Calcification of Untreated Mediastinal Hodgkin’s Lymphoma: A Case Report

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Abstract
Calcification occasionally occurs in Hodgkin’s lymphoma after therapy due to tissue necrosis. Rarely, calcification may be detected prior to treatment. This likely represents a dystrophic process when bulky tumours outgrow their blood supply. Due to this rare presentation, pre-treatment calcified Hodgkin’s lymphoma is often mistaken for germ cell tumours on imaging. It is thus important to include Hodgkin’s lymphoma in the differential of this presentation. We present such a case of pre-treatment calcification of Hodgkin’s lymphoma in a young male and discuss the incidence, pathophysiology, and imaging findings.

Case Presentation
A 24 year old male presented to the Emergency Room complaining of shortness of breath that was ongoing for three weeks. The patient was using a budesonide/for-moterol inhaler with no relief. His symptoms became worse when he lay on his right side and back. The patient was otherwise healthy and had no constitutional symptoms. He had a five year history of smoking and occasional alcohol use.

On examination, the patient was afebrile with stable vital signs. There were no auscultatory findings on respiratory examination. There was palpable right supraclavicular lymphadenopathy. Abdominal and cardiac examinations were unremarkable.

Laboratory examination revealed a decreased leukocyte count of 3.2 x 10⁹/L with an absolute neutrophil count of 0.8 x 10⁹/mmm³. All other laboratory investigations were within normal range. Chest radiograph showed a soft tissue density mass involving the right hilum and anterior mediastinum (Figure 1). Calcifications were not demonstrated radiographically.

Computed tomography (CT) of the chest with intravenous contrast was performed which confirmed a large homogenous mass with soft tissue attenuation involving the anterior and middle mediastinum and right hilum. The mass contained a single, lobulated and coarse calcification measuring 12 mm in diameter (Figure 2A). The mass resulted in marked narrowing of the right main pulmonary artery and mild mass effect on the right mainstem bronchus (Figure 2B). Bilateral supraclavicular, prevascular and pericardial adenopathy was also noted. There were no abnormalities seen in the upper abdomen.

A needle core biopsy was taken from the right supraclavicular node suggesting the diagnosis of Hodgkin's lymphoma of nodular sclerosing type. Immunohistochemistry for CD15, CD20, CD30 and fascin confirmed the diagnosis. Bone marrow biopsy was negative.
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Case Report

Background and Epidemiology
Hodgkin’s lymphoma has an annual incidence of 2.8 out of 100,000 persons in the United States.1 The World Health Organization (WHO) recognizes five subtypes of Hodgkin’s Lymphoma: nodular sclerosing, mixed cellularity, lymphocyte rich, lymphocyte depleting, and lymphocyte predominating.2 The former four encompass the classical type based on similar histological morphology, which account for 95% of cases, with the most common being nodular sclerosing (65-70%).1 The mean age at diagnosis is 38 years.1
Calcification in lymphoma is rare, occurring 1-5 years after chemotherapy or radiation therapy with an incidence of 2%.3 This process has been shown to be associated with a good prognosis with 75% of patients being disease free eight years after therapy.3,4 In comparison, calcification before treatment in Hodgkin’s lymphoma is an even more rare finding, occurring in 0.4% of patients.5 Non-Hodgkin’s lymphoma has a higher rate of pre-treatment calcification at 1%.3,5,10

Pathophysiology
Even though the pathophysiology of pre-treatment calcification has yet to be established, two mechanisms have been proposed. The first mechanism is metastatic in nature, resulting from an excessive serum concentration of unstable calcium ions.11 Hypercalcemia can be caused by osteolytic metastases, tumour secretion of parathyroid hormone related protein, or by tumour production of calcitrol, which is the most common process occurring in lymphomas.12 However, hypercalcemia in Hodgkin’s lymphoma is very rare with only one case reported in the literature.13 A metastatic process is unlikely to be the cause of pre-treatment calcification in our patient as his serum calcium concentration was within normal limits (2.47 mmol/L).

The second potential mechanism is dystrophic calcification that is due to tissue necrosis. This occurs when excessive calcium enters the mitochondria of dying cells to form extracellular hydroxyapatite crystals. This process can occur in bulky tumours that outgrow their blood supply which present with multifocal areas of calcification.6 It has been suggested that the nodular sclerosing type of Hodgkin’s lymphoma may be more susceptible to calcification before and after treatment. In the reported cases of pre-treatment calcified Hodgkin’s lymphoma,6,8 only one was found not to be of this type, but rather of mixed cellularity.6 Predisposing factors include collagen fibrosis, cellular degeneration, and necrosis.6

Differentials and Diagnosis
Awareness of this phenomenon is important as the finding of calcification might otherwise be used to exclude lymphoma from one’s differential diagnosis of an anterior mediastinal mass. All four of the common anterior mediastinal masses (thyroid and thymic masses, germ cell tumours, and lymphoma) may present with calcification, thereby limiting this finding as a distinguishing feature.11

A mediastinal mass in a young adult will most commonly be a germ cell tumour or Hodgkin’s lymphoma. Findings on chest radiograph between these two processes are often indistinguishable, requiring CT for further investigation. Distinguishing features on CT include inhomogeneity of soft tissue components in germ cell tumours, including cystic or fatty components, versus relative homogeneity in Hodgkin’s lymphoma. Secondly, Hodgkin’s lymphoma may involve any compartment whereas germ cell tumours typically develop in the anterior mediastinum with posterior displacement of structures.6 Therefore, in order to differentiate between mediastinal masses, a CT scan is essential.

Back to the Case
Upon additional investigations including a CT of the abdomen and pelvis, a stage of 2A was assigned. A stage of 2A refers to two or more lymph node regions on the same side of the diaphragm being involved with no “B” symptoms.3 The patient was referred to the Oncology service and is currently undergoing chemotherapy.

References