Brief Report

Late relapse of testicular cancer. A case report and a review of the literature

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A case of disseminated testicular cancer relapsing after 6 and 8 yr is reported, and the literature on late relapses is reviewed. About 4% of potentially cured testicular cancer patients do relapse after two or more years. Early detection is important and we recommend an indefinite follow-up, because salvage therapy can be effective when the extent of disease is limited. Neth J Med 1991;39:353–355.

Key words: Testicular cancer; Late relapse

Introduction

Non-seminomatous testicular cancer is considered a highly curable disease. Cisplatin-based combination chemotherapy has resulted in the cure of approximately 80% of patients with metastatic disease [1]. Recurrences typically occur within the first 2 yr after diagnosis and treatment [2]. Patients who survive disease-free beyond 2 yr are generally believed to be cured because recurrence after this time interval is rare [3]. We report a patient who suffered two relapses, 6 and 8 yr after first induction chemotherapy, and include a review of the literature.

Presentation of the case

A 61-year-old man underwent left orchietomy in May 1979 because of an enlarged testis. Histopathology revealed an embryonal cell carcinoma. Subsequent staging disclosed metastasis of the disease to the retroperitoneal lymph nodes. The serum concentrations of beta-human chorionic gonadotrophin (β-HCG) and lactate dehydrogenase (LDH) were within normal limits, but the alpha-fetoprotein (AFP) was 2452 ng/ml (normal < 5 ng/ml).

He was treated with four courses of cisplatin, vinblastine, and bleomycin after which he achieved a complete remission, and the AFP decreased exponentially to a normal level.

A routine chest film during regular follow up revealed a pathological mass (2 × 2 cm) in the lingula in November 1985. At that time serum AFP was again abnormal (1554 ng/ml), while serum β-HCG was normal. No other abnormalities were found during a complete staging procedure including a CT-scan of the chest and the abdomen. Thus, it was likely that the lingual mass represented a metastasis from the testicular cancer of 1979. Combination chemotherapy was initiated; this consisted of VP-16 (etoposide) and carboplatin, both at a dose of 50 mg/m² i.v. on 5 consecutive days every 4 weeks. The mass in the lingula decreased markedly in size; however, it
did not disappear completely. Serum AFP decreased slowly (half-life 14 days) to 14 ng/ml.

Because of the residual mass a thoracotomy with wedge excision was performed in April 1986. Histological examination revealed still viable cells of the embryonal cell carcinoma. A tumour-free margin of at least 0.5 cm was noted. After surgery, serum AFP dropped to the normal level of less than 5 ng/ml.

It was decided to give two consolidation cycles of carboplatin and VP-16. However, due to intolerance he received only one cycle. In addition, the operation area was treated with 3000 cGy radiotherapy in 15 fractions. Unfortunately, in January 1987, serum AFP levels started to rise again. The chest X-ray revealed recurrence of the lingual mass.

Restaging revealed no other lesions. The patient was observed for 6 months. In August 1987 it was evident that the mass in the lingula was the only site of disease. Therefore a second thoracotomy was performed excising the whole lingula. At that time the AFP had risen to 1934 ng/ml. Pathological examination again revealed viable embryonal cell carcinoma. After the operation, AFP levels dropped exponentially to normal. To date (October 1991) the patient remains in complete remission with normal AFP levels.

**Discussion**

We consider this patient's history to be particularly interesting. In general, recurrence of testicular cancer means generalized disease and chemotherapy is the only treatment option to achieve a remission. The precise role of the chemotherapy in this patient at recurrence is unclear. It is clear that the chemotherapy used was not highly effective as the AFP did not decrease exponentially. However, because the patient was relatively old, more aggressive chemotherapy was not possible. We cannot exclude the possibility that radical surgery alone when used at the onset of the recurrence would have led to the same result.

In general, a duration of complete remission of 2 yr has been considered equivalent to cure in patients with testicular cancer [2]. However, late relapses have been reported, mostly as single case reports [4–10]. Recently four reports on larger numbers of patients called attention to late relapses. Borge et al. [11] reported that 15 of 1008 (1.5%) patients with testicular cancer relapsed 36 months or more after the initial treatment consisting of radiotherapy, chemotherapy, or both. Six patients had pure seminoma initially (clinical stage I–III) and relapsed after an average of 54.5 months (range 36–108 months). Nine non-seminoma patients (initially stage I–IV) relapsed after an average of 85 months (range 36–194 months). Thirteen of these patients had symptoms as a result of the recurrent tumour leading to the diagnosis. With chemotherapy and radiotherapy, 4 of the 6 seminoma patients entered a second complete remission as did 2 of the 7 non-seminoma patients. Two initially non-seminoma patients underwent surgical excision of pure mature teratoma as their only treatment, both achieving a complete remission. De Leo et al. [12] reported five (6%) late recurrences 58 to 195 months after the initial treatment in 81 patients treated for advanced disease. One patient with seminoma achieved a complete remission with salvage chemotherapy while two of the four non-seminoma patients did so.

Levi et al. [13] reported four relapses (2%) 28 to 60 months after the initial treatment in a group of 183 patients treated for advanced disease. In two patients a second complete remission was observed with salvage chemotherapy.

Roth et al. [14] reported seven late relapses (4%) 41 to 83 months after the initial treatment in a group of 175 complete responding disseminated testicular cancer patients. Four of these seven non-seminoma patients achieved a complete remission with salvage chemotherapy lasting 34 + 81 + months.

Late recurring germ cell tumours often respond poorly to chemotherapy. Most cited cases, however, had bulky disease at the time of recurrence. Because tumour bulk at diagnosis is recognized as a prognostic factor [15], early detection of these recurrences seems to be critical. The probability of a second long term complete response to salvage therapy appears to be in the order of 20% [16].
While the first 2 years following the attainment of complete remission continue to be regarded as the critical period of observation, there is little consensus in the literature regarding the length of follow-up.

Borge et al. [11] state that active follow-up is not justified as most patients in their series (13/15) seemed to be aware of the clinical signs and symptoms leading to the diagnosis of the relapse. They stress informing testicular cancer patients about typical signs and symptoms that can be related to a relapse. This advice is questionable, because they discontinued follow-up in most patients after three tumour-free years. Nevertheless, Borge et al. advise life-long follow-up in order to evaluate the long-term effects of the administered treatment.

De Leo et al. [12] advise at least an annual evaluation, but they do not mention for how long or in which way. Levi et al. [13] advise maintaining indefinite follow-up for these patients. A proposed reasonable follow-up scheme would be every third month in the third year, every fourth month in the fourth year, twice yearly in the fifth year and yearly thereafter [17]. A physical examination, a chest X-ray and determination of the serum tumour markers should be performed at each visit. The value of an annual survey of the retroperitoneal region with ultrasound or preferably CT scan is debatable, but should be performed when a relapse is suspected. All patients should be taught the technique of self-examination of the remaining testicle and told to return between routine visits for any noticed change such as abdominal or low back pain, shortness of breath or persistent cough, and lymphadenopathy.

With ongoing follow-up it is clear that about 20% of patients with disseminated disease treated with initial chemotherapy will fail to obtain a durable complete remission and that about 4% of potentially cured advanced testicular cancer patients do relapse after two or more years [14]. When a relapse occurs, salvage therapy can be effective.

References