

CASE REPORT

Bronchopulmonary cancer and chronic lymphocytic leukemia: a unique combination for which prognosis?

Le cancer bronchopulmonaire et la leucémie lymphoïde chronique: une combinaison unique pour laquelle le pronostic?

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ABSTRACT

The association of lung cancer and chronic lymphocytic leukemia has already been described by some authors. The central issue remains the prognosis of both diseases, would it be worse or not by the association, or does there exist a causal link between the two diseases. We report the case of 56 year old, chronic smoker, with a bronchopulmonary cancer and being followed-up for chronic lymphocytic leukemia. He benefited from a right upper lobectomy preceded by a radical mediastinal lymphadenectomy with uncomplicated postoperative outcome. We focus on a systematic search of these secondary cancers to establish early treatment strategies to improve prognosis.

KEYWORDS: Lung Neoplasm, lymphocytic leukemia, prognosis, lobectomy, thoracotomy.

RÉSUMÉ

L'association du cancer du poumon et de la leucémie lymphoïde chronique a déjà été décrite par certains auteurs. La question centrale reste le pronostic des deux maladies, serait-il pire ou non par l'association, ou existe-t-il un lien de causalité entre les deux maladies. Nous rapportons le cas d'un fumeur chronique âgé de 56 ans, atteint d'un cancer bronchopulmonaire et suivi d'une leucémie lymphoïde chronique. Il a bénéficié d'une lobectomie supérieure droite précédée d'une lymphadénectomie médiastinale radicale avec un résultat postopératoire non compliqué. Nous nous concentrons sur une recherche systématique de ces cancers secondaires afin d'établir des stratégies de traitement précoce pour améliorer le pronostic.

MOTS CLÉS: Tumeur pulmonaire, leucémie lymphocytaire, pronostic, lobectomie, thoracotomie.

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INTRODUCTION

Chronic lymphocytic leukemia (CLL) is the most common leukemia in Europe representing 1% of cancers while lung cancer would be around 12.9%, responsible for 21% of cancer deaths [1,2]. The association of lung cancer and CLL was described by some authors [3]. The central issue remains the prognosis of both diseases, would it be worse or not by the association or does there exist a cause and effect between the two. Through observation we report on this rare association.

CASE REPORT

Mr O.A aged 56, chronic smoker for 40 years, presented to our department for stage II Sadoul dyspnea evolving since 3 months. He was being followed for chronic lymphocytic leukemia (CLL) Stage B in remission and had already received six courses of rituximab, fludarabine and cyclophosphamide (RFC). Clinical examination found a patient in good condition with a WHO score 0. A chest radiograph showed a mid-thoracic opacity with central spiculated contours. A CT brain-thorax-abdomen and pelvis was performed. It showed an upper lobar right lung tissue lesion measuring 41 x 24 mm (*Figure 1*) with ipsilateral hilar lymphadenopathy above the carina (*Figure 2*) and abdominal. A scan-guided biopsy was performed on the lung tissue lesion. Pathological findings in favor of a primitive lung infiltrating adenocarcinoma. After discussion of the patient file in a multidisciplinary meeting group, surgery was decided. The approach was the right posterolateral conservative thoracotomy. Exploration of an upper right lobe tumor limited to the lobe without invasion of adjacent structures was done. Mediastinal lymph node dissection with frozen section was the first approach. The results excluded pathological tumor in these lymph nodes.

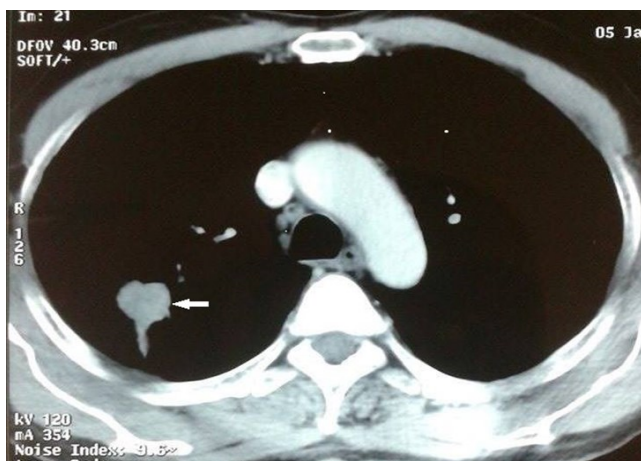


FIGURE 1. Upper lobar right lung tissue lesion measuring 41 x 24 mm (arrow).

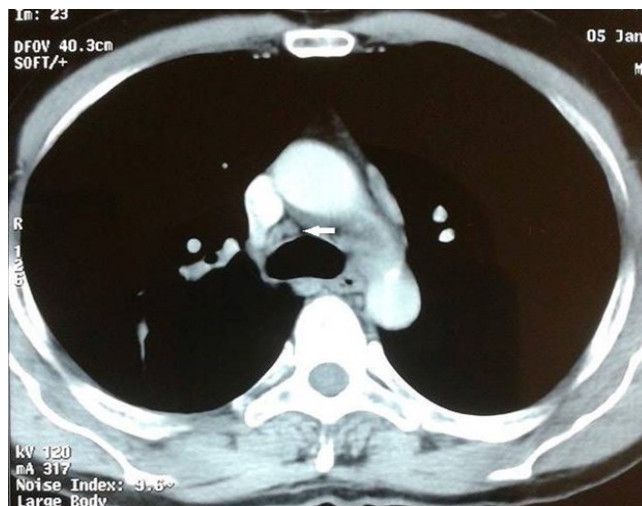


FIGURE 2. Lymphadenopathy above the carina (arrow).

A right upper lobectomy was performed with protection of the bronchial section with a pleural flap. The postoperative course was uneventful and the patient was discharged on postoperative day 4.

DISCUSSION

Chronic lymphocytic leukemia (CLL) is characterized by lymphocytosis a malignant monoclonal proliferation of mature B lymphocytes especially greater than $5 \times 10^9/L$ for at least 3 months [1]. Its prevalence increases with age, more than 5% after 60 years. The combination of a concomitant CLL or in following chemotherapy for CLL has been shown by several authors [4]. There is a consensus in the literature about the increased risk of a secondary cancer in patients with chronic lymphocytic leukemia.

In an Australian study, Royle found a doubling of risk of developing a second cancer in patients with CLL. [5] For other authors, younger patients are the most affected with a male predominance [4]. Preferred sites are the colon, rectum, skin (melanoma), prostate, kidneys and lungs [5]. Hisada meanwhile found a prevalence of melanoma and lung cancer [6]. Among these, adenocarcinoma is the most common [4]. They would be responsible for 2% of deaths in patients with CLL [7]. One reason for this increase in secondary cancers is linked to early detection because of prolonged surveillance of the CLL. The second reason is controversial and would be linked to the nature of the treatment of CLL

Thus the role of fludarabine has been implicated by some authors [8] including Benjamini in a study that compiled 234 cases of CLL and showed an increased risk of secondary cancer after chemotherapy with rituximab, fludarabine, and cyclophosphamide [9]. This protocol was the one used in our patient.

A dose-response action was noted. Thus the risk is reduced when the cumulative dose of cyclophosphamide is less than 11250 mg / m² [9]. The secondary immunosuppression would be responsible for the increase of secondary cancer because it was also generally observed in renal transplant patients under immunosuppressive therapy. [5] But the biology and genetics common to these cancers could not be excluded.

Indeed, overexpression of HER2 / neu in non-smoking patients with lung cancer and CLL made a reasonable correlation for which Potti et al proposed a systematic search of all lung cancer patients with CLL [10]. And above and beyond the search for this cancer, one of the problems is to be able to classify and stage it according to the TNM classification for determining its status that may be biased because of the possibility of lymph node involvement by CLL. Thus, the discovered nodes, will they be considered as metastatic lung cancer or rather within the scope of the CLL? It is known that PET CT has better performance for judging lymph node tumor involvement. Its role in the CLL was especially clear to discriminate between point A and B Binet classification [11]. But in the case of an association of two potential lymph node malignancies, careful attention deserves to be made as to its interpretation.

Thus the fact that the lymph node lesions of CLL are mostly bilateral and symmetrical, they will be bilateral cervical, bilateral axillary bilateral clavicular addition, bilateral hilar, bilateral inguinal and bilateral external iliac involvement. The first fact could be a discriminative argument between CLL and lung cancer. But latero-tracheal and anterior mediastinal level this rule is not always respected as the lymph nodes may be asymmetrical [11]. Thus the difference could also be on the extent of the SUV_{max} . Indeed in lung cancer the threshold of the SUV_{max} remains

higher. This value ranges from 5 to 15 in the lung cancer while it is at most 2.74 in the CLL particularly in Stage B [11]. Still, the certainty of a lymph node involvement could only be obtained by histology. Lymph node biopsies by various invasive methods or not fully find their place in this type of association. The EBUS (endobronchial ultrasound) and EUS (endoscopic ultrasound) has a respective sensitivity of 78 and 89% in lymph node biopsies are superior to mediastinoscopy in the search for tumor localization [12]. Histological examination will show in the case of a CLL, lymphoid cells with a small homogeneous cytoplasm, weakly basophilic and devoid of nucleolus. The core has dark reinforcements clearly separated by lighter spaces, giving the impression of chromatin clods [13]. Our attitude was to attempt a posterolateral thoracotomy and mediastinal lymph node dissection first before any act of parenchymal resection. The negativity of dissection during a frozen section has enabled us to achieve a lobectomy. The prognosis of CLL depends on its stage as classified by Binet. The median survival of Stage C is 2 years while that of stage B resembles practically that of the general population [14]. For stage B as is the case in our patient, the median survival is 5 years. With this relatively poor prognosis like that of lung cancer that also relies the stage of the disease.

Thus the risk of cancer death in CLL patients is increased by 72% and deaths represent 64.8% in this population. Among these cancers, lung cancer and melanoma have a poor prognosis [5].

Ultimately, the CLL patients are known carriers of a risk of developing a second cancer. Several theories have attempted to explain this phenomenon, and particular attention should be paid to the role of chemotherapy. Lung cancer is part of this set of secondary cancers whose combination worsen further prognosis. A systematic search of these cancers should be attempted in order to establish early treatment strategies for improving the prognosis.

CONFLICT OF INTEREST

None declared

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