A 23-year-old female presented with 3 months of central chest pain and fever. Clinico-radiological investigations were consistent with an anterior mediastinal mass. This clinicopathologic conference discusses the differential diagnoses of such a presentation and their management options.

**KEY WORDS:** Female, mediastinal mass, young

**PRESENTATION OF THE CASE**

**Dr. Rohit**

A 23-year-old nonsmoker female presented to the Pulmonary Medicine outpatient with complaints of central chest pain of 3 months and low-grade fever. The fever was intermittent, low grade (maximum recorded was 100°F), without any diurnal variation or any night sweats. It was not associated with chills or rigors. She denied the presence of cough, shortness of breath, wheezing, loss of appetite, and loss of weight. She had no history of any major medical or surgical illness or any exposure to a patient of active tuberculosis.

Clinical evaluation and imaging at another hospital revealed a mediastinal mass and she was referred to our center for further assessment.

On physical examination, the vital signs and oxygen saturation while breathing room air were normal. Respiratory system examination revealed dull note in the right parasternal area in the second and third intercostal region. Rest of the systemic examination was unremarkable.

A contrast-enhanced computed tomogram (CT) scan of the thorax revealed an ill-defined solid mass predominantly in the anterior and middle mediastinum measuring 85 mm × 50 mm without any postcontrast enhancement [Figure 1]. The mass did not have any cystic component nor any areas of calcification or necrosis. The mass did not have any well-defined borders and was encasing the left brachiocephalic vein and compressing the right upper lobe bronchus. However, it did not have any definite infiltration into the adjacent structures. Her complete blood count, liver, and kidney function tests were normal and viral serologies were negative. Tumor markers (serum beta human chorionic gonadotropin, alpha-fetoprotein and lactate dehydrogenase), serum immunoglobulins (serum immunoglobulin G [IgG], IgA, IgA,
Iyer, et al.: Anterior mediastinal mass in young female

**DIFFERENTIAL DIAGNOSIS**

*Dr. Hariharan Iyer*

Bronchogenic carcinoma (small cell type)

Bronchogenic carcinoma predominantly small cell type can present with a predominantly central lesion. However, considering the young age and the absence of smoking status makes this an unlikely cause.

Lymphoma

Classic Hodgkin’s lymphoma commonly presents with lymph node enlargement of the neck. Mediastinal lymph node enlargement can be seen in 50%–60% of the cases and can be asymptomatic or associated with symptoms such as retrosternal chest pain, cough, and dyspnea. The patient also had an accompanying fever which constitutes a “B symptom.” This disease usually has a peak age of presentation between 15 and 35 years. Considering the clinico-radiological profile of this patient, this etiology will be high on the list of differential diagnosis.

Thymoma/thymic carcinoma

Thymoma may occur in patients of all age groups, with a peak incidence between 40 and 60 years and an equal gender predilection. Paraneoplastic syndromes, most commonly myasthenia gravis presenting with muscle weakness are a frequent accompaniment. Usually, a thymic tumor is found to be located between the sternum and the great vessels. Thymoma usually presents with a smooth or lobulated contour arising from one lobe of the thymus. Furthermore, these tumors may have an associated cystic component and peripherally located calcification. On the other hand, thymic carcinomas are aggressive tumors which occur in the age group of 50–70 years and are characterized by imaging findings of anterior mediastinal mass with areas of necrosis, hemorrhage, calcification with locoregional (pleural or pericardial dissemination), and distal spread. Our patient had a younger age without any associated paraneoplastic features. The mediastinal mass described was devoid of any cystic or calcified component (usually seen in thymomas), nor there were any radiological features typically described in thymic carcinomas. Considering this clinical picture, both these etiologies though possible, would be less common in the present case.

Retrosternal extension of thyroid

This disease also should be considered in the differential diagnosis of anterior mediastinal mass. However, these lesions usually show contiguity with the thyroid, which was absent in the present case. Furthermore, these lesions are known to frequently present with breathlessness, dysphonia, difficulty in swallowing, or a superior vena cava obstruction, which were absent in the present case. Radiologically, after IV contrast is administered there is a pronounced enhancement seen in these masses, however in our case, there was no postcontrast enhancement seen. These masses usually have well-defined borders and are associated with punctate calcification. Due to the absence of these features, possibility of this etiology is less.

Fibrosing mediastinitis

This is a rare disease which is characterized by dense fibrous tissue proliferation in the mediastinum either as a localized form or as a diffuse infiltration. It can either be a response to various infective (histoplasmosis,
tuberculosis, and aspergillosis) or noninfective (IgG4 related) causes or may be idiopathic. The disease can affect any age group with equal predilection for both genders. However, in the case of IgG4-related fibrosing mediastinitis, associated with an elevated IgG4 levels in the blood and tissue, the median age of affected patients reported is 56 years with a distinct male preponderance (11:4). Furthermore, the most common radiological pattern of involvement in this disease is periaortic and paravertebral fibrosis. Clinically, most patients are symptomatic and the symptoms depend on the mediastinal structure involved. Constitutional symptoms such as fever and weight loss are infrequent. However, our patient had only fever and chest pain. Radiologically, either a focal mass (most common) with calcification commonly in the right paratracheal and subcarinal location or a diffuse pattern which is seen infiltrating multiple mediastinal compartments is seen. Usually, such a diffuse pattern is devoid of calcification and is seen in conjunction with other fibrosing diseases such as retroperitoneal fibrosis. Considering these features, this entity seems to be a possible cause in our patient as well.

**Infectious causes of mediastinal mass**

Tuberculosis is one of the important conditions which can present with a mediastinal lymph nodal mass. The presence of constitutional symptoms of fever also makes this a likely cause in the present case. Other than tuberculosis, invasive pulmonary aspergillosis may rarely present with a mediastinal mass.

**Granulomatous diseases**

Diseases such as sarcoidosis are well-known causes of mediastinal lymph node enlargement. However, in sarcoidosis, the nodes are homogeneous, well defined without any invasion of adjacent structures. The pattern of mediastinal involvement in our patient was not consistent with the above distribution; moreover, the encasement of the left brachiocephalic vein and right upper lobe bronchus by the mass, makes sarcoïdosis an unlikely cause in the present case.

**Clinical diagnosis**

In view of multiple diagnostic possibilities, a definite clinical diagnosis is possible only after histopathological evaluation.

**Dr. Anant Mohan**

Based on clinico-radiological possibilities, can we have the histopathological evaluation of the specimen?

**Dr. Deepali Jain**

Histopathological examination of the CT-guided biopsy specimen was suggestive of markedly sclerosed tissue which shows ill-formed granulomas and giant cells with occasional septate fungi representing *Aspergillus* [Figure 2].

**FINAL DIAGNOSIS**

**Invasive aspergillosis of the mediastinum**

**Dr. Hariharan Iyer**

*Aspergillus* is a ubiquitous spore-forming fungi which causes a wide spectrum of diseases in humans which are mainly dependent on the host immune responses. In immunocompetent hosts, diseases such as asthma and ABPA occur whereas in immunocompromised individuals, Invasive Aspergillosis (IA), a condition associated with high mortality is known to occur. Although underlying immunodeficiency, for example: recipients of hematopoietic stem cell transplant, long-term steroid intake, chronic granulomatous disorder, neutropenia, AIDS, or structural lung diseases constitute the most important risk factor for IA, it has been reported in immunocompetent persons as well. While common immunodeficient conditions such as HIV, immunoglobulin levels are usually tested for, when they are negative it is necessary that patients be tested for diseases such as chronic granulomatous disorder. This is an inherited disease in which phagocytes are unable to generate reactive oxidant species against microbes leading to defective innate immunity. When no other cause is identified, tests for CGD should be performed as invasive fungal infections such as *Aspergillus* are commonly seen in such patients.

*Aspergillus* infection is also known to present as a mass-like structure in the lungs. This is usually due to colonization of a pre-existing cavity which is usually referred to as aspergilloma. It may also mimic a lobar collapse. However, such mass-like lesions are rarely reported involving the mediastinum. The possible routes for mediastinal involvement by this fungus could be either due to contiguous spread from the adjacent lung lesions or hematogenous dissemination. However, in the absence of infection in the lung as in our case, the plausible explanation could be inhalation of spores followed by mediastinal deposition due to some trauma to the airways providing an entry point to the fungal spores. Various patterns of mediastinal involvement by the fungi presenting as a mass have been described. There is a report of mediastinal infection in a postcardiac surgery patient mimicking a mass due to *Aspergillus* infection. The
infection may be associated with non-specific symptoms and diagnosed incidentally after biopsy or in some cases the fungus may infiltrate the mediastinal structures such as superior vena cava (SVC) leading to the development of SVC syndrome.\cite{20,21} Most importantly there are no specific radiological features that can pinpoint a diagnosis of mediastinal aspergilloma. Although certain radiological features such as low attenuation areas (which could be due to the presence of microabscesses) and ill-defined margins (which could represent ongoing inflammation and invasion of contiguous structures) may be seen in mediastinal aspergillosis, in most of the reported cases, the diagnosis has been established only after biopsy and histopathological examination.\cite{22}

One of the challenges in the diagnosis of IA in immunocompetent persons has been the lack of early suspicion and initiation of treatment. In a tuberculosis endemic country, most of these patients are empirically treated with Anti-Tb drugs which can not only lead to delay in the diagnosis but also allow for hematogenous dissemination of the fungus which is associated with higher mortality. Another important learning point from this case was that it is very essential to achieve a definite diagnosis prior to initiation of any form of treatment. The patient underwent CT guided biopsy twice from the lesion, which finally gave a confirmatory evidence of *Aspergillus* infection.

**HOW DO WE MANAGE SUCH PATIENTS AND WHAT IS THEIR PROGNOSIS?**

Dr. Rohit  
*Treatment and follow-up*

Based on the above report she was started on voriconazole 200 mg twice daily. After starting the treatment, she had improvement in symptoms. A repeat imaging with magnetic resonance imaging of the thorax was done after a year which was suggestive of marked resolution of the mediastinal lesion [Figure 3]. The patient had a recent follow-up after 3 years [Figure 4] which showed further regression.

The Infectious Diseases Society of America recommends the use of voriconazole as the first-line therapy for invasive aspergillosis.\cite{21} Our patient was treated with voriconazole for a period of more than a year. The optimal duration of therapy is not known. Guidelines of the Infectious Diseases Society of America recommend at least 6–12 weeks of therapy.\cite{23} However, for IA in immunocompromised patients, it is reasonable that treatment should extend throughout the period of immunosuppression and until radiological clearing of lesions.

**SUMMARY**

The above case highlights the importance of keeping IA as a differential diagnosis of mediastinal mass in an immunocompetent person. Timely diagnosis can help in reducing the hematogenous dissemination and help reduce the mortality.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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