

Pulmonary metastasis: very late relapse of testicular embryonal carcinoma

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Abstract

Testicular carcinoma recurrences represent a rare finding (1-6% in non-seminomatous germ cell tumours). However, cases of recurrence have been described many years later. We report a case of late recurrence of embryonic testicular carcinoma, after 26 years, with pulmonary metastases. Following evidence of increase of alpha-feto-protein (AFP), the patient underwent a total body computed tomography scan that exhibited two pulmonary nodules, one in upper left lobe and other in left hilar region with multiple mediastinal and retrocrural lymph node enlargements. All consolidations showed increased sugar uptake value at PET CT. Biopsies of lung consolidations confirmed diagnosis of recurrence of testicular carcinoma.

Introduction

Late relapses (LR) of a testicular cancer, defined as tumour recurrence more than 2 years after complete remission following primary treatment, are rare occurrences with 2.6 % of incidence rate

[1]. However, very late recurrences of testicular cancers that occur even more than 5 years after the treatment are reported. The most frequent location of LR of testicular cancers is the retroperitoneal space, while the lungs and the mediastinal lymphnodes are less frequently involved [1]. When it is located in lung, differential diagnosis with primary lung cancer is required; in these cases, histological assessment and bio-molecular profiling assist diagnosis [2-7]. Chemo-resistance is common in late relapses especially of non-seminomatous germ cell tumours, resulting in poor prognosis [8].

Case Report

We report a case of a 50-years old man, smoker of 18 pack-years with medical history of testicular neoplasia, an embryonic carcinoma, twenty-six years ago, treated with right orchifunicectomy followed by 4 cycles of adjuvant chemotherapy with Platinum/Etoposide/Bleomycin (PEB). No alterations were ever detected during the annual follow-ups of both imaging and blood serology.

After 26 years from the primary treatment, during an annual follow-up, an increase of alpha-fetoprotein (AFP), 400 UI/ml (n.v. 0.1-5.5), was found. Total body computed tomography scan and positron emission tomography scan PET/TC revealed two pulmonary nodules, one in upper left lobe (10 mm SUV max 2.8) the other in left hilar region (23 mm SUV max 4.6) (Figure 1). Furthermore, multiple mediastinal and retrocrural lymph node enlargements were detected (SUV max 9.3) (Figure 2). He presented in good general condition of health. He reported only mild exertional dyspnoea, no asthenia or weight loss. Laboratory tests, spirometry and blood gas analysis were otherwise normal, except for a slight reduction in alveolar-capillary diffusion capacity and a slight increase of specific neuron enolase (17.4 ng/mL). Bronchoscopy and TBNA of station 4L were performed. The pathological assessment revealed carcinoma neoplastic cells resulting AFP + TTF- at immunohistochemical staining compatible with embryonic carcinoma metastases (Figure 3). The final diagnosis was pulmonary relapse of embryonic carcinoma. The patient was referred to oncology department and started chemotherapy protocol, started a second line chemotherapy protocol with Cisplatin (P), Etoposide (E), Ifosamide (I) (PEI). Chemotherapy treatment is still ongoing, normalization of tumour markers has been detected and the first imaging control after therapy is scheduled

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Discussion

Despite good response to initial treatment, about 10-30 % of patients with testicular cancer develop recurrence, usually within

the first 2 years after complete response to treatment. In a pooled analysis of 5880 patients with testicular cancer Oldenburg *et al.* found late relapses in 3.2% of non-seminoma and 1.4% of seminoma

patients [1]. Generally, LRs happen in the first 5 years after treatment. In a population-based analysis, Oldenburg *et al.* report recurrence beyond 5 years, called very late relapses (VLR) in 0.5%

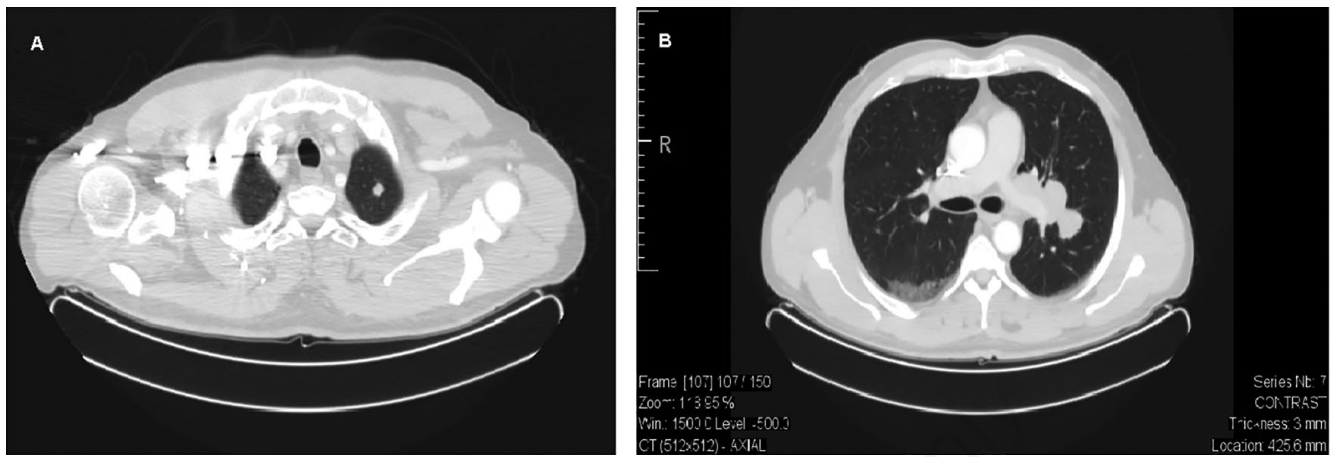


Figure 1. Thoracic CT scan. A) Nodule in upper left lobe (10 mm). B) Nodule in left hilar region (23 mm).

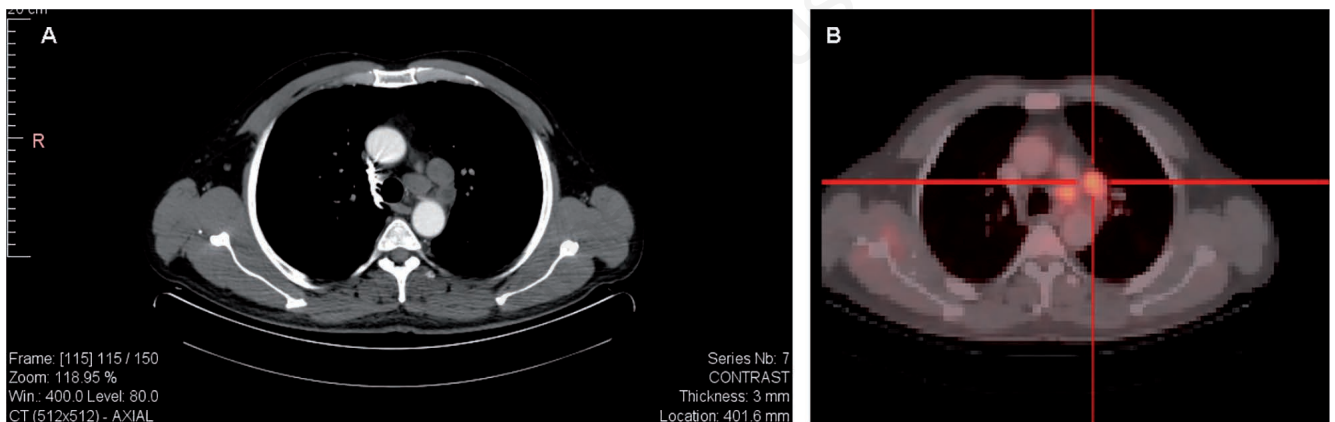


Figure 2. Multiple mediastinal lymphnode enlargement. A) Multiple pre-vascular lymphadenopathies, in the APW and posterior mediastinum medially to the descending aorta (max diameter 25 mm). B) Lymphadenopathies aortopulmonary window (diameter 25 mm SUV max 6.4).

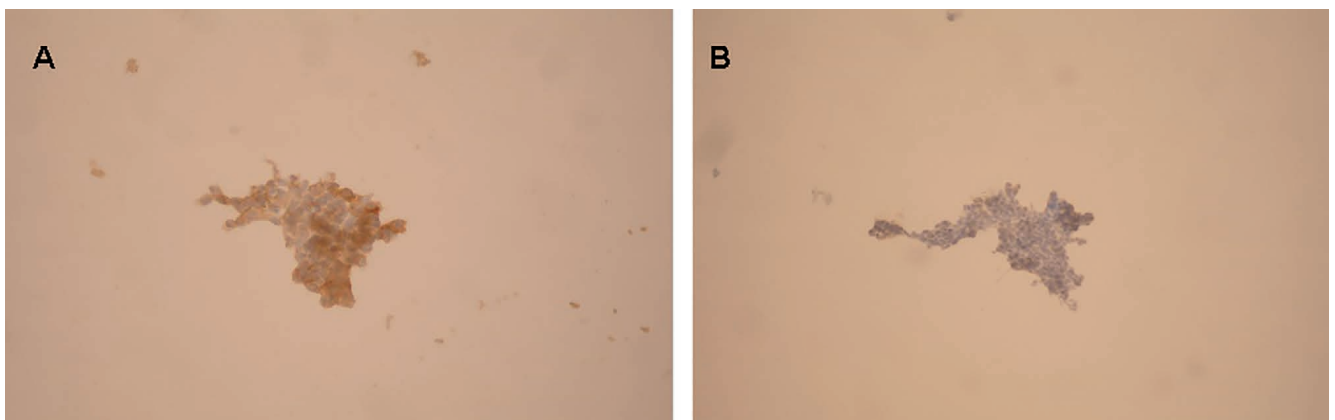


Figure 3. Neoplastic cells AFP+ (A) and TTF1- (B).

of patients [8]. Geldart *et al.* describe 9 years of median time to relapse, while other authors reported 5.4-7.1 years of median time to relapse [9]. Our patient presented a recurrence of embryonic carcinoma after 26 years. VLR after 20 years from initial presentation are extremely rare. Few cases are reported in literature in testicular cancer: Kalaitzis *et al.* (choriocarcinoma and embryonal carcinoma 23 years), Pavic *et al.* (teratoma 32 years), Mukhtar *et al.* (42 years) and Akar *et al.* (non-seminomatous 24 years), Arafat (teratoma 27 years) [10-14]. The most frequent location of late relapse of both seminomatous and non-seminomatous germ cell tumours are retroperitoneal space followed by lung and mediastinum (25%) [1].

Among the different subtypes, teratoma is the most frequent subtype in the LRs of germ cell tumours, followed by yolk sac tumour alone or with teratoma. The others subtypes, including embryonic carcinoma, represent 20% of patient with late recurrence. Choriocarcinoma and seminoma are rarely seen [1]. Early relapses have good response to salvage regimens in a significant proportion of patients [15]. Conversely, LRs of non seminomatous germ cell cancer have poor response to chemotherapy. Complete surgical resection in localized disease is related to the best outcome and represent the most important part of treatment approach [8]. Successful management of LRs is dependent on early recognition. The recurrence onset is, in the majority of case, symptomatic. However, up to 50% of patients have elevated tumour markers at presentation of relapse [15]. At the moment an international consensus about the optimal management for LRs of testicular cancer is still lacking and follow-up after 5 years is generally not recommended in testicular cancer [16]. George *et al.* proposed an annually follow up for life with history and physical, tumour markers, and chest X-Ray [17]. All testicular cancers are potentially at risk for early and late relapse. Our case underlines the importance of extended follow up of more than five years to prompt detection of late relapses. However, considering of the potential difficulties to perform lifelong follow-up, we suggest, in a patient with a history of embryonic carcinoma, to not underestimate the possibility of late metastasis.

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