirus disease 2019 (COVID-19) pandemic, the patient did not follow through with the discharge recommendations for surgical consultation. Over a year later, the patient presented to the emergency room for congestive heart failure exacerbation, and chest computed tomography revealed the mass had increased in size to 8.2 cm x 7.7 cm. A multidisciplinary approach was used to determine the patient's course of treatment. Due to the patient's debilitated state and concern for local invasion, radical thymectomy with mediastinal lymph node dissection was planned. Despite medical optimization and coordination with a multidisciplinary team, following surgery, the patient became symptomatically bradycardic with acute hypoxic respiratory failure. The patient ultimately passed away after pulseless electrical activity and the family's decision to discontinue resuscitation.

Conclusion
It is imperative to consider the negative impacts of the COVID-19 pandemic. Delay in treatment allowed the thymoma to rapidly grow, thus leading to a decreased chance for cure. An extensive surgery increased perioperative risks that led to unforeseen complications resulting in the untimely death of the patient.

Keywords
thymoma; thymic carcinoma; thymus; COVID-19; long term adverse effects

Introduction
Anterior mediastinal masses most commonly include thymomas, thyroid goiters, teratomas, and lymphomas. Thymomas are the most common anterior mediastinal mass and are described as slow-growing neoplasms that originate from thymic epithelial cells generally located in the anterior mediastinum.[1] The thymus is a primary lymphoid organ and the site responsible for T-cell maturation. Although thymomas are a rare form of malignancy with a reported estimate of 390 cases per year in the United States, they are considered the most common tumor of the thymus.[1] Thymomas

are quite uncommon in childhood, yet become more prevalent in middle-aged patients, with the highest incidences reported in Asians and Pacific Islanders.[1]

Most patients present asymptomatically, but thymomas can have a variety of clinical presentations that are associated with local thoracic symptoms, superior vena cava syndrome, or paraneoplastic syndromes. Local thoracic symptoms are limited to the thymus or adjacent organs and present with shortness of breath, chest pain, cough, dyspnea, orthopnea, or hemoptysis.[2] Severe cases present with symptoms associated with superior vena cava syndrome, such as chest and neck swelling, respiratory compromise, or neurologic manifestations.[2] Systemic syndromes can be caused by paraneoplastic disorders, most commonly myasthenia gravis, but can also include neuromuscular, dermatologic, or hematologic disorders, such as pure red cell aplasia, hypogammaglobulinemia, or pure white blood cell aplasia.[2] These autoimmune conditions are systemic syndromes caused by immunologic mechanisms, which commonly occur due to abnormal T-cell maturation in the thymus.[1]

Thymomas can be classified as benign or malignant based on histology and staging criteria. Histology categorizes thymomas into medullary patterns presenting with benign behavior, cortical patterns exhibiting malignant behavior, or mixed patterns displaying intermediate behavior. Thymomas are further classified based on cellular histology as type A (bland spindle cells with few lymphocytes), AB (mixed thymoma), B1 (lymphocytes with few epithelial cells), B2 (increased epithelial cells forming clusters, cytologic atypia, and possible anaplastic behavior), or B3 (polygonal tumor cells and cytologic atypia with few lymphocytes).[3,4] Thymoma staging is determined by the Masaoka-Koga staging criteria and defined by the level of invasion: Stage I: no capsular invasion; Stage II: capsular or pleural invasions; Stage III: invasion of surrounding tissue; Stage IVa: dissemination into the thoracic cavity; and Stage IVb: distant metastases, most commonly to the lungs or bones.[5] Prognosis and survival rates are determined by a variety of factors, such as the stage of the thymoma, cellular histology, and complete resection. The 5-year overall survival rate is 84.9%, with Stage I: 91.7%; Stage II: 88.9%; Stage III: 72.0%; and Stage IV: 34.3%.[6]

Early-stage thymomas can be treated with minimally invasive surgical procedures, such as video-assisted thoracic surgery or robotic-assisted thoracic surgery, yet the most effective and reliable treatment remains open, complete resection of the thymoma capsule with conventional median sternotomy. Management can vary depending on the size of the mass and the extent of invasion, which is categorized as resectable, potentially resectable, or unresectable. Complete resection is indicated as the initial treatment for encapsulated thymomas.[2] Potentially resectable thymomas suggest a level of invasion and therefore require preoperative chemotherapy and postoperative radiation therapy.[2] Unresectable thymomas signify greater complications due to metastasis. These can be managed with neoadjuvant systemic therapy using chemotherapy and radiation or with salvage cytoreductive surgery.[2]

In this report, we consider the clinical presentation and complications manifested in a patient presenting with a large thymoma and discuss the impact of the coronavirus disease 2019 (COVID-19) pandemic on the patient's case.

Case Presentation

In 2020, a 71-year-old White male with a past medical history of hypertension, hyperlipidemia, diabetes mellitus, atrial flutter, cerebrovascular accident, congestive heart failure (CHF) with reduced ejection fraction (EF) (35-40%), chronic coronary artery disease, and end-stage renal disease requiring hemodialysis, and with a pertinent past surgical history of left brachiocephalic arteriovenous fistula creation, presented to the emergency department after a mechanical fall complaining of backache, rib pain, and headache. Chest computed tomography (CT) imaging incidentally revealed a soft tissue mass in the anterior mediastinum with a cross-sectional diameter of 3.8 cm x 6.0 cm (**Figure 1**). No acute processes were revealed. Prior hospital imaging, including a magnetic resonance imaging of the neck in 2017 and a chest x-ray in 2018, did not reveal any anterior chest mass or mediastinal widening. The patient denied symptoms related to mass or systemic syndromes caused by autoimmune

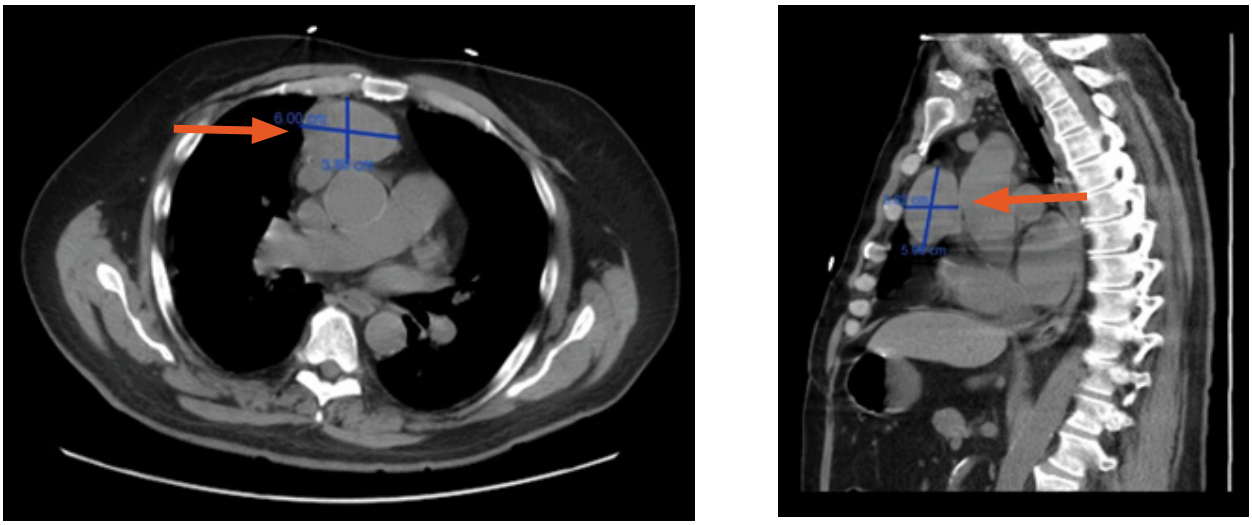


Figure 1. An initial chest CT scan without contrast shows an anterior mediastinal soft tissue mass measuring 3.8 cm x 6.0 cm in cross-sectional diameter abutting the ascending aorta posteriorly and the mediastinal pleura anteriorly (orange arrows).

conditions. The patient was discharged from the emergency room with recommendations to follow up as an outpatient with a cardiothoracic surgeon but failed to pursue consultation due to the ongoing COVID-19 pandemic. During this time, the patient was living with his daughter who was his primary caretaker. The patient remained in social isolation due to the social distancing guidelines and his multiple comorbidities with a sedentary lifestyle.

A year and 4 months later, the patient presented to the emergency department with bilateral knee pain, vomiting, and acute-on-chronic decompensated CHF with elevated B-type natriuretic peptide (BNP) levels (2522 pg/ml). An EKG revealed sinus rhythm with first-degree atrioventricular block and a troponin I level of 0.241 ng/L. Transthoracic echocardiogram revealed an EF of 35-40%, mild tricuspid and mitral regurgitation, and inferior and inferolateral wall hypokinesis. Cardiac catheterization revealed a chronic total occlusion of the distal right coronary artery (RCA) with collateral flow, which was unchanged from prior catheterization. Chest CT revealed the anterior mediastinal mass had grown to 8.2 cm x 7.7 cm in cross-sectional diameter with unclear margins, trace pericardial effusion, and lymphadenopathy (**Figure 2**). The mass was consistent with a neoplastic process and thus a CT-guided biopsy was performed. The final pathology report revealed type A thymoma with a requested second opinion favoring malignant thymoma. After confirmation of unchanged cardiac catheterization medical stabilization, and pending a final pathology report, the patient was discharged with instructions to follow up as an outpatient with cardiothoracic surgery, oncology, cardiology, and nephrology.

One month later, a PET/CT scan revealed mediastinal and abdominal lymph nodes that were concerning for metastatic disease. Two months later, the patient presented to our office for a cardiothoracic surgery consultation. The patient's case was discussed in depth with a multidisciplinary team, including oncology, cardiology, nephrology, and critical care. It was concluded that due to the rapid growth of the tumor and the strong possibility of local invasion with associated compressive symptoms the patient would not tolerate neoadjuvant chemotherapy and radiation followed by surgery. Furthermore, due to the patient's moderate to severe frailty, the patient's current state would be worsened by chemotherapy and radiation.[7] Although he had a Class IV cardiac risk index, in this case, his RCA occlusion remained stable with evidence of collaterals, and cardiology determined coronary revascularization was not indicated.[8] The best possible outcome was ensured by performing a radical thymectomy and mediastinal lymphadenectomy with consideration of chemotherapy and radiation postoperatively. The preadmission and surgery dates were coordinated with the hospital to ensure preoperative dialysis and postopera-

tive intensive care. Due to the high capacity of COVID-19, the earliest date the patient could be admitted was 2 weeks later. During the surgery, a standard median sternotomy with radical thymectomy was performed with clean dissection from the surrounding vasculature and phrenic nerves. The mass along with the dissected lymph nodes were sent to pathology for permanent section. Two Blake drains were placed, and the sternum was reapproximated and closed with sternal plates and wires. There were no complications, and the patient was transferred to the intensive care unit in stable condition.

The patient remained hemodynamically stable, draining serosanguineous fluid from his drains. On postoperative day 4, telemetry revealed junctional escape rhythms with a heart rate as low as 20 beats per minute (bpm) along with acute hypoxic respiratory failure requiring a 15 L nonrebreather mask. Despite providing dopamine and midodrine, vitals remained unstable. A temporary pacemaker was placed in the right ventricle. The patient's hemodynamic status improved with telemetry revealing sinus rhythm with a heart rate between 50 to 70 bpm, yet the following day after dialysis, the patient complained of feeling ill and became unresponsive with pulseless electrical activity (PEA). Code blue was called and cardiopulmonary resuscitation was initiated. The patient's next of kin was contacted who indicated they did not want resuscitation to be continued. Advanced Cardiovascular Life Support measures were then stopped, and the patient was pronounced dead.

The final pathology report revealed the mass to be a type A thymoma measuring 10 cm in its greatest dimension, focally invading the thymic capsule and contacting the surrounding fat (**Figure 3**). Lymphovascular invasion was not identified, and all 9 separate lymph nodes that were submitted were negative for metastatic malignancy. The American Joint Committee on Cancer (AJCC) 8th edition staging system found the mass to be T1aN0M0, and the modified Masaoka stage was IIa.

Discussion

Thymomas are neoplasms that originate from thymic epithelial cells and are of unknown etiology.[1] Their significance is due to the low occurrence of thymomas leading to a limited number of case presentations and literature. Though the rate of diagnosed thymomas has increased due to higher rates of imaging, thymoma remains one of the most uncommon malignancies, with a reported estimated number of cases remaining under 400 per year.[1,9] Due to the limited quantity, each case report is relatively informative as each illuminates a unique disease course of how a thymoma presents and is treated.

This case demonstrates a unique presentation of a rapidly growing thymoma with direct implications for the outcome associated with

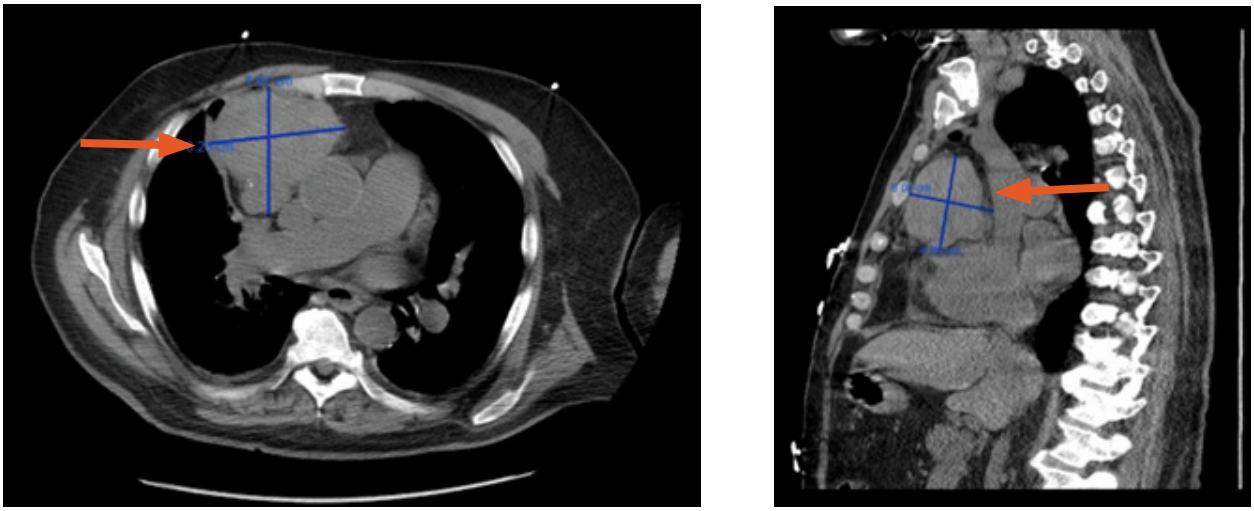
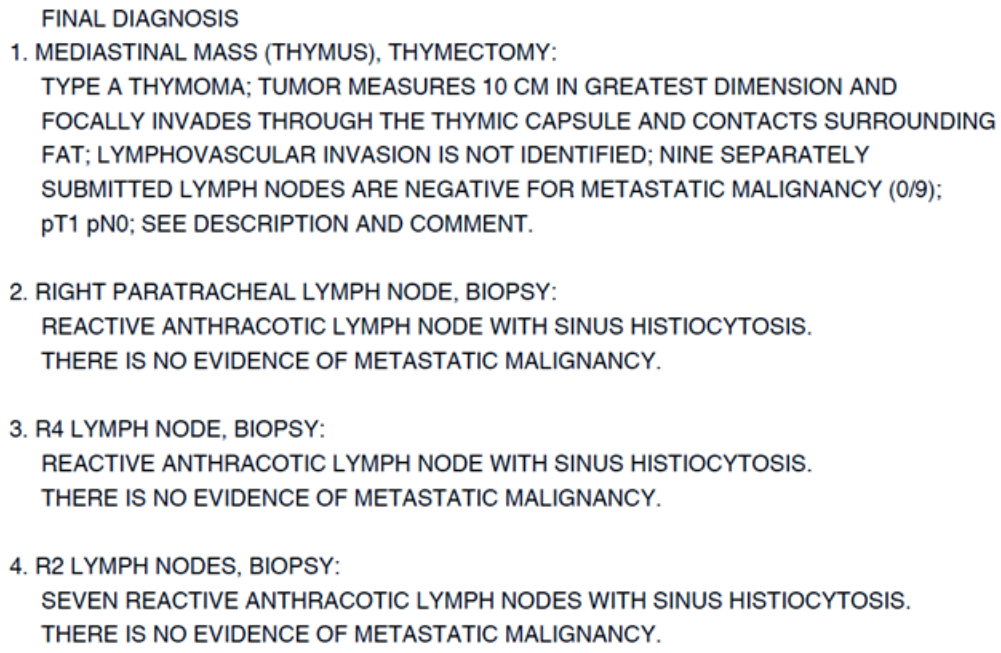


Figure 2. A secondary chest CT scan without contrast shows a large anterior mediastinal mass, approximately 8.2 cm x 7.7 cm in greatest axial dimension, consistent with a neoplastic process (orange arrows).



FINAL DIAGNOSIS

1. MEDIASTINAL MASS (THYMUS), THYMECTOMY:
   TYPE A THYMOMA; TUMOR MEASURES 10 CM IN GREATEST DIMENSION AND FOCALLY INVADES THROUGH THE THYMIC CAPSULE AND CONTACTS SURROUNDING FAT; LYMPHOVASCULAR INVASION IS NOT IDENTIFIED; NINE SEPARATELY SUBMITTED LYMPH NODES ARE NEGATIVE FOR METASTATIC MALIGNANCY (0/9); pT1 pN0; SEE DESCRIPTION AND COMMENT.

2. RIGHT PARATRACHEAL LYMPH NODE, BIOPSY:
   REACTIVE ANTHRACOTIC LYMPH NODE WITH SINUS HISTIOCYTOSIS. THERE IS NO EVIDENCE OF METASTATIC MALIGNANCY.

3. R4 LYMPH NODE, BIOPSY:
   REACTIVE ANTHRACOTIC LYMPH NODE WITH SINUS HISTIOCYTOSIS. THERE IS NO EVIDENCE OF METASTATIC MALIGNANCY.

4. R2 LYMPH NODES, BIOPSY:
   SEVEN REACTIVE ANTHRACOTIC LYMPH NODES WITH SINUS HISTIOCYTOSIS. THERE IS NO EVIDENCE OF METASTATIC MALIGNANCY.

Figure 3. The final pathology report revealed a type A thymoma.

the COVID-19 pandemic. Under most circumstances, immediate intervention of the smaller thymoma with consideration of a minimally invasive approach (MIA) is implemented to prevent its growth. However, social isolation led to decreased follow-up visits during the COVID-19 pandemic. The delay in treatment allowed the thymoma to rapidly increase in size, leading to a more extensive surgery, increased perioperative risk, decreased chance for cure, and unforeseen complications, which resulted in the untimely death of the patient. Furthermore, despite the urgent need for surgical intervention, the patient's preadmission and surgery dates were prolonged due to the limited resources and available space in the intensive care unit as a result of the high capacity of COVID-19 patients.

Studies have shown that Masaoka stages I and II thymomas can effectively be removed with an MIA with comparable survival to an open approach, yet we decided not to pursue an MIA due to the large size of the mass, associated difficulty of surgical manipulation, possible invasion into surrounding structures, and increased risk of thymoma capsular injury.[10,11] Although the surgery was successful in removing the thymoma, the patient experienced postoperative complications requiring intervention with the placement of a temporary pacemaker. Nonetheless, the patient subsequently became unresponsive with PEA during dialysis. There are some potential etiologies due to the unfortunate death. The patient's RCA was occluded indicating the possibility of decreased perfusion to the patient's atrioventricular node; however, prior coronary artery catheterization and stress testing revealed consistent collateral vascularization. We, therefore, decided not to perform concurrent coronary artery bypass grafting and prolong anesthesia time for a sick patient. In hindsight, intraoperative, temporary pacemaker wire placement could have been beneficial in preventing postoperative bradyarrhythmia. Other possible explanations include pulmonary embolism or heart block secondary to medications, sick sinus syndrome, or decreased preload during dialysis. Such complications are a combination of his poor pre-existing health conditions compounded with the stress of an extensive surgery, which ultimately led to the patient's demise. However, without surgical intervention, the patient's prognosis remained poor due to the increase in severity and frequency of symptoms, as well as the decrease in quality of life.

Conclusion

This is one of the first cases reported discussing the secondary impact of COVID-19 on a patient presenting with a thymoma. We

believe an earlier surgical intervention would have greatly benefited the patient in terms of reducing the risk of postoperative complications. There are no randomized clinical trials that provide definitive guidance for the management of thymomas.[2] In general, it is important to address how this case highlights the significance of a case-by-case approach when formulating treatment plans, especially for rare and complicated diagnoses that present under unique circumstances.

Conflicts of Interest

The authors declare they have no conflicts of interest.

Drs Lalonde and Tauriainen are employees of Medical City Arlington, a hospital affiliated with the journal's publisher.

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