# Patient taking chemotherapy for a small cell lung cancer: not every cerebral nodule is a metastasis: the tree that hides the forest.

## Patient sous chimiothérapie pour un cancer à petites cellules du poumon: Tout nodule cérébral n'est pas une métastase : l'arbre qui cache la forêt

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**RÉSUMÉ**

Nous rapportons le cas d'un homme âgé de 53 ans chez qui le diagnostic d'un cancer pulmonaire à petites cellules a été obtenu par la biopsie d'une masse tumorale au niveau du muscle trapèze. La bronchoscopie souple a mis en évidence une tumeur endobronchique dont l'étude histologique était en faveur d'une origine tuberculeuse. La tomodensitométrie thoracique a révélée une masse tumorale suspecte de malignité avec des nodules et micronodules évoquant une tuberculose pulmonaire. Le scanner cérébral a montré un nodule de 4, 5 mm de diamètre rehaussant après injection du produit de contraste évoquant une métastase cérébrale. Le patient a été mis sous traitement antituberculeux pour sa tuberculose pulmonaire. Quinze jours après, le malade a reçu une chimiothérapie à base de carboplatine-étoposide. Le scanner cérébral de contrôle réalisé à la fin de la chimiothérapie (soit à 2 mois de traitement antituberculeux) a révélé des multiples nodules corticaux et subcorticaux infracentimétriques rehaussant après injection de produit du contraste avec un emplacement tentorial et subtentorial considérés comme étant en relation avec miliaire tuberculeuse cérébrale. Le nodule découvert sur ??Le premier scanner cérébral était donc à posteriori considéré comme ayant été d'origine tuberculeuse. L'état général du patient s'aggravé rapidement. Il a présenté un état de confusion mentale et le décès a survenu en quelques jours.

**Mots-clés**

Traitement antituberculeux, tuberculose cérébrale, Chimiothérapie, Miliaire tuberculeuse, Cancer à petites, cellules du poumon

**SUMMARY**

We report the case of a 53- year-old man in whom the diagnosis of small cell lung cancer (SCLC) was made by the biopsy of a mass of the right trapezius muscle. A tumor was revealed on flexible bronchoscopy which pathological study showed tuberculosis (TB). Chest computed tomography (CT) scan revealed findings related to the SCLC associated to micronodules and nodules compatible with pulmonary TB. Cerebral CT scan revealed a nodule of 4.5 mm in diameter presenting enhancement after contrast material injection thought to be a metastasis. The patient was administered antitubercular treatment. Fiveteen days later, the patient started chemoptherapy with etoposid and carboplatin. A control cerebral CT scan realized after the end of the chemotherapy (2 months and a half of antitubercular treatment) revealed numerous cortical and subcortical infracentimetric nodules with contrast enhancement with a tentorial and subtentorial location considered to be in relation with cerebral miliary TB. The nodule discovered on the first cerebral scan was therefore a posteriori considered to have been of tubercular origin. The PS of the patient rapidly worsened. He presented mental confusion and died in some days.

**Key-words**

Anti tubercular treatment, cerebral tuberculosis chemotherapy, Miliary tuberculosis, small cell carcinoma, pulmonary cells

Small cell lung cancer (SCLC) is known to frequently metastasize to the brain that is why a nodular lesion of the brain in that case is usually thought to be a metastasis. We demonstrate by this case report that this is not always the case. In fact, in this case cerebral tuberculosis should also be evoked. Tuberculosis (TB) is nowadays still a major problem of public health especially in some particular circumstances such as lung cancer. The pulmonary location of the disease is relatively easy to be diagnosed, however extrapulmonary ones notably the cerebral location are more difficult to be assessed. Extrapulmonary TB mainly concerns immuocompromised patients such as those with cancer or taking chemotherapy [1]. Cerebral involvement is of special concern as its prognosis is bad because of the diagnostic delay and the therapeutic failure [2]. The aim of our work is to report a rare case of cerebral tuberculosis in a patient with SCLC that has worsened after chemotherapy.

## OBSERVATION

A 53- year-old man, smoking 80 pack-years, was admitted to our department for a superior vena cava syndrome associated to a cervical tumefaction that appeared 2 months before. His questioning didn't reveal any past medical history and he didn't have tubercular contagium. On physical examination, his performance status (PS) was at 0. He had an oedema of the face, a thoracic venous collateral circulation, a right non tender, fixed, firm mass of the right trapezius measuring 2 cm of diameter. Chest X –ray film showed a right upper lobe opacity and a collapse of the same lobe associated to an opacity related to a homolateral pleural effusion.Acid-alcohol-resistant bacilli were absent from the sputum. Flexible bronchoscopy revealed a macroscopic aspect of inflamed mucosa, a tumor of the right upper lobe bronchus and an extrinsic compression of the segmental bronchi of the right upper lobe. Acid-alcohol-resistant bacilli were absent from the bronchial fluid which cytologic examination showed inflammatory cells. Biopsies of the tumor revealed confluent granuloma consisting on epitheloid cells associated to Langerhans cells with a central fibrinoid necrosis. The biopsy of the right trapezius mass revealed a metastasis of a small cell carcinoma in this muscle. Chest and abdominal computed tomography (CT) scan showed a proximal right upper lobe mass which surrounded the right mainstem bronchus with an occlusion of its segmental bronchi. The mass invaded the mediastinum and caused deviation of the trachea to the left side and a deformation of its wall. It surrounded the carina and get over the median mediastinal line. The mass also envaded the aortic arch and the superior vena cava which was completely thrombosed. It also surrounded the right pulmonary artery. The mass was not distinguishable from bulky adenomegalies of the pre and the sub carinal chains. There were also adenomegalies of the left latero tracheal and anterior mediastinal chains. Micronodules and nodules on the right upper lobe and subpleural nodules on the middle lobe and the inferior right and left lobes were present (Fig.1). There was also a right pleural effusion without pleural thickening. No abdominal abnormality was found in the abdomen. The cerebral CT scan revealed a fronto-parietal nodule of 4.5 mm in diameter presenting enhancement after contrast material injection. The diagnosis of dissemitated SCLC with cerebral metastasis associated to venous thrombosis and lung tuberculosis was made and the patient was administered anticoagulants and antitubercular treatment consisting on isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E). Fiveteen days later, the patient started chemoptherapy with etoposid and carboplatin during 5 cycles. On two months of antitubercular treatment, the patient was doing well and was administered just H and R for his tuberculosis. A CT realized after the end of the chemotherapy (2 months and a half of antitubercular treatment) revealed a reduction of the pulmonary tumoral mass estimated at 54% but the appearance of a bone lysis of the third right costal arch. Lung nodules enlarged. Abdominal CT scan showed a left adrenal gland mass. Control cerebral CT scan revealed numerous cortical and subcortical infracentimetric nodules with contrast enhancement with a tentorial and subtentorial location involving the cerebral trunck (Fig.2). These findings were considered to be in relation with cerebral miliary TB. The PS of the patient rapidly worsened and he presented mental confusion and died in some days.

**Figure 1 :** Chest CT scan: Opacity of the right upper lobe surrounded by nodules and subpleural micronodules.

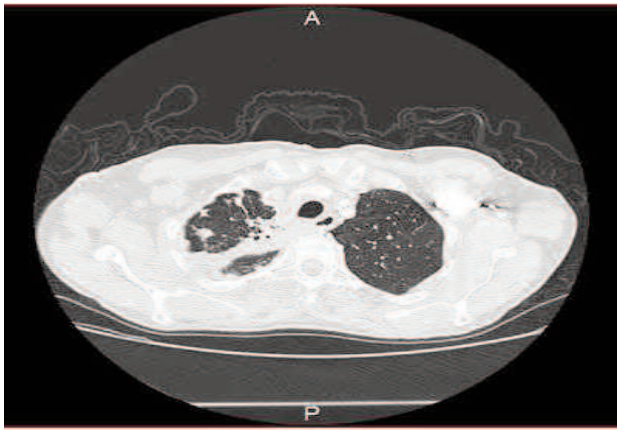
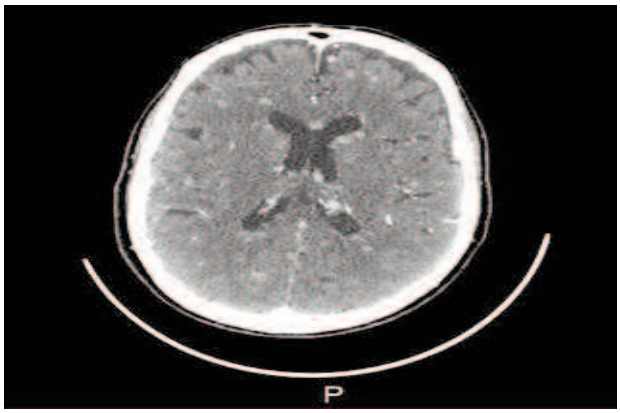



**Figure 2 :** Cerebral CT scan: infracentimetric nodules with contrast enhancement.




## DISCUSSION

We present a case of SCLC associated to lung and cerebral TB who developed miliary cerebral TB when taking chemotherapy because an initial cerebral nodule was thought, in a context of cancer, to be a

metastasis. Pulmonary TB was diagnosed by bronchial biopsy which showed granuloma formed by epitheloid and Langehans cells. This form of tuberculosis is called tuberculoma. The patient is from Tunisia, an endemic country of TB that's why the most probable diagnosis consisting with these pathologic findings is tuberculosis. Moreover, chest CT scan showed micronodules and nodules on an upper lobe. Nodules and micronodules are consisting of the diagnosis of TB and their location on an upper lobe increases the probability of TB. However, the possibility that these nodules are in relation with metastasis can not be excluded. In this patient, the cerebral nodule was first diagnosed on CT as being a metastasis of his SCLC as this cancer is known to metastasize frequently and rapidly. On the cerebral CT scan the multiplicity of the cerebral small nodules that enhanced with contrast material in a patient known to have pulmonary TB and that was a few times ago taking chemotherapy made the diagnosis of miliary TB. Nowadays, the coexistence of cancer notably that of the lung, and tuberculosis is more and more frequent [3]. In our patient both pathologies were diagnosed at the same time. In a study interesting 61.931 new cases of tuberculosis, the incidence of the association between tuberculosis and cancer was 0.9 per 1000 new cases of cancer per year [4]. In another study, achieved in an endemic country for TB, this incidence was 0.5 per 1000 new cases of cancer per year [5]. Moreover, chemotherapy induces an immunodepression that makes any infectious disease and particularly TB more susceptible to occur or to disseminate. We think that our patient had a cerebral nodule in relation to cerebral TB and that brain location of TB disseminated because of the chemotherapy. This treatment was initiated soon after the diagnosis of pulmonary TB because the treatment of SCLC should be urgent. TB The initial cerebral nodule was first thought to be a metastasis but we finally think that it has been in fact a tubercular nodule because after chemotherapy there were many nodules in the brain that enhanced after contrast material injection and looked like the first nodule. So the more like probability is that the cerebral miliary tuberculosis developed when he was taken chemotherapy. Most of the time, the occurrence of TB in patients taken chemotherapy occurs in those who have a past history of tuberculosis [5,6]. The lung is the most frequent organ affected by TB in patients undertaking chemotherapy and represents 87.88% of all the locations [6]. Our patient had a pulmonary TB but also a rare location of the disease that is why the diagnosis for the cerebral nodule was metastasis which was more often to happen that cerebral tuberculosis. Cerebral involvement is one of the most severe expressions of TB [7, 8, 9]. Whatever the clinical presentation or complementary examinations are, the patient questioning is very important for TB suggestion. However, this possibility is most of the time evoked too late especially in the low TB incidence countries [10].The presence of an associated extracerebral site of tuberculosis is of great value and should be looked for very cautiously. This happens in 40 à 66 % of the cases [11, 12]. Clinical presentation of cerebral TB is not specific. A retrospective study achieved in Budapest in a department of neurology revealed that headache and consciousness trouble occurred in 53% of the cases while headache associated to fever and neck stiffness occurred in 33.3% of the cases [8]. In our patient, there were first none of these signs then he complained of a decrease of the general status and a mental confusion and died in some days. In patients with lung cancer and ever when they take chemotherapy, cerebral TB is always misdiagnosed, the development of imaging techniques should make the diagnosis sooner and therefore the prognosis more favorable [13]. In our patient, the diagnosis of cerebral TB complicating chemotherapy was diagnosed when CT scan revealed finding comptatible with a miliary form of the disease in the tentorial and infratentorial sites of the brain. These findings are in accordance with what is reported in the literature [14, 15]. Resonance magnetic imaging can be helpful for the diagnosis [13]. This investigation was impossible in our patient as his PS become very quickly too poor.

## CONCLUSION

This case highlights the fact that all abnormalities encountered in a patient with lung cancer undertaking chemotherapy are not obligatory in relation with his cancer. A special care must be taken for infectious diseases, especially tuberculosis in endemic zones such as the case in our patient, that can occur or disseminate in such a circumstance.

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