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## Case Report

# A Synchronous Presentation of AITL with Adenocarcinoma of Lung

### Abstract

Angioimmunoblastic T-cell lymphoma (AITL) is a frequent subtype of peripheral T – cell lymphoma (PTCL) characterized by generalized lymphadenopathy, hepatosplenomegaly, and frequent B - symptoms. Extranodal manifestations are quite common in this subtype of Non Hodgkins Lymphoma which is characterized by frequent skin involvement. However, the extranodal disease should be evaluated thoroughly and a tissue diagnosis must be obtained to confirm lymphomatous involvement when the presentation is not classical. Here we report a case of AITL who presented with lung mass suspected to be due to lymphomatous involvement, but turned out to be a synchronous presentation of an adenocarcinoma of the lung. The possible relation between the two conditions is also elucidated.

## Introduction

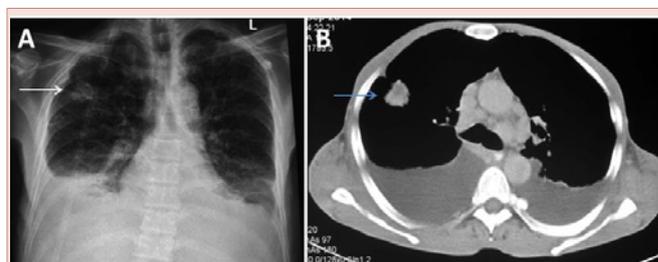
Angioimmunoblastic T-cell lymphoma usually presents in Stage III or IV disease and pulmonary involvement is seen in up to 10% of these cases [1]. However all pulmonary masses in these patients are not due to lymphoma. Any atypical lung mass, even in a proven case of disseminated lymphoma, should be subjected to pathologic evaluation for exact characterization of its nature.

## Case Report

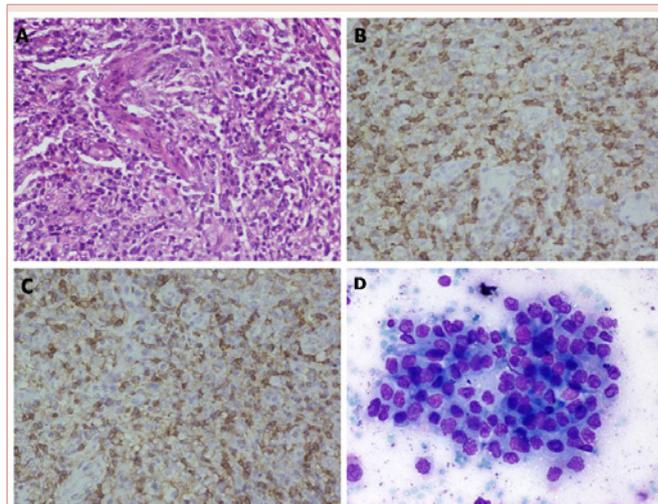
A 62-year-old man presented with progressive dyspnea and fever for two months. The physical examination revealed generalized lymphadenopathy with ascites, bilateral pleural effusion and pedal edema. He also had bilateral wheezes and hepatosplenomegaly. Hemogram revealed microcytic hypochromic anemia. (Hb = 8.8g/dl, MCV = 74.3fL & PCV = 30 %), platelet count of  $108 \times 10^9/L$  and WBC count of  $11.3 \times 10^9/L$  with eosinophilia (Neutrophils 74%, Lymphocytes 10%, Monocytes 6%, Eosinophils 10%). Renal and liver function tests were normal. Chest X-ray revealed an opacity in the right upper lobe (Figure 1A).

Excision biopsy of the axillary lymph node showed effacement of architecture. There was proliferation of high endothelial venules. These were surrounded by atypical lymphoid cells, which were 1-1.5 times the size of mature lymphocytes. These cells were immunoreactive for CD3 & CD4. Scattered CD 8 positive cells were also noted (Figure 2A-C). BM examination revealed infiltration by lymphoma cells. Patient was high risk by Prognostic index for AITL [2], (4/5 risk factors).

The CT Chest showed a 2.2 x 2.4 x 2.6 cm mass with speculated margins in the right upper lobe (Figure 1B). In view of the presence of an aggressive lymphoma first possibility of lung infiltration by AITL was kept in mind. However, non-contiguous, speculated isolated mass is an odd presentation for lymphomatous involvement, besides the patient was a heavy smoker for >20 years. Therefore an alternative possibility of synchronous carcinoma of lung was considered. A CT guided fine needle aspiration cytology (FNAC) was obtained from the right upper lobe lesion which revealed tumor cells arranged in clusters forming glands and papillae suggestive of adenocarcinoma



**Figure 1:** (A) Chest x ray showing left upper lobe lesion (white arrow). (B): Corresponding CT section showing 2.2\*2.4\*2.6 cm mass with speculated margins (blue arrow) and bilateral pleural effusion.



**Figure 2:** (a) The axillary lymph node showed effacement of architecture. There was proliferation of high endothelial venules. These were surrounded by atypical lymphoid cells. 1-1.5 times the size of mature lymphocytes. These cells were immunoreactive for CD3 and CD4 (Figures b-d). Scattered CD 8 Positive cells were also noted. Figure d shows cluster of malignant cells with moderate nuclear enlargement in aspiration cytology smear from the lung (May grunwald giemsa x 240).

(Figure 2D). Pleural fluid cytology was negative for malignant cells thrice.

Patient was sick with ECOG performance status of 4. Therefore he was unfit for any surgical intervention or intensive chemotherapy. In view of predominant B-symptoms we decided to start treatment of AITL first, so the patient was given prophase with prednisolone 60mg/m<sup>2</sup> for 5 days. Following this therapy fever and B symptoms both subsided and patient's performance status improved. The family opted against further therapy and the patient succumbed to his illness 2 months later.

## Discussion

AngioImmunoblastic T-cell Lymphoma is an aggressive peripheral T cell lymphoma (PTCL) subtype originally described by Frizzera in 1974 [3]. AITL accounts for 15% - 20% of PTCL. It generally affects elderly adults with median age of 65 and slight male predominance [1]. The classical presentation of AITL is with high-grade fever, generalized lymphadenopathy and skin rash. Less commonly reported presentations are arthralgia, pleural effusion, ascites, edema and involvement of the lungs, gut and nervous system. Spleen, liver and bone marrow are frequently involved and most cases are at an advanced stage at presentation [4].

Among the laboratory parameters Coombs positive hemolytic anemia, polyclonal gammaglobulinemia and eosinophilia are commonly present but almost any lab value can be abnormal in AITL. Other findings include thrombocytopenia, elevated lactate dehydrogenase and ESR levels and autoantibody formation [5].

Our case had most of the classical clinical features of AITL except for the skin rash. This is consistent with the reported low incidence of skin rash in India (only 5%) [6]. This case had the typical histopathological pattern of lymph node involvement (Pattern III) [7] and it also fulfills 4 out of 5 histological criteria suggested for the diagnosis of AITL [8].

Several case reports of synchronous presentation of AITL with a second hematologic malignancy exist in literature. Wang et al have

collated and reported the co-occurrence of nearly 40 cases of AITL with Diffuse Large B Cell Lymphoma (DLBCL) [9]. However, there are very limited data available on synchronous AITL with a non-hematologic malignancy. Literature search on Medline and Excerpta Medica Database (EMBASE) revealed total 8 cases of co-occurrence of AITL with a carcinoma (Table 1) [1,10-15]. Two cases had lung carcinoma, of which one was a squamous cell carcinoma [11] and another one had the erstwhile broncho-alveolar carcinoma of the lung [10]. But both of these cases developed lung cancer after 18 and 84 months after developing AITL respectively. To the best of our knowledge this case is the first report of synchronous presentation of adenocarcinoma of the lung with AITL.

In six of the eight cases shown, the diagnosis of AITL preceded the diagnosis of carcinoma by at least 3 months. It has been postulated that the impairment in T cell function due to AITL leads to development a solid organ tumor [16]. In the case reported by Sztern et al., the diagnosis of carcinoma preceded that of AITL by 11 months. This led them to suggest that prolonged antigenic stimulation by the slow growing solid organ tumors, as the stimulus for the development of AITL [11]. In our case there was a relatively small carcinoma presenting simultaneously with a disseminated lymphoma. It is likely that AITL induced immune dysfunction lead to development of carcinoma in the lung. However co-occurrence by chance is a more likely possibility.

The two large case series of synchronous / metachronous malignancies in literature suggest that synchronous malignancy is more likely to occur in males, who are smokers or alcohol consumers and usual site of the synchronous malignancy being the aerodigestive tract (head & neck, lung and esophagus). The field cancerization effect of tobacco has been suggested as the reason for this predilection, but the authors were not able to explain why it is more frequently seen with synchronous than with metachronous malignancies [17,18]. While our patient fits into the profile mentioned by them, the other two cases of synchronous presentation did not fit this profile as they did not involve the aerodigestive tract.

**Table 1:** Shows the reported cases of AITL with a carcinoma.

No	Age/Sex	Year	Initial Diagnosis	Treatment	Second diagnosis	Treatment	Time to diagnosis	Survival	Ref
1	52/M	1978	AITL	CVP	Adenocarcinoma Pancreas	Excision	3 months	4 months	9
2	78/F	1983	AITL	MOPP	Bronchio alveolar carcinoma	NA	18 months	Diagnosed on autopsy	10
3	70/M	1984	Squamous Cell Carcinoma Lung	Refused treatment	AITL	Refused treatment	11 months	Was alive at 48 months	11
4	NA	1986	AITL	NA	Adenocarcinoma stomach with liver Mets	NA	Synchronous	12 months	12
5	66/M	1988	AITL	PTC-VCR-P	Adenocarcinoma Colon	Excision	108 months	Alive at 22 months	13
6	64/M	1997	AITL	Nil	Squamous Cell Carcinoma Tonsil	Excision + Radiotherapy	84 months	Alive at 12 months	14
7	79/F	2012	AITL	Excision	Adenocarcinoma Colon	NA	Synchronous	NA	15
8	60/M	2014	AITL	ongoing	Adenocarcinoma lung		Synchronous	Died after 2 months	This report

CVP – Cyclophosphamide, Vincristine & Prednisolone. MOPP – Mechlorethamine, Vincristine, Procarbazine & Prednisone. PTR-VCR-P – Peptichemo, Vincristine & Prednisolone.



The involvement of the pulmonary parenchyma is well-documented in literature and usually consists of a well-circumscribed parenchymal infiltrate [1]. The reported incidence of such infiltrates was up to 10% of cases in a large case series by de Leval et al., [4]. AITL usually presents in an advanced stage (Ann Arbor III & IV) [4,8] and pulmonary infiltrate can be easily mislabeled as a pulmonary manifestation of AITL. In our case, a high index of suspicion, driven by the atypical radiological findings for lymphoma in the lung and the significant smoking history led us to the diagnosis of a co-existing lung adenocarcinoma

## Conclusion

Angioimmunoblastic T-cell lymphoma usually presents with advanced-stage disease and pulmonary involvement is seen in up to 10% of these cases. However, not all pulmonary masses in these patients are due to lymphoma. Any atypical lung mass should be subjected to pathologic evaluation for exact characterization of its nature. The management of synchronous malignancy remains a challenge with the disease with poorer prognosis driving the outcome.

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