Case Report

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Successful Treatment of Stage-IIIB Seminoma with Single-Agent Carboplatin Therapy

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Key Words

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Abstract

Single-agent carboplatin chemotherapy has recently been introduced into the therapy of limited seminoma. Because of poor compliance due to Down's syndrome we successfully treated a 32-year-old man with relapsed stage-IIIB seminoma with a dose-modified carboplatin monotherapy schedule leading to complete remission even after a follow-up of 4 years.

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Case Report

In December, 1990, a 30-year-old man, suffering from Down's syndrome, underwent orchiectomy because of pure seminoma of the right testis (pT1). Abdominal ultrasound and conventional chest X-ray film revealed no other tumor manifestation. AFP and beta-HCG were within the normal range. Because of poor compliance no further treatment or follow-up investigation was performed.

In August 1992, the patient presented with back pain and a palpable abdominal tumor. A CT scan revealed retroperitoneal lymphomas up to 7 cm in diameter and a large mediastinal tumor measuring up to 15 cm infiltrating the left upper lung lobe accompanied by pleural effusion (fig. 1). Beta-HCG was increased to 167 U/l, and lactate dehydrogenase (LDH) to 631 U/l (normal range < 240 U/l), whereas AFP was within the normal range. A single-agent chemotherapy with carboplatin was started with 200 mg/m² on days 1 and 8, and repeated on day 22. Four courses were given between August and December 1992. Only mild side effects with nausea and vomiting only after the first therapy cycle could be observed. Hematological toxicity included mild anemia (Hb 12.9 g/dl) and leukopenia (2,500/μl). Besides transient microhematuria, no nephrotoxicity or even ototoxicity or neuropathy developed. After the first course there was

prompt regression of the tumor. Beta-HCG declined to 9.2 U/l, and LDH to within the normal range. After four courses of therapy, in December 1992, there was only a small residual tumor in the upper mediastinum. The retroperitoneal tumor showed complete remission. Beta-HCG has been within the normal range since October 1992. Unfortunately, the patient refused further treatment. However, a follow-up investigation at the end of 1996 revealed complete remission.

Comment

Cisplatin-based polychemotherapy is the established therapy for advanced seminoma, leading to complete remission in 65-90% [1]. However, the neuro-, nephro- and hematotoxicity of this regime is high. Furthermore, the risk of therapy-induced second neoplasms cannot be underestimated in this collective of very young patients treated. Therefore the much less toxic cisplatin analogue, carboplatin, was introduced into therapy. The regular dose in phase-II studies for limited [2-4] and advanced [1, 5] seminoma is 400 mg/m² given in 4-6 cycles every 3 weeks. Side effects include mild nausea and vomiting. Hematotoxicity did not exceed grade III according to WHO criteria [1], and nephrotoxicity was of no clinical relevance leading only to a minor decrease in creatinine clearance [6]. No neurotoxicity could be observed. In our patient this minor toxic profile was essential because of his extremely poor compliance due to Down's syndrome which was the reason for his refusal of adjuvant radiotherapy after the initial diagnosis in 1990. To reduce toxicity even more, we split the total dose of 400 mg/m² to 200 mg on days 1 and 7 of each cycle. Therefore toxicity was tolerable even for this patient.

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Fig. 1. a Abdominal CT scan showing retroperitoneal lymphoma measuring 7 cm in diameter, b Thoracic CT scan showing the mediastinal tumor measuring 15 cm in diameter with infiltration of the left upper lung lobe.

The effectiveness of carboplatin monotherapy in advanced seminoma has been investigated in several phase-II studies. Horwich et al. [5, 7], after more promising initial results, treated 70 patients with advanced seminoma. After a median follow-up of 36 months, complete remission was observed in 77% of patients. Sixteen patients relapsed. Twelve of them could be successfully treated by salvage polychemotherapy. The rate of relapse could be reduced by radiation following carboplatin therapy. Similar results have been reported by Schmoll et al. [1]. Complete remission was achieved in 30 of 42 patients. The rate of relapse-free survival was 60% after a median follow-up of 31 months. Visceral disease was associated with a poorer response to carboplatin monotherapy. Of 8 patients relapsing and 4 more with progressive disease, 10

responded to salvage polychemotherapy, leading to an overall survival of 93%. In a more recent report, Kawakita et al. [8] achieved only 1 complete remission in a group of 5 patients with seminomas of stage II to IIIB. In conclusion, approximately 60% of patients have been cured by this less toxic first-line chemotherapy without compromising the effectiveness of cisplatin-based salvage polychemotherapy.

Our patient presented with retroperitoneal and mediastinal bulky disease accompanied by lung involvement. Therefore, he belonged to the high-risk group. Nevertheless, carboplatin monotherapy seems to be effective even after a follow-up of 4 years. However, it has to be underlined that up to now single-agent carboplatin therapy is an experimental approach in patients with advanced seminoma. Firm recommendations regarding its use must await the results of a recently started phase-III trial comparing carboplatin monotherapy and cisplatin-based polychemotherapy.

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