Severe Thrombosis after Chemotherapy for Metastatic Choriocarcinoma of the Testis Maintaining Complete Remission for a Long Period

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We report the favourable outcome of a patient who suffered from severe arterial and venous thrombosis during chemotherapy for testicular pure choriocarcinoma. An increased paraneoplastic stimulus of HCG secondary to the marker surge phenomenon is suggested as responsible for transient hypercoagulability and subsequent thromboembolism.

Key words: choriocarcinoma, testis, chemotherapy, thromboembolism, hyperestrogenism, β-HCG, vascular toxicity, complication.

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Pure choriocarcinoma of the testis is a relatively rare neoplasm. It is the most malignant among testicular germ cell tumours, grows rapidly and commonly metastasizes to the lung. Combination chemotherapy with reliable non-invasive techniques to assess the extent of disease and its response to therapy may achieve high rates of remission even in metastatic germ-cell tumours (1, 5). Vascular toxicities during chemotherapy for testicular tumours have been reported infrequently but they are of clinical interest as such complications arise in young patients who have a high chance of cure, and unfortunately may be fatal (3). Herein, we would like to report the favourable outcome of a patient who suffered from severe arterial and venous thrombosis during chemotherapy for testicular pure choriocarcinoma.

CASE REPORT

A 40-year-old man presented with bilateral gynecomastia, impotence and a painful right testicular enlargement. Testicular ultrasonography confirmed the presence of a solid 2 cm intraparenchymal mass of the right testis and showed a normal but atrophic left testis. He had no risk factors for atherosclerosis and no history of cardiovascular disease or coagulopathy. A CT-scan showed multiple nodules in both lungs but did not show any retroperitoneal lymph nodes enlargement or hepatic lesions. Serum level of β-human chorionic gonadotropin (β-HCG) was 147,000 IU/l. Preoperative hematologic evaluation revealed normal counts, and prothrombin and partial thromboplastin times were also normal. A right orchidectomy was performed and histopathologic examination of the specimen revealed pure choriocarcinoma. The patient began chemotherapy consisting of cisplatin 20 mg/m^2 for 5 days, vinblastine 0.2 mg/m^2 for 2 days, and bleomycin 30 mg weekly. Because of leukocytopenia (leukocyte count: 1800/βl), G-CSF 300 ng/day for 4 days was successfully administered. Pulmonary nodules did not reduce in size and, paradoxically, the serum level of β-HCG increased to 595,000 IU/l. On day 2 of the second chemotherapy course, the patient had an abrupt ischemia of the right lower limb. Chemotherapy was immediately discontinued. An angiogram showed complete occlusion of the right superficial femoral artery. Intra-arterial thrombolytic therapy with bolus injection of 100,000 U of urokinase improved symptoms and restored flow to his right lower limb, but when he was given intra-arterial continous infusion urokinase therapy (25,000 U/day), ischemic signs and symptoms occured also in the controlateral leg. Angiogram showed occlusion of the left posterior tibial artery which was first treated with local thrombolytic therapy and thereafter with continuous intravenous infusion heparin therapy (30,000 U/24 h for 4 days). His condition gradually improved and a repeated angio-

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graphy 8 days later showed a disobliteration of the arteries of both lower extremities.

One month later, the serum level of β-HCG was 340,000 IU/l and a third chemotherapy course plus systemic intravenous infusion of heparin (40,000 U/24 h) was administered. Unfortunately, after completion of therapy, the patient complained of acute lower legs edema and pain. CT-scan and ultrasonographic examination revealed a thrombosis of both the iliac veins with a well-developed collateral venous circulation and a non-occlusive thrombosis of the abdominal aorta involving the right renal artery. Electrocardiogram and echocardiogram were normal and a ventilation/perfusion lung scan showed no perfusion defects. Peripheral intravenous urokinase (1000 U/kg per hour) was promptly administered for 12 h, followed by continuous intravenous infusion of heparin (40,000 U/24 h) and the patient's clinical status rapidly improved. Arteriography and venacavography 24 h later showed a 90% clearing of venous and arterial thrombi with a normal perfusion of the right kidney. After 10 days of heparin therapy warfarin treatment was instituted. One month after an uneventful recovery with relief of his symptoms, the serum level of β-HCG became normal and a CT-scan of the chest showed a reduction in size of all pulmonary lesions. The patient refused pulmonary metastasectomy and he had a fourth uneventful chemotherapy course with cisplatin 20 mg/m^2 for 5 days plus etoposide 100 mg/m^2 for 5 days resulting in a complete disappearance of all clinical, radiologic, and biochemical evidence of tumor. Warfarin therapy was maintained for 3 months. Three years and 7 months later, there are no signs of vascular disease or evidence of tumor recurrence.

DISCUSSION

Hypercoagulability producing thromboembolic complications may be acquired in association with several diseases, among which is malignant neoplastic disease, and with various forms of treatment, including chemotherapy. In many patients, the association of underlying vascular disease and transient hypercoagulability may explain such complications (2). However, the young age of patients with testicular tumours and the lack of vascular risk factors in most of the reported cases suggest that cumulative vascular damage due to chemotherapy cycles may be responsible for such events (3). In our opinion, a hypercoagulable state may be also due to an increased serum level of β-HCG. It is well documented that the similarity of the subunits of HCG and luteinizing hormone (LH) allows each hormone to stimulate receptors of the other hormone when they are secreted in supraphysiological quantities by tumours (4). In this patient, gynecomastia and impotence were already present as clinical signs of this cross-reaction between HCG and LH. An increased paraneoplastic stimulus of HCG secondary to the marker surge phenomenon was observed in our patient after the first chemotherapy course and it may have resulted in a further increase in the serum level of estrogens which was probably responsible for transient hypercoagulability and subsequent thromboembolism.

It would seem advisable to investigate further the hemostatic system and the hormonal status of all patients with testicular cancer to better understand the pathophysiology of thromboembolic complications and thereby to minimize the risk of their occurrence during chemotherapy.

REFERENCES

1. Bagshawe KD. Choriocarcinoma. A model for tumour markers. Acta Oncol 1992; 31: 99–106.
2. Donaldson MC, Whittemore AD. Thromboembolism from occult subclavian arterial stenosis during chemotherapy for breast carcinoma. Arch Surg 1995; 130: 224–226.
3. Gerl A, Clemm C, Schleuning M, Wilmanns W. Fatal cerebrovascular accident associated with chemotherapy for testicular cancer. Eur J Cancer 1993; 29A: 1220–1221.
4. Gleason PE, Elliot DS, Zimmerman D, Smithson WA, Kramer SA. Metastatic testicular choriocarcinoma and secondary hyperthyroidism: case report and review of the literature. J Urol 1994; 151: 1063–1064.
5. Lekili M, Minareci S, Nergis N, Serim U, Ayder AR. Management of testicular cancer with combined-modality treatment. Int Urol Nephrol 1995; 27: 423–429.