Chemotherapy induced myocardial infarction in a young male with non-seminomatous germ cell tumor of testis

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Abstract:
Chemotherapy induced myocardial infarction is a rare complication. We report a case of acute myocardial infarction developing in a patient with germ cell tumor of testis being treated with combination chemotherapy containing cisplatin. Twenty nine year old male without any associated cardiac illness developed acute myocardial infarction after third cycle of combination chemotherapy. Prompt thrombolysis helped in reducing the morbidity and earlier recovery of cardiac function.

Keyword: Cisplatin Thromboembolism Myocardial infarction

Introduction:
The cardiotoxicity as a side effect of chemotherapeutic drugs is common and well known. Chemotherapeutic drugs produce variety of cardiac abnormalities including acute events like conduction abnormalities (arsenic and cytarabine) and ischemic changes (fluoropyrimidines and taxanes); long term complications like heart failure (anthracycline) (1,2). These cardiotoxic can be dose dependent or can manifest because of variation with the route and duration of administration. Incidence of cardiac side effects increases with presence of associated cardiac comorbidities. We report a rare ischemic side effect of chemotherapeutic agent cisplatin in a patient with non-seminomatous germ cell tumor of testis.

Case report:
29 year old gentleman, with no known associated cardiac illness presented to us in August 2012 with history of painless left cervical adenopathy of one year duration. He had noticed it one month after herniorrhaphy for right inguinal hernia. He was subsequently proven to have carcinoma upon biopsy of the cervical node at a private hospital. On clinical examination his ECOG performance score was 1 and had left supraclavicular 4cms node along with previous lymph node excision biopsy scar. He also had a cricket ball size vague palpable mass in right iliac fossa. His contrast enhanced computed tomography (CECT) imaging of chest and abdomen
showed multiple retroperitoneal nodes largest measuring 5cms. His ultrasonogram of testes revealed hypoechoic mass in the right testis measuring 0.8 x 0.2cms. Serum AFP (254mg/ml), -HCG (1227mlU/ml) and LDH (969U/L) levels were elevated. He was diagnosed as a case of non-seminomatous germ cell tumor of testis (NSGCT) stage IIIB. He underwent right high inguinal orchiectomy. Histopathological examination revealed anaplastic seminoma without any teratomatous, embryonal or yolk sac components. Considering the elevated levels of AFP he was treated on lines of NSGCT rather than seminoma with Bleomycin, Cisplatin and Etoposide (BEP) chemotherapy. He tolerated two cycles of BEP chemotherapy fairly well. However on day 8 of 3rd cycle of BEP chemotherapy he developed acute onset of chest pain. Electrocardiogram (ECG) revealed acute anterior wall ST elevation myocardial infarction (Image 1). He underwent thrombolysis for the same under the care of cardiologist. Echocardiogram done at time of cardiac event showed an Ejection Fraction of 40% with hypokinetic interventricular septum and apex. Post thrombolysis he recovered well with an increase in ejection fraction increasing to 60%. The regional wall motion abnormality of the interventricular septum and apex persisted. His serum AFP and -HCG levels had normalized by now but had residual retroperitoneal adenopathy of 4.5 centimetres on CECT of abdomen. No further chemotherapy was contemplated considering the significant cardiac side effects after chemotherapy. He underwent retroperitoneal lymph node dissection. Histopathology of the dissected nodes showed residual mature teratoma without any embryonal or yolk sac components. He was hence was kept on follow-up. Unfortunately during follow-up his serum AFP and -HCG levels started increasing. CECT of chest and abdomen showed multiple lung metastases.

He is presently being treated with salvage chemotherapy.

Discussion:
Thromboembolism in cancer patients is common complications. Cancer itself is a precipitating factor for thromboembolism (3). Cancers of brain, pancreas, lung, prostate and hematological malignancies have been associated with high incidence of thromboembolism. Other factors which have been associated with increased risk of thromboembolism are advanced or metastatic cancer, metastases to bone and viscera, pelvic surgeries, and type of chemotherapeutic agents (4,5).

Cisplatin is the backbone of combination chemotherapy used in the first line treatment of germ cell tumors of testis. The main side effects of cisplatin are peripheral neuropathy, ototoxicity and nephrotoxicity (6). Thromboembolic complications due to cisplatin are very rare (7) and only few cases of arterial thromboembolism have been reported worldwide. Arterial thromboembolic complications due to cisplatin are mainly myocardial infarction, aortic thrombosis, cerebrovascular accidents (3). Many risk factors have been attributed to increased risk of thromboembolism including liver metastasis, use of antiemetic therapy and associated cardiac comorbidities (8–11). The mechanism for increased risk of thromboembolic complications by cisplatin is not fully elucidated. It has been attributed to many causes like damage to endothelium by the chemotherapeutic drug itself or by interaction of cisplatin with von Willebrand factor. It has also been proposed that the hypomagnesemia produced by cisplatin may cause vasospasm (12).
There are very few published case reports with chemotherapy induced myocardial infarction in patients with NSGCT (13). Myocardial infarction has been reported with even one cycle of chemotherapy. Our patient had developed ST-elevation MI after 3rd cycle of chemotherapy which recovered after thrombolysis. He was non-smoker and was not suffering from any illness which would precipitate myocardial infarction like diabetes mellitus, dyslipidemia, or hypertension. Considering that he didn’t had any significant other risk factors for myocardial infarction, cisplatin would be the likely agent for the event. He recovered well post thrombolysis without any major complications indicating the effectiveness of the thrombolysis in such emergent conditions due to cisplatin.

**Conclusion:**
Cisplatin induced myocardial infarction is a rare side effect. Early diagnosis and management probably helps in effective treatment. Reexposure to cisplatin may be deleterious and probably not advised.

**References:**
Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3409130/

