Nasopharyngeal and pulmonary cancer plus tuberculosis

Cancer nazofaringian și pulmonar plus tuberculoză

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Abstract

The malignancy is associated with an increased risk of tuberculosis. We report the case of a 48-year-old patient with nasopharyngeal tumor treated with radiotherapy. Two years after the cancer diagnosis, he developed bacteriologically confirmed pulmonary tuberculosis (TB). Surprisingly, shortly after the TB diagnosis, a second cancer, in stage IV, located in the lung, was discovered. Despite the fact that antituberculous therapy was promptly initiated, the evolution was serious and fatal three months after the TB diagnosis. The particularity of our case was the coexistence of pulmonary tuberculosis and a lung cancer, two years after the diagnosis of the nasopharyngeal tumor.

Keywords: *tuberculosis, cancer, immunosuppression*

Rezumat

Malignitatea este asociată cu un risc crescut de tuberculoză. Raportăm cazul unui pacient de 48 de ani, cu tumoră nazofaringiană tratată prin radioterapie. La doi ani după diagnosticarea cancerului, el a dezvoltat tuberculoză pulmonară (TB) confirmată bacteriologic. În mod surprinzător, la scurt timp după diagnosticul de TB, a fost descoperit un al doilea cancer, în stadiul IV, situat în plămân. În ciuda faptului că terapia antituberculoasă a fost inițiată cu promptitudine, evoluția a fost gravă și fatală la trei luni după diagnosticarea tuberculozei. Particularitatea cazului nostru a fost coexistența tuberculozei pulmonare și a cancerului pulmonar, la doi ani după diagnosticarea tumorii nazofaringiene.

Cuvinte-cheie: *tuberculoză, cancer, imunosupresie*

Introduction

Tuberculosis is an infectious disease that occurs in patients with impaired immunity, as for example in patients with malignancy. This association aggravates the evolution of both diseases, posing problems of diagnosis and treatment. In this paper we present the case of a patient with two solid malignancies that develops tuberculosis concomitant with the second malignancy.

Case presentation

A 48-year-old patient presented to the pneumology clinic with the following symptoms: productive cough, weight loss (five kilograms in two months), loss of appetite, nocturne perspiration; the symptoms started two months before. He had a history of smoking of 30 pack-years and quit smoking one year before.

The patient's medical history revealed that he was diagnosed two years before with a nasopharyngeal tumour, with biopsy revealing undifferentiated carcinoma. The cancer was treated with local radiotherapy (70 gray) and was declared healed. There was no history of contact with a TB patient in the last year. In his family, the father was diagnosed with lung cancer.

The clinical examination showed a patient with a low BMI (17 kg/m^2), with pale and sweaty skin. The pulmonary system examination was normal, with no rales at auscultation, and spontaneous oxygen saturation was 97% at rest. Blood pressure and heart rate were within normal limits.

Routine blood investigation revealed: mild anaemia (hemoglobin: 11 g/dl, total leukocyte count: 7500 /mm^3 with lymphopenia 10.7% predicted). The inflammation marker had an increased value (erythrocyte sedimentation rate = 60 mm/1 hour).

Standard chest X-ray found a consolidation in the medium right pulmonary field, with apical fibronodular opacities (Figure 1). The radiological investigations were completed with a thoracic CT scan which showed pulmonary nodules, predominantly in the right lung, and tree-in-bud appearance in the upper right lobe (Figure 2).

The bronchoscopy did not reveal pathological lesions of the mucosa. Bronchial aspirate smear was positive for acid fast bacilli (AFB); no tumor cells were found. The Genexpert molecular test detected the presence of *Mycobacterium tuberculosis* sensitive to rifampicin. ELISA test for Human Immunodeficiency Virus was negative. Cultures on Löwenstein-Jensen medium were positive for *Mycobacterium tuberculosis*.

Based on the clinical, radiological and bacteriological results, the diagnosis of right pulmonary tuberculosis has been made and the antituberculous therapy was started. The standard six-month antituberculous treatment, as stated in the National Tuberculosis Control Program, was a combination of four drugs daily for two months (isoniazid, rifampicin, pyrazinamide and ethambutol), followed by two drugs (isoniazid and rifampicin) three times per week for four months. After the antituberculous treatment was started, the patient's condition presented a slow improvement, recovering the appetite and gaining weight. The bacteriological sputum exam after one month of treatment was negative for acid-fast bacilli in microscopy.

Two months after TB diagnosis, the patient was readmitted in our clinic with poor general status: productive cough, dyspnea at rest, complete loss of appetite, night sweats, severe asthenia. The oxygen saturation was 90% in ambient air. Sputum smear for acid-fast bacilli was negative. The biological serum analysis revealed severe

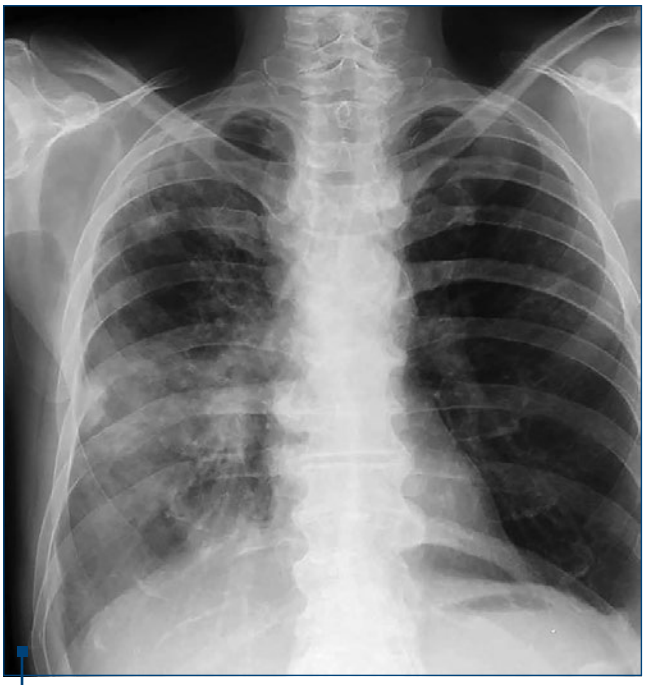

Figure 1. *Chest X-ray – consolidation in the medium right pulmonary field, with apical fibronodular opacities*

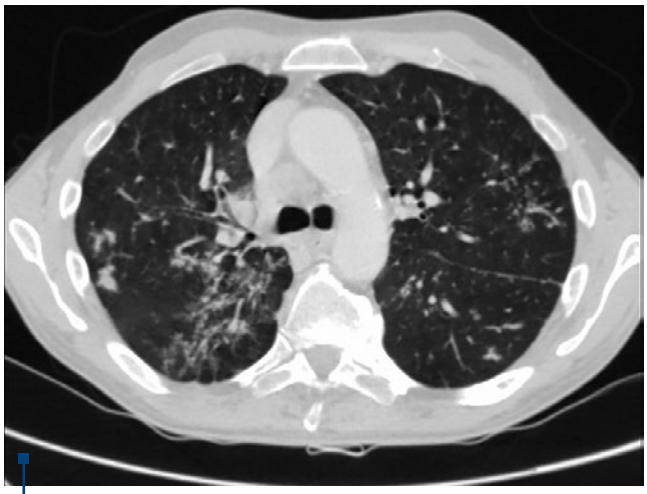

Figure 2. *Thoracic CT scan – pulmonary nodules, predominantly in the right lung and tree-in-bud appearance in at the upper right lobe*

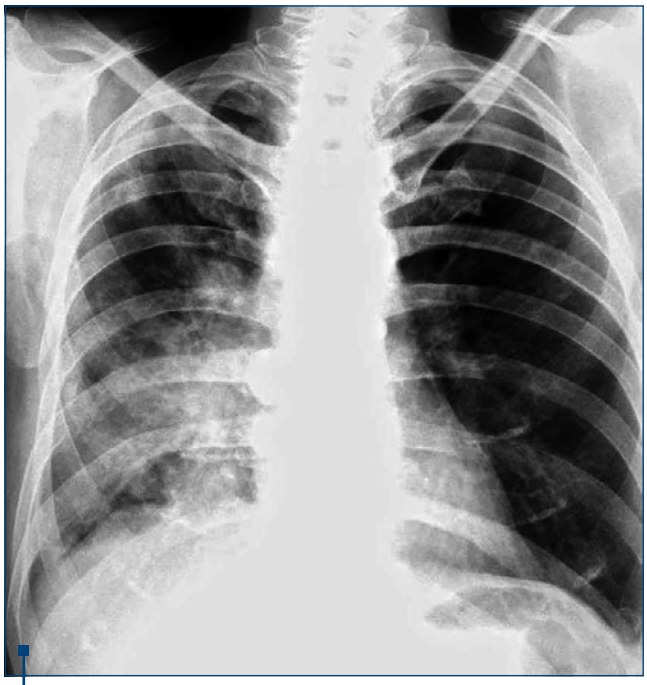

Figure 3. *Chest X-ray – the persistence of right pulmonary consolidation (two months after the antituberculous therapy was started)*

hepatocytolisis, requiring the cessation of antituberculous treatment. Chest X-ray showed no improvement, with the persistence of right lung consolidation (Figure 3).

The new CT scan performed revealed the presence of a right partial pulmonary atelectasis through a pulmonary tumor (Figure 4), with pulmonary, suprarenal, hepatic and bone metastases. A second bronchoscopy was performed, showing stenosis of mean lobar bronchia by extrinsic compression and mucosal infiltration. In the right lower lobar bronchia, small tumours were present, with bronchial biopsy positive for non-small cell lung carcinoma. The immunohistochemical tests revealed pulmonary squamous cell carcinoma.

The evolution was severe and progressive, leading to respiratory failure and exitus one month after the hospital readmission.

Discussion

Lungs are one of the favourite sites of complications in malignancy, most common being metastasis, pulmonary embolism and infectious pulmonary diseases. The main infectious pulmonary diseases encountered in cancer patients are tuberculosis, bacterial pneumonia and pulmonary aspergillosis.

The presence of tuberculosis may be due to general immunosuppression associated with cancer itself or cancer-specific therapy (chemotherapy, radiotherapy)[1]. This risk is higher in countries with a high incidence of tuberculosis. The cytostatic therapy leads to immunodepression that favors the occurrence of the TB. Also, radiotherapy acts by making structural changes related to ionization and destroy the DNA of malignant and normal cells. The analysis made by Simonsen on Danish national medical databases focused on the association between TB and cancer, and found that, while TB risk in cancer patients was 2.48 greater than in general population, it grew to 6.78-fold for cancer patients receiving chemo- or radiotherapy[2].

The risk for developing tuberculosis in malignancy varies: from 2-3 fold higher than in general population[2,3] to 9-fold higher in the US population[4]. In the recent analysis of Dobler, this risk was higher for solid organs malignancy than for lymphoproliferative disorders[5]. In patients with solid tumors, such as lung and head and neck cancers, TB appears early in the course of the neoplastic disease, in contrast with lymphoproliferative disorders, where the infection develops later in the course of the disease[6].

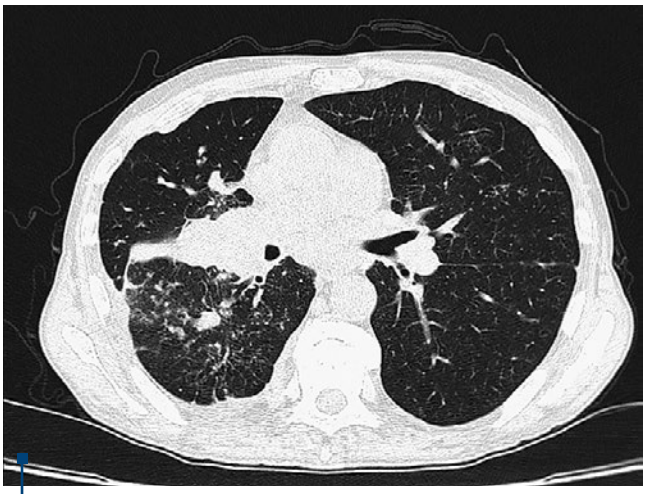

Figure 4. Thoracic CT scan – right partial pulmonary atelectasis through a pulmonary tumor and right pulmonary nodules

An issue in this assessment of the TB risk associated with malignancy is represented by the fact that these patients are performing complete radiological examinations at the time of cancer diagnosis, which might result in an increased number of overdiagnosed TB cases.

In our case, the patient was firstly diagnosed with nasopharyngeal cancer, for which he received radiotherapy. Due to immunosuppression (malignancy plus cancer therapy) pulmonary tuberculosis occurred. The surprise was the presence of a second malignancy, respectively stage IV lung cancer, found shortly after the tuberculosis diagnosis. Most probably, pulmonary opacities found at the time of tuberculosis diagnosis were already hiding lung cancer, although the first bronchoalveolar lavage was non-diagnostic.

In fact, lung cancer can be sometimes unwillingly diagnosed and treated as TB[7]. The symptoms (cough, weight loss, asthenia) may be similar, as in the case we presented. Sometimes, the presence of pulmonary nodules on chest X-ray, especially if some of them are with excavation, must lead to a differential diagnosis between lung cancer and tuberculosis, especially in countries with high prevalence of TB. In the presence of TB suspicion, sputum smear for AFB must be performed as soon as possible.

Although the association between nasopharyngeal malignancy and TB is rare, this connection is more common in the case of lung cancer. In a Korean study, from 36 patients with lung cancer and TB, in 10 cases tuberculosis was diagnosed at the same time with lung cancer, while in 26 cases tuberculosis occurred after the diagnosis of lung cancer[8].

One of the main problems related to the association between cancers and tuberculosis is that the presence of active TB is delaying the start of specific cancer therapy. In these cases, antituberculous treatment must be started first, in order to obtain the absence of *Mycobacterium tuberculosis* in the sputum. However, the study conducted by Cuellar showed that in 76 patients with cancer and TB, only in 11% of cases the diagnosis of tuberculosis affected the cancer treatment[9].

In our patient's case, the evolution was fatal three months after the TB discovery, respectively one month after the lung cancer detection. It is known that TB occurrence may increase lung cancer mortality. A large cohort study from Hong Kong showed that tuberculosis is an independent predictor of mortality in lung cancer[10]. The same result was found by the Engels study, showing that the presence of tuberculosis increases the lung cancer mortality (25 vs. 3.1 per 1,000 person-years) [11].

The particularity of our case was the coexistence of pulmonary tuberculosis with a second pulmonary cancer two years after the diagnosis of a nasopharyngeal tumor. The immunohistochemical analysis confirmed the pulmonary origin of the second malignancy. To note, smoking represents a risk factor for both nasopharyngeal and pulmonary neoplasia. ■

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