Case Report

Late relapse of testicular tumour at 23 years invading the ischium with pulmonary involvement and thoracic - abdominal adenopathy. Case report

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SUMMARY. Late relapse of testicular germ cell tumour is uncommon, especially with skeletal metastases. It appears that late relapse of non-seminomatous germ cell tumours presents with more aggressive biological features and is clinically distinct from early relapse. This report describes the case of a non-seminomatous germ cell tumour which recurred 23 years after the initial diagnosis and treatment. A 52-year-old man developed an ischial bone osteolytic mass which was discovered during investigation of severe pain in the hip joint. ***Pneumon 2010, 23(1):107-110.***

INTRODUCTION

Approximately 60% of testicular germ cell tumours (GCTs) are seminomas and 40% are non- seminomatous (NSGCT). The NSGCTs often consist of more than one histological type, and the types represented are: intermediate malignant teratoma, undifferentiated malignant teratoma, trophoblastic malignant teratoma (choriocarcinoma), yolk sac tumour and differentiated teratoma[1].

Testicular cancer is considered to be a curable neoplasm. Almost 95-100% of patients with early stage disease and 70-80% with stage III disease are curable[2]. Late relapse is defined as metastasis arising 2 years after initial diagnosis and complete response to treatment, in the absence of a contralateral GCT, extragonadal GCT or non-testicular secondary cancer[3]. The incidence rate of relapse is 1.3% to 28%. Recurrences usually occur within 2 years and only a few cases have been reported more than 10 years after the initial presentation[4]. Recently alterations in gene expression have been indentified that are specific for each type of NSGCT, which may serve as novel markers for diagnosis or tumour progression[5].

CASE REPORT

A 52 year-old man was admitted because of severe joint pain in the right ischium. He had a history of right radical orchidectomy for GCT 23 years earlier. The initial diagnosis was stage IIIc (pulmonary involvment) GCT. Following diagnosis he had received five cycles of chemotherapy with bleomycin,VP15 and actinomycin,and retroperitoneal lymph node dissection (RPLND) was performed because of retroperitoneal lymph node metastases (i.e., mature teratoma). Because of elevated post-RPLND serum tumour markers he recieved five further cycles of bleomycin, VP15 and actinomycin. He was followed up for 5 years after the initial diagnosis, during which serum tumour markers were negative.

The patient presented with a 3 month history of severe joint pain in his right ischium. Clinical examination was unremarkable exept for the absence of the right testis. The left testis was normal on palpation. The blood count and biochemical blood studies were unremarkable. Serum tumour markers CEA, CA125, CA 15.3 CA19.9, PSA and β-hCG were in the normal range. He had raised serum levels of alpha-fetoprotein (AFP) (169.48 ng/ml, normal range 0.0-7.0 ng/ml), lactate dehydrogenase (LDH) (1155 U/L, normal range 230-460 U/L) and alkaline phosphatase (104 U/L, normal range 3-128 U/L).

Pelvic X-ray showed an osteolytic lesion in the right ischium. CT scan of the chest showed 4 small peripheral lessions, two in the apex of the left lung and two in the right lung, and mediastinal adenopathy. CT scan of abdomen showed adenopathy of the left renal hilum and an osteolytic lession on the right os ischii and hip joint. Bone scan was positive for metastatic disease.

Biopsy of the testis was negative. Biopsy of the lytic bone lesion was carried out to confirm the diagnosis. Histological and immunohistochemical examination of the biopsy cylinders showed an anaplastic seminoma. Immunohistochemical testing was positive for AFP and negative for β-HCG, panceratins and CEA.

The patient recieved two cycles of chemotherapy with cisplatin, etoposide and bleomycin, and local radiotherapy for relief of the bone pain.Treatment was discontinued ten days later due to systemic complications. He developed high fever, leucopenia and upper gastrointestinal tract haemorrhage and died ten days later.

DISCUSSION

Late recurrences are rare in patients with testicular

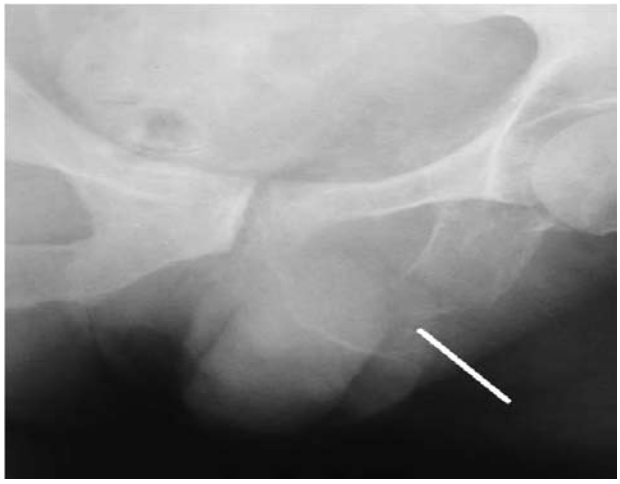

FIGURE 1. Plain X-ray film of pelvis showing lytic lesion of the right ischium.

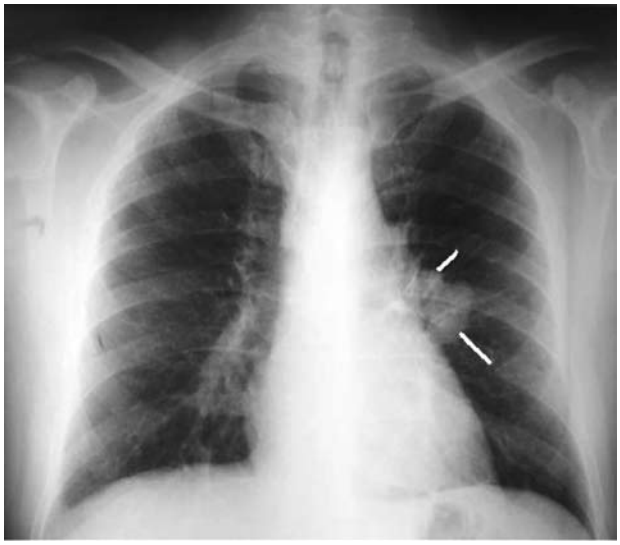

FIGURE 2. Chest X-ray showing lung metastases and hilar lymphadenopathy.

GCTs and follow-up to detect recurrence may not be needed 5 years after the initial diagnosis, except in those presenting with metastatic NSGCTs[6]. Early first relapse is probably a risk factor for late relapse in non- seminoma tumours, and the cumulative relapse risk is 9% at 5 years for patients with early relapse[7]. Residual viable cancer cells after initial treatment (inappropriate chemotherapy) persist with an atypical biological behaviour pattern, and may predispose to late recurrence. In addition, the presence of pure teratoma at initial diagnosis, as has been previously noted, is a risk factor for late recurrence[6].

Studies have shown that the median interval for late

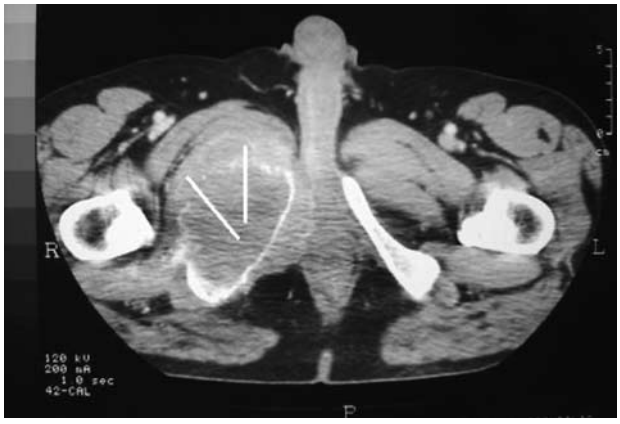

FIGURE 3. CT showing lytic lesion of the right ischium.

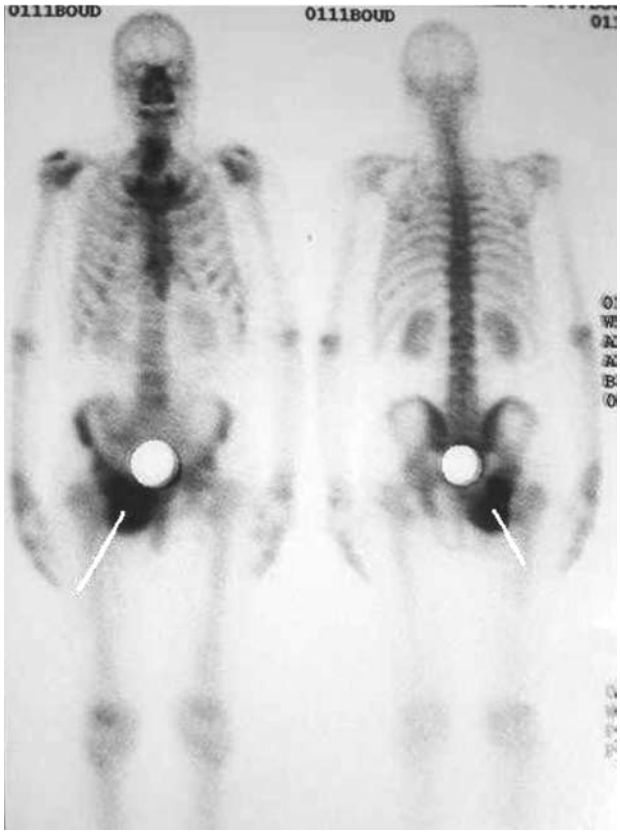

FIGURE 4. Bone scan showing warm area of the right ischium.

recurrence of non-seminoma GCT is 73 months, and the longest interval that has ever been reported was 32 years (384 months) [8, 9, 0. In the case reported here, the diagnosis was straightforward because the patient presented with an elevated serum level of AFP, metastatic GCT was

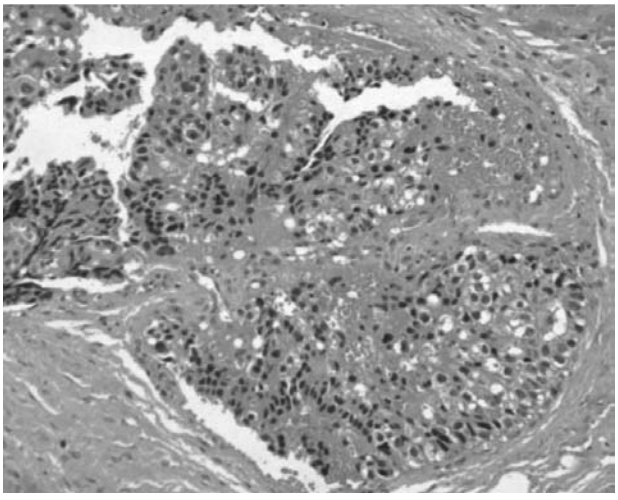

FIGURE 5. Bone biopsy showing a focus of metastatic germ cells with abundant clear or weakly eosinophilic cytoplasm (Haematoxylin and eosin).

found was found in the bone biopsy, and no other primary site was detected.To the best of the authors' knowledge, this case is the second longest long-term interval for a metastatic GCT (23 years or 276 months) and the first presenting with ischial bone and lung metastases and with concomitant thoracic and abdominal adenopathy. Only a few cases of late bone metastases have been reported, which involved the axial skeleton (vertebrae-ribs) and the lesions were also lytic[11].

Dieckmann et al reported that the recurrence interval in NSGCTs is significantly associated with previous chemotherapy and this could explain the shorter intervals of seminoma, for which chemotherapy is rarely administered[3].

A number of studies have determined the clinical features in late relapse. It appears that late relapse lymphadenopathy most commonly occurs in the retroperitoneum (50-80%) followed by the mediastinum (12%) and the neck[12]. Lung metastases constitute the most common extra-nodal disease site, accounting for 21% of cases[13].

George DW et al reported that an increase in serum AFP is a critical point in late recurrence and is a characteristic of non-seminoma GCTs[14]. Likewise Dieckmann KP et al[3] noted a elevation in AFP levels in 67% of Patients, while β-HCG was elevated in only 27%. He also noted that levels greater than100U/l were significantly associated with an unfavourable outcome. Shahidi M et al made the same observation in his series[6], and this opinion is supported by Gerl A et al who observed that AFP-producing tumours are relative slow developing and reported

that the median AFP doubling time following primary chemotherapy was 155 days[7].

A standard treatment for late recurrence NSGCT has not yet been established. Hartmann et al[15] evaluated the feasibility of intensified chemotherapy with etoposide, ifosfamide and cisplatin combined with paclitaxel, plus peripheral blood haematopoetic stem cell treatment. The survival rates of 2 and 5 years were 77.6% and 75.2% respectively. Kondagunta et al, using a combination of paclitaxel, ifosmamide and cisplatin reported a 70% complete response rate, and a 2-year progression-free survival rate of 65%[16].

Chemotherapy has only minor curative potential in the treatment of late recurrence, but patients with localized resectable disease can be cured. Unfortunately the patient reported here did not complete the chemotherapy due to lethal systemic complications.

CONCLUSION

The clinical case reported here draws attention to the current insufficiency of diagnostic tools for late relapse of NSGCT and emphasizes the need for novel diagnostic markers and for annual follow-up which would be more accurate in the detection of relapse in the asymptomatic phase, which appears to be mandatory for selected patients (i.e., those with NSGCT). This regime is recommended in the latest (2009) update of the EAU guidelines.

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