Clinics in diagnostic imaging (215)

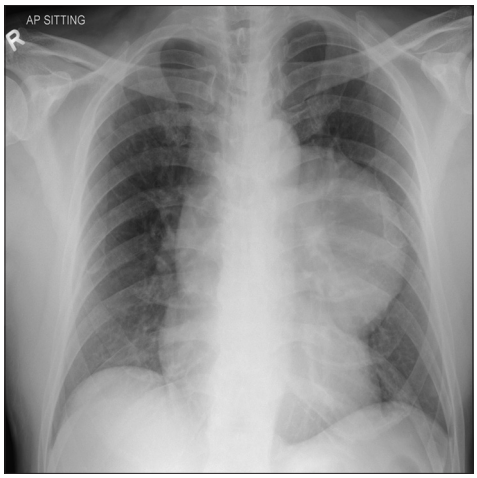

Figure 1: Anterior-posterior chest radiograph.

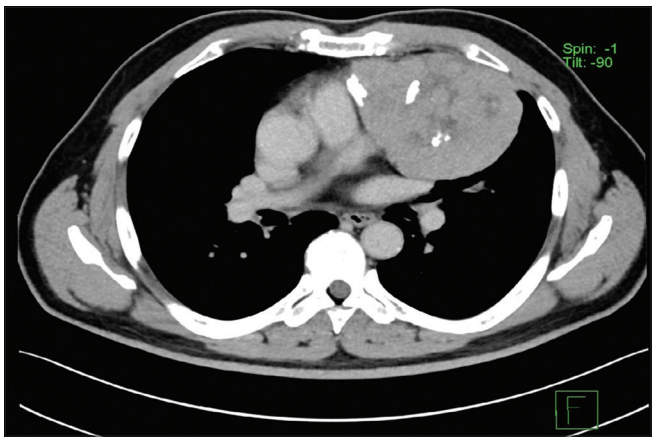

Figure 2: Axial contrast-enhanced CT of the thorax.

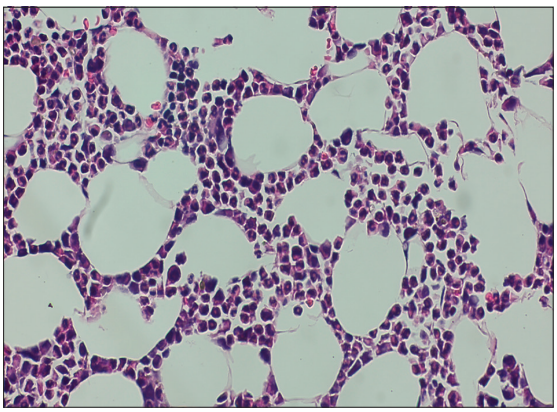

Figure 3: Photomicrograph of the bone marrow trephine biopsy (H&E stain, x40).

CASE PRESENTATION

A 57-year-old man was referred to the emergency department of our hospital from an outpatient clinic because of low haemoglobin (Hb) and on/off palpitations for the past one month. He has a past medical history of hypertension and adolescent pulmonary tuberculosis, with no prior history of autoimmune or connective tissue disease. Initial blood workup revealed normocytic normochromic anaemia (Hb 4.9 g/dL, serum ferritin 1742 mcg/dL, serum transferrin 154 g/dL, total iron binding capacity 40 mcg/dL and iron saturation 83%), with total white cells 19,100/µL and platelets 626,000/µL. The reticulocyte count was reduced (0.4%) and parvovirus B19 IgM antibody was negative. His coagulation profile, thyroid function tests, renal and liver panels were within the normal range. No mass was detected on digital rectal examination. The patient was transfused with four units of packed cells on admission. A chest radiograph [Figure 1], contrast-enhanced computed tomography (CECT) of the thorax [Figure 2], and marrow trephine biopsy [Figure 3] were performed. What do these images show? What is the diagnosis?

IMAGE INTERPRETATION

Chest radiograph [Figure 1] reveals a left-sided mass with a broad base to the mediastinum, in keeping with a mediastinal mass. The hilum is seen through the mass, and no definite erosion of the thoracic vertebra is seen, placing the mass in the anterior mediastinum. CECT [Figure 2] shows a heterogeneously enhancing left anterior mediastinal mass, confined to the prevascular space, with smooth lobulated margins containing areas of amorphous calcifications. No internal area of fat or necrosis and no definite invasion of the adjacent sternum and vascular structures is seen. No suspicious lymphadenopathy is identified. The bone marrow appears mildly hypocellular without erythropoiesis [Figure 3]. Cytogenetics of the bone marrow aspirate shows normal male chromosomal pattern and rules out clonal, numerical, or structural abnormalities.

DIAGNOSIS

Pure red cell aplasia (PRCA) with thymoma.

CLINICAL COURSE

The patient was then referred to interventional radiology for a computed tomography (CT)-guided biopsy, which revealed a thymoma. He underwent elective total thymectomy with wedge resection of the left lung. Diagnosis of type AB thymoma was confirmed by pathological analysis of the resected specimen. On follow-up imaging, no recurrence of thymoma was detected. However, he continued to have symptomatic anaemia necessitating regular transfusion at three weekly intervals.

DISCUSSION

PRCA was first described in the 1920s.[1] In this condition, there is a selective absence of the red cell precursors in the bone marrow, resulting in normocytic normochromic anaemia. It is likely related to the abnormal function of T-cells and presence of antibodies (IgG) that act against erythroblasts. Conditions associated with PRCA include large-cell granular lymphocyte leukaemia, viral infections, certain autoimmune conditions, and some haematological malignancies.[2] PRCA can be rarely associated with thymoma.[1,3] Within the limited number of cases reported worldwide, fewer than 5% of patients with PRCA were noted to have thymoma.

Thymomas are tumours arising from thymic epithelial cells. They may be incidentally detected or may manifest with symptoms such as breathlessness, chest discomfort or pain. Rarely, they may show aggressive features. Thymomas may also be associated with a few other paraneoplastic syndromes such as myasthenia gravis, myositis, and neurological conditions such as acquired neuromyotonia or encephalitis.[4] The pathophysiology of PRCA in thymoma remains to be fully understood. A plausible explanation is the development of auto aggressive T-cell clones due to damage induced by tumour growth within the thymus, resulting in blockade of erythroid progenitors. However, the clonal expansion of pathogenic T cells differs among patients.[2] Thymoma with PRCA has a worse prognosis compared to isolated thymoma.[5]

PRCA is diagnosed by bone marrow aspirate and biopsy, along with complete hematologic workup and CECT of the thorax to rule out an associated thymoma or lymphoid malignancy. Although there are some overlapping features between thymoma and lymphoma, the absence of conglomerate lymph nodes, encasement of the great vessels of the thoracic aorta, and confinement to the pre-vascular space (as in our case) with PRCA, the mass is in keeping with a thymoma, and surgical resection is indicated, precluding the need for tissue biopsy. In our case, a biopsy was performed as we were not aware of the association between thymoma and PRCA at the time of investigation.

Surgical resection of thymoma associated with PRCA is recommended as it leads to remission; however, it is worth noting that only 30% of patients will improve after thymectomy.[1] In the largest series of PRCA with thymoma, none of the patients went into remission of anaemia after surgery.[6] The average survival for patients with PRCA is around 12 years,[7] with the main causes of morbidity and mortality being iron overload and multi-organ failure.

A wide variety of pathologic entities occur in the mediastinum. Imaging is crucial in establishing a presumptive diagnosis and guiding further confirmatory testing. Localising the mass into the anterior, middle and posterior mediastinum will help narrow the differentials. Using CT along with the overall clinical history, a presumptive diagnosis can be made with a high degree of confidence based on imaging alone.

On chest radiography, visualisation of the hilum through the mediastinal mass is known as the hilar overlay sign.[8] This indicates that the mass is not arising from the middle mediastinum, which would obliterate the hilum. In addition, the absence of erosive or destructive changes of the thoracic vertebra excludes a posterior mediastinal pathology. The most common anterior mediastinal masses are classically termed the "4 Ts": thymomas, teratoma, thyroid nodule and "terrible" lymphoma. The lateral radiograph helps to localise the mediastinal mass. Based on Felson's classification, the mediastinum can be divided into the anterior, middle and posterior mediastinum. In the lateral radiograph, a line is drawn from the anterior tracheal wall to the posterior wall of the inferior vena cava. This line separates the anterior from the posterior mediastinum. A second line is drawn around 1 cm posterior to the anterior vertebral margin. This line separates the middle and posterior mediastinal compartments. CT is performed to confirm the exact location and characterisation of the lesion.[9] Although the lateral radiograph provides useful information, it is not performed in all centres, as easy access to CT imaging has largely resulted in a steady decline of the use of lateral chest radiograph.

Thymoma is the most commonly occurring anterior mediastinal mass in the adult population; however, it only accounts for less than one per cent of all adult malignancies.[9] Thymomas usually present with smooth and lobulated contours, appearing as homogenous soft tissue masses, occasionally with calcifications and small cystic changes.[10] Thymic masses rarely present as aggressive and invasive neoplasms in the form of thymic carcinoma, which usually displays anterior invasion of the sternum, mediastinal fat invasion and vascular invasion of the great vessels.[11]

Germ cell tumours (GCTs) are tumours containing primitive germ cells, with teratoma being the most common GCT. Although GCTs mainly arise in the gonads, they represent 15% of anterior mediastinal masses.[12] Due to the presence of at least two of the three germ cell layers (ectoderm, mesoderm and endoderm), teratomas contain a mixture of soft tissue, fluid, fat and calcium. On CT, these tumours appear heterogeneous, with walls of variable thickness and enhancement. Fat is a distinct feature of teratomas [Figure 4], which is reported to be present 76% of the time, while fat-fluid level within the mass is a highly specific sign for teratomas.[12] Calcification is another hallmark feature, appearing focal or rim-like; however tooth-like calcification is only present in 56% of all teratomas.[13]

Intrathoracic, substernal goitre accounts for 3%–6% of mediastinal masses.[14] On radiography, goitres usually appear as a homogenous, smooth, sharply marginated paratracheal mass, with the cephalic portion of the mass displaying indistinct margins when extending above the level of the clavicles; this is known as the cervicothoracic sign [Figure 5].[8] Large goitres may exert mass effect on the trachea, resulting in displacement away from the goitre. On CT, goitres will demonstrate a connection with the cervical thyroid gland. On unenhanced CT, goitres are hyperattenuated due to the presence of high iodine content.

Lymphomas account for 20% of mediastinal neoplasms in adults, most commonly in the anterior mediastinum. Around 50%–70% of mediastinal lymphomas are due to Hodgkin disease.[14] Lymphomas usually appear as large homogenous or less commonly heterogeneous anterior mediastinal mass with low density (cystic) areas [Figure 6]. Lymphomas typically encase the vessels, without evidence of vascular invasion and with a high prevalence of associated mediastinal lymphadenopathy.[14] Following chemotherapy, 20% of lymphomas can show areas of calcification, ranging from coarse-like to egg-shell calcifications.[14]

Percutaneous mediastinal biopsies are almost always performed under image guidance, to allow accurate localisation and documentation of the biopsy needle within the target area.

Fine-needle aspiration (20 to 23 gauge) and core biopsy needles (14 to 19 gauge) are accepted methods for obtaining tissue samples. The exact location of the mass, with care to avoid vital structures are taken into consideration during needle placement planning. Lesions in the anterior and middle mediastinum are generally accessed in a parasternal approach, while posterior or subcarinal lesions are preferably accessed via a paravertebral approach; the suprasternal approach is the

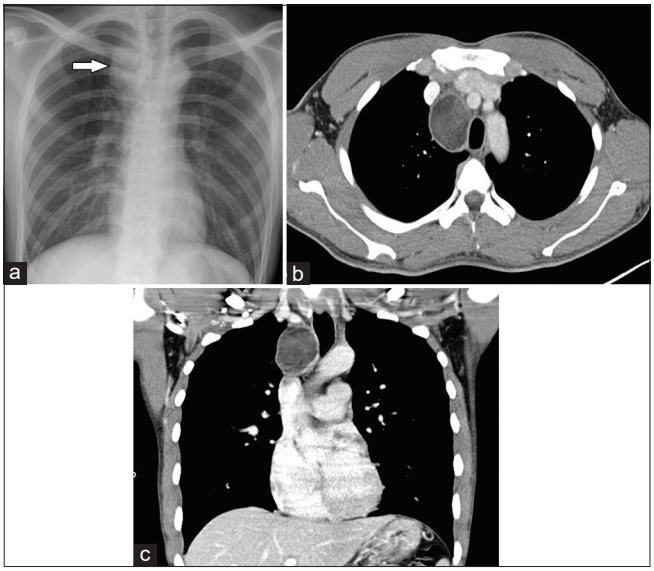

Figure 4: A 27-year-old man with an incidental mass seen on health screening radiograph. (a) Frontal chest radiograph shows a mass with a broad base to the pleura, in keeping with a mediastinal mass. (b) Axial and, (c) coronal contrast enhanced CT images of the thorax show a soft tissue mass centred in the anterior mediastinum. Hypodense components within the mass are in keeping with macroscopic fat, with Hounsfield unit measuring -26 HU. Imaging and histological features are consistent with that of a mature teratoma.

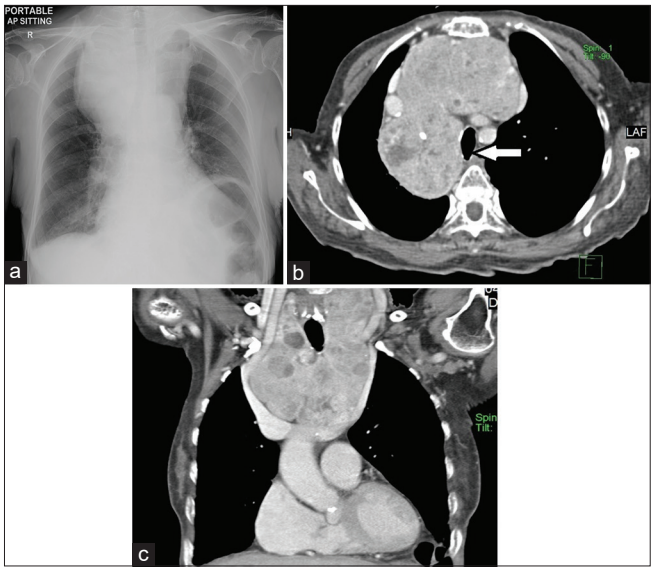

Figure 5: Multinodular goitre of an 80-year-old woman. (a) Frontal chest radiograph shows a smooth marginated paratracheal mass extending above the clavicles, in keeping with the cervicothoracic sign. (b) Coronal and, (c) axial contrast enhanced CT images of the thorax show the retrosternal extension of goitre into the mediastinum, narrowing the trachea (arrow).

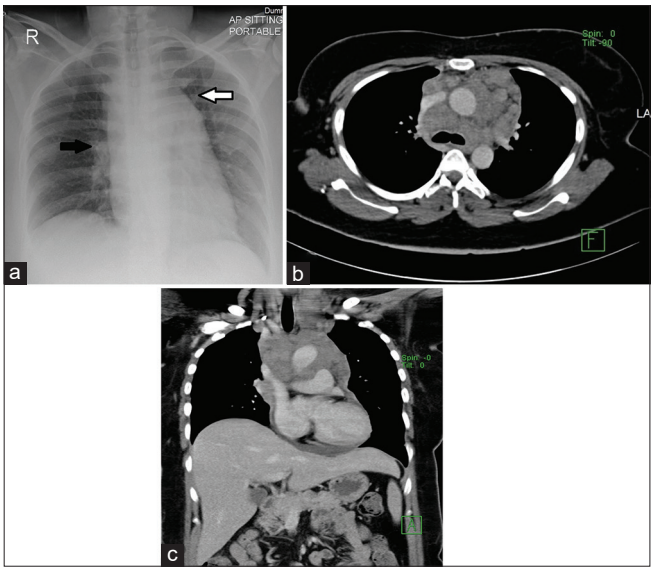

Figure 6: (a) Frontal chest radiograph of a 40-year-old woman, shows a widened mediastinum (white arrow), and bulky lobulated hilum (black arrow). (b) Axial and, (c) coronal contrast enhanced CT images of the thorax confirm multiple enlarged conglomerate lymph nodes encasing the major branches of the thoracic aorta. This was histologically proven to be Hodgkin's lymphoma.

best for targeting superior mediastinal lesions.[15] Occasionally, lesions might not be accessible via these approaches, and more invasive approaches such as transsternal or transpulmonary needle placements can be considered, despite increased risk of haemorrhage and pneumothorax.[15]

In conclusion, although rare, it is important to be aware that an anterior mediastinal mass on imaging with PRCA is most likely a thymoma. Utilising radiographs and CECT, a presumptive diagnosis of a thymoma would have negated the need for biopsy, opting for surgical resection in the first instance. A combination of thymectomy and medical therapy is often necessary for such patients in the treatment of anaemia.

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Conflicts of interest

There are no conflicts of interest.

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SMC CATEGORY 3B CME PROGRAMME

Online Quiz: https://www.sma.org.sg/cme-programme

Deadline for submission: 6 pm, 20 January 2023

Question	True	False
1. The following are anterior mediastinal masses:		
(a) Thymomas		
(b) Lymphoma		
(c) Teratomas		
(d) Hilar lymphadenopathy		
2. Regarding thymomas:		
(a) Most commonly occurring mediastinal mass in adults.		
(b) Thymic neoplasms are always present in the prevascular space.		
(c) Thymic neoplasms are never invasive.		
(d) Isolated thymomas have a better prognosis compared to pure red cell aplasia associated with thymoma.		
3. Regarding germ cell tumours:		
(a) Represent 30% of anterior mediastinal masses.		
(b) Ectoderm, mesoderm and endoderm are present in all germ cell tumours.		
(c) Teratoma is the most common germ cell tumours.		
(d) Fat fluid level on imaging is a not a specific sign for teratomas.		
4. Regarding mediastinal lymphoma:		
(a) It most commonly occurs in the middle mediastinum.		
(b) Non-hodgkins lymphoma is the most common mediastinal lymphoma.		
(c) It commonly shows areas of vascular invasion.		
(d) It calcifies following chemotherapy in 20% of cases.		
5. Regarding biopsy of mediastinal masses:		
(a) Only core biopsies are performed.		
(b) Posterior mediastinal masses are most commonly biopsied via a paravertebral approach.		
(c) A transpulmonary approach is absolutely contraindicated.		
(d) A transsternal approach may be considered if no appropriate biopsy window is identified.		