# Lymphocytic Leukaemia /Small Lymphocytic Lymphoma, A Case Report with Review of Literature

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## Abstract

**Metastasis of a cancer to another coexisting tumor is a very rare event. When this occurs, it confers a diagnostic dilemma. So far, only very few cases have been reported regarding primary squamous cell carcinoma metastatic to lymph nodes replaced by chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), most of which were metastasis from primary skin cancers. Here we present a rare case of squamous cell carcinoma of lung metastatic to CLL/SLL-involved mediastinal lymph node. The patient was an 82-year-old male who had a history of CLL/SLL and recurrent stroke. His disease has been stable with a white cell count maintained around 60,000 for the previous 3 years without medication. He presented with left-sided facial droop, confusion and slurred speech with a white cell count of 110,000. CT Scan performed recently showed a 2.6 cm right lung mass with enlarged bilateral hilar and mediastinal lymph nodes. Mediastinal lymph node biopsy was performed and sent for frozen section. Frozen section was misinterpreted as "negative" due to diagnostic difficulty. On permanent sections, aggregates of cohesive epithelioid cells (Figure 1) were found in a background of homogenous population of small lymphocytes. The normal architecture of lymph node was effaced (Figure 5). The epithelioid cells showed increased nuclear/cytoplasm ratio, clumpy chromatin, and were positive for CK5/6 (Figure 2) and negative for BerEp4, Mucicarmine (Figure 2) and TTF-1 (Figure 1). The small lymphocytes in the background were positive for CD5, CD20 and CD23 (Figure 6-8), and negative for CD3. These morphological and immunohistochemical features are diagnostic for poorly differentiated squamous cell carcinoma metastatic to a lymph node involved by CLL/SLL. We compared this case with other similar cases available in the literature and discussed diagnostic pitfalls in such situation.** *[N A J Med Sci. 2008;1(1):25-28.]*

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## Introduction

Synchronous tumors are unusual clinical entities in which two histologically distinct tumors present in the same location. Synchronous presentation of lung carcinoma and mediastinal lymphoma has been reported for a number of lymphomas (e.g. CLL/SLL, Mantle cell lymphoma) and lung subtypes.[1,2] These cases show considerable diversity in the anatomic site (e.g. lymphoid organs, skin, lungs etc) and the temporal pattern of presentations.[2,3,4,5] In some of these cases, simultaneous diagnosis of both collision tumors was made right at the onset of presentation. In others, previously diagnosed tumors present with secondary neoplasms.

Concurrent presentations of tumors pose interesting academic and clinical questions in terms of etiology, predisposing factors, diagnosis and management options. The possibility of intersection of etiologies of distinctive tumor types arises particularly in those neoplasms that increase the incidence of secondary malignancies. Chronic lymphocytic leukemia for instance is known to predispose patients to an increase in secondary malignancies.[1] The question of whether this predisposition is the result of underlying genetic abnormalities or predisposition, immune status compromise or identical environmental factors has not been fully explored. No similarities in cytogenetic abnormalities in a case of concurrent presentation of chronic lymphocytic leukemia and malignant melanoma have been observed to date.[5] Nevertheless, environmental exposure and predisposing lifestyle are factors that may identify etiologies in a predisposed individual.

Concurrent presentations of collision tumors also confer a diagnostic and treatment dilemma. In some case reports, certain diagnostic techniques were insufficient to identify the presence of simultaneous tumors in a specific site.[2] In situations where biopsies are not completely representative or where involvement by one of the neoplasm is limited, it is likely that the diagnostic utility of the specimen will be compromised.

Here we present a case of synchronous CLL/SLL and squamous cell carcinoma of the lung. We discuss the diagnostic difficulties in this case and in similar cases in the literature in which further ancillary and sophisticated techniques were required to arrive at the proper diagnosis. We also discuss etiological implications and the impact of collision tumors on management and treatment options.

## Case Report

This was a 79 year old African American man with a long standing diagnosis of CLL/SLL. His disease has been stable with a white cell count maintained around 60,000 for the previous 2-3 years without medication. He was a previous smoker who quit four years ago. He had smoked 1 pack a day for 30 years. He presented with leftsided facial droop, confusion and slurred speech. He had had two recurrent episodes of cerebrovascular disease, 4 and 7 weeks ago, involving the right middle cerebral artery (MCA) territory and resulting in an MCA infarct. Magnetic resonance imaging showed an acute right frontal and right parietal lobe infarct including post central gyrus. MRA of the neck showed no hemodynamically significant stenosis within the carotid artery. MRA of the head showed moderate atherosclerotic disease involving M1 and M2 segments of the right middle cerebral artery. His white cell count was 110,000, Hb 8.6, hematocrit 25% platelets 171,000. His recurrent cerebrovascular disease has been attributed to CLL with hyperviscosity syndrome. During his previous admission, CAT scan showed irregular, noncalcified peripheral mass in the right upper lobe, adjacent to the pleural surface measuring 2.6 x 2 x 0.9 cm. suggestive of a primary bronchogenic neoplasm, and nonspecific mild bilateral hilar and mediastinal lymphadenopathy, nonspecific focus of vague infiltrates in the left lower lobe with associated honeycombing fibrosis, mild upper retroperitoneal lymphadenopathy versus unopacified small bowel loops. A mediastinoscopy was therefore performed and mediastinal lymph node biopsy was done. Frozen section of the mediastinal lymph node biopsy was misinterpreted as "negative" due to diagnostic difficulty. On permanent sections, aggregates of cohesive epithelioid cells were found in a background of homogenous population of small lymphocytes. The normal architecture of lymph node was effaced. The epithelioid cells showed increased nuclear/cytoplasm ratio, clumpy chromatin, and were positive for CK5/6 and negative for BerEp4 and Mucicarmine. The small lymphocytes in the background were positive for CD5, CD20 and CD23, and negative for CD3. These morphological and immunohistochemical features are diagnostic for poorly differentiated squamous cell carcinoma metastatic to a lymph node involved by CLL/SLL.

Patient progress:
The patient developed acute renal failure with laboratory values of sodium 139, chloride 109, $CO_2$ 21, BUN 53, creatinine 4.2, calcium 8.2. His prognosis was determined to be poor. Aggressive management for his disease was declined and he was discharged for hospice care.

## Discussion

Simultaneous occurrence of metastatic carcinoma and lymphoma in a single lymph node is a rare occurrence. Increased incidence of secondary tumors has been reported for CLL.[1] These include additional lymphomas, melanomas, lung carcinomas etc. CLL is known to predispose to increase in secondary malignancies. These malignancies also tend to be more aggressive than usual and metastasize with greater frequency.[6,7] One study showed an incidence of lung carcinoma in CLL patient of 2%, a 33 times increase compared with the normal population.[8] Of these tumors, 25% were squamous cell carcinoma. These patients tended to be smokers (85%). There appeared to be a 10 year interval between the diagnosis of CLL and the later diagnosis of lung cancer. Median survival interval of these patients was 25 and 6 months for those treated surgically and nonsurgically respectively for their lung cancer. The patients tended to die as a result of the lung cancer and not the CLL or other malignancies. Another study determined a sixty percent increase in lung cancer in CLL patients < 50 years but not in those > 70 years.[9] Median time to develop lung cancer was 5 years and median survival ranged from 5-9 months. It has been postulated that similar etiological factors may underlie the simultaneous occurrence of these tumors.[10] Defects in the cellular and humoral immunity are known to occur in CLL/SLL. This may predispose individuals to the development of other malignancies including lung carcinomas. Immune deficiency may explain the increased aggressive nature of these tumors when they occur. Reports of simultaneous occurrence of carcinoma and lymphoma in a single lymph node are even rarer.

These cases may present with diagnostic difficulties both at the time of frozen section and subsequently on permanent section. In one case report of collision tumor, a diagnosis of recurrent lymphoma was made after a FDG PET scan revealed multiple foci of hypermetabolism in the bilateral hilar and mediastinal lymph nodes.[11] All but one of the multiple foci of hypermetabolism detected regressed with chemotherapy. This focus was later determined to be the site of squamous cell carcinoma. In a second case, extensive metastatic small cell carcinoma was detected in the background of very inconspicuous MCL.[2] The presence of MCL required confirmation by immunohistochemistry and fluorescence in situ hybridization (FISH). However, fine needle aspiration cytology has been shown to be of use together with ancillary immunocytological and flow cytometry techniques in detecting these collision tumors in lymph nodes.[12] In the case we report, the diagnosis was overlooked at frozen section. Immunohistochemical staining of the permanent section was necessary to identify the concurrence of poorly differentiated squamous cell carcinoma in a background of a lymph node with architectural effacement by CLL.

CLL is an indolent disease and therapeutic goals should be directed at the more lethal pulmonary neoplasm. However, therapy for the concurrent lung cancer is complicated by the compromised health status of patients with underlying CLL. This presents therapeutic challenges in these patients. In the case we present, complications from CLL prompted further investigations before the lung carcinoma was detected. However, the poor health status of the patient limited therapeutic intervention for the more lethal squamous cell carcinoma of the lung. This is similar to other reported cases that the most appropriate therapy determined by the poor health status of the patient was withholding of aggressive treatment of the lung carcinoma.[4]

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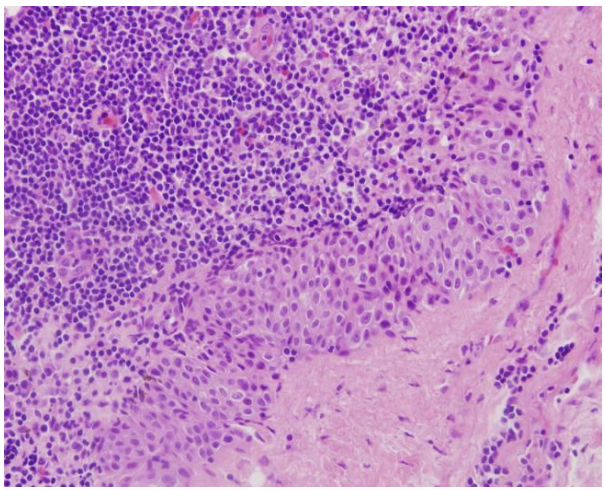

**Figure 1.** Lymph node with Metastatic SCC x100.

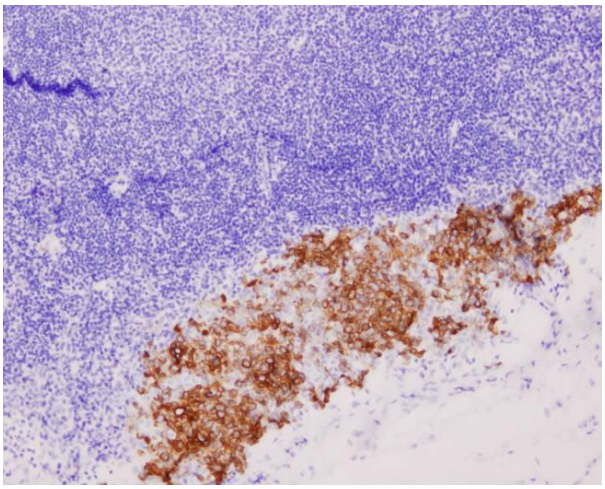

**Figure 2.** CK 5/6 Immunostaining x100.

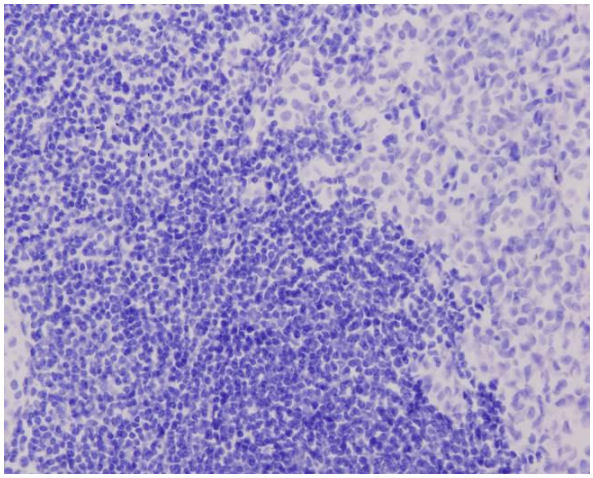

**Figure 3.** Mucin immunostaining x100.

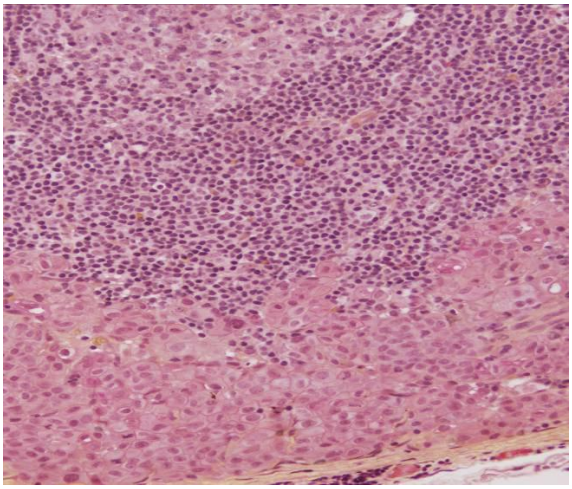

**Figure 4.** TTF immunostaining x100.

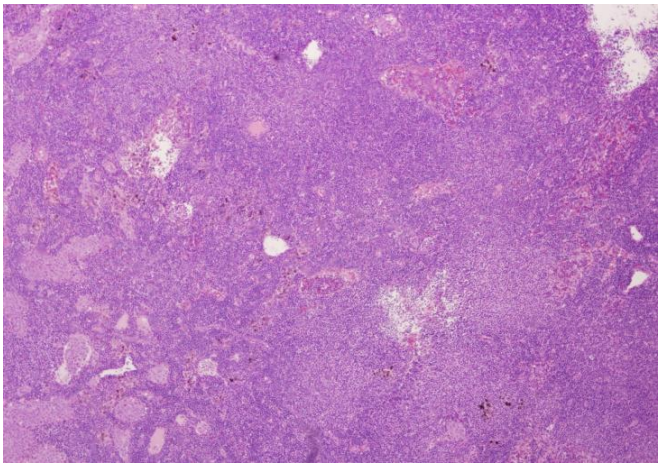

**Figure 5.** Lymph node with architectural effacement x40.

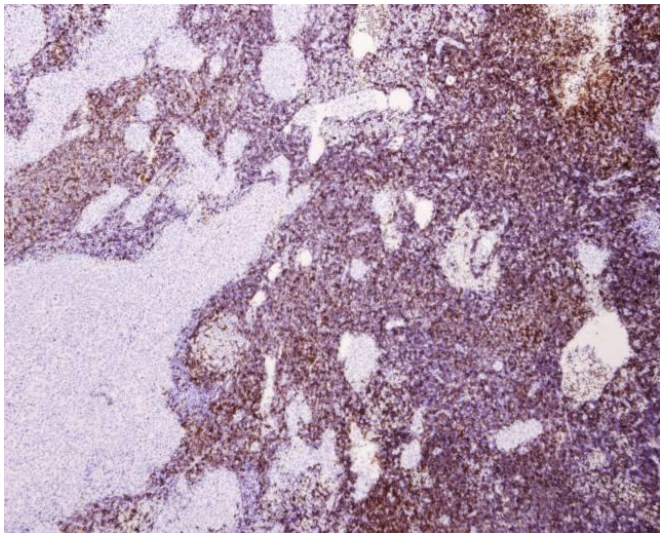

**Figure 6.** CD 5 immunostaining x40.

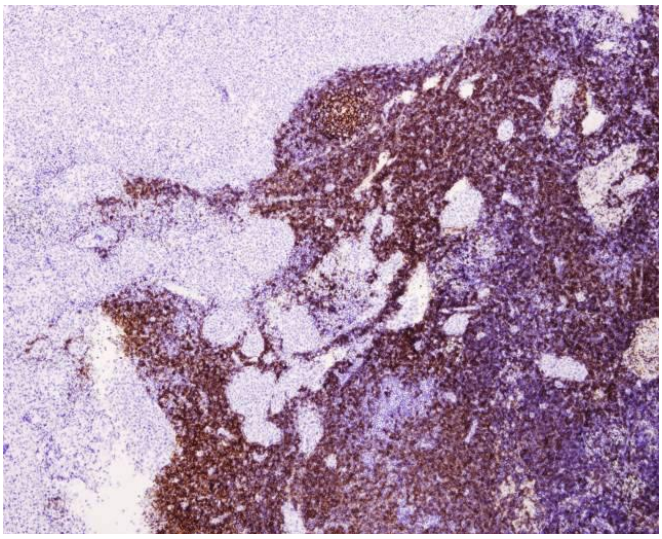

**Figure 7.** CD 23 immunostaining x40.

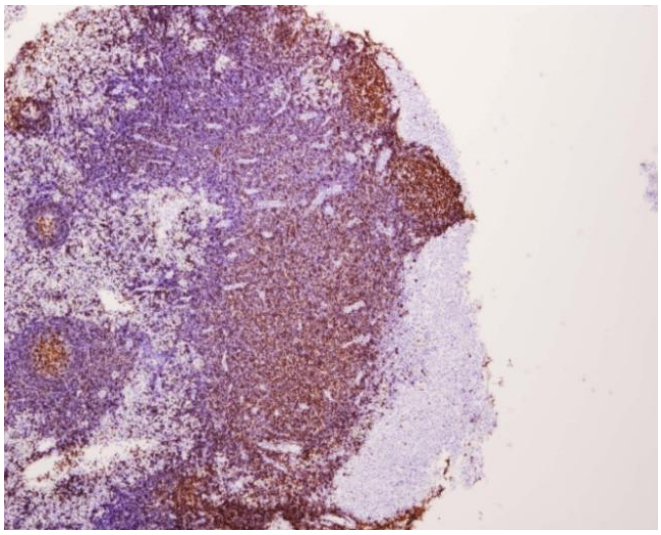

**Figure 8.** CD 20 immunostaining x4.