DOI: 10.7860/JCDR/2017/22582.9313

Case Report

Oncology Section

Disseminated Intravascular Coagulation and Excessive Fibrinolysis (DIC XFL) Syndrome in Prostate Cancer: A Rare Complicated Disorder

AZHAR BIN AMIR HAMZAH[1], YEW MAW CHOO[2], MOHAMED AZMI HASSALI[3], FAHAD SALEEM[4], ASHUTOSH KUMAR VERMA[5]

ABSTRACT

Disseminated Intravascular Coagulation (DIC) develops in patient with prostate cancer, which is manifested by systemic, intracranial, intracavitary or intracutaneous bleeding indicating uncompensated or excessive fibrinolysis (XFL). This case report is a description of a 61-year-old male with metastatic prostate cancer that progressed to manifest DIC. The condition is rare in clinical practice, and even rarer when is coupled with XFL. Treatment was mainly replenishing coagulation factors, platelets and controlling the disease progression with aggressive hormonal therapy. The patient progressed to coagulopathy further with fibrinolysis, hence leading to mortality. This case study discusses the pathophysiology of this complication and various methods to monitor the disease progression are discussed.

Keywords: Fibrinolysis, Hormonal therapy, Intravascular Coagulation, Metastatic prostate cancer

CASE REPORT

A 61-year-old male patient presented with history of haematuria from one month prior to admission. It was associated with progressive worsening back pain since last 5 months duration. The patient was diagnosed for prostate cancer 3 years back after the prostate biopsy confirmed an adenocarcinoma with Gleason score of 4+4. Staging CT and bone scan confirmed metastasis of the spine and pelvic bones. He was started on Luteinizing Hormone Releasing Hormone (LHRH) agonist IM Leuprolide (11.25 mg/3 monthly and bicalutamide 50 mg TDS) after he refused castration. The patient was again brought to the hospital with haematuria after 1 month, which soon became coarse. Haematuria was further complicated with blocking of the irrigation catheter due to blood clots for which regular flushing of the catheter had to be done. Patients' examination reported a normotensive Blood Pressure (BP) but with a tachycardiac pulse rate (95 to 100 beats per minute). There was an enlarged liver that was non-tender and with macro-nodules palpable suggestive of liver metastasis. Shifting dullness was observed with presence of ascites. Per-rectal examination revealed firm prostate (size 30 gm) with irregular surface. Respiratory examination revealed equal breath sounds bilaterally with rales at bilateral basal regions suggestive of atelectasis.

His haemoglobin (Hb) was 9.8 g/dL, platelet count was 36000 cells/uL and PT/aPTT was in normal range. Irrigation commenced and gross haematuria was resistant. Subsequently he went into DIC whereby his fibrinogen was only 42 mg/dL, D-dimer was 5.6 µg/mL and PT/aPTT was prolonged. Hb level further plummeted along with platelet counts. Sixteen units of platelets, 8 units fresh frozen plasma, 16 units of cryoprecipitate and 10 pints of packed cells were transfused throughout his admission. Haematuria was resistant and was further complicated with haemoptysis due to pulmonary haemorrhage. Haemostatic radiotherapy of 5cGy each day for 5 cycles was subjected but haematuria improved for 1 day followed by reoccurrence of bleeding. Finally, patient's family were explained of the complication of chronic DIC. Then the patient's family decided to withdraw patient from hospital take back home where the patient died a day later.

DISCUSSION

DIC is the most frequent coagulation disorder in prostate cancer and it usually occurs in its advanced disease state [1]. The indexed case initially presented with haematuria and further went on to develop pulmonary haemorrhage due to chronic DIC coupled with XFL which are also reported in literature [2,3]. The patient was on optimal hormonal therapy, but still he developed DIC that did not responded to the further treatment. The reason could have been a hormone resistant prostate cancer that was secreting high levels of mucin that acts as a tissue factor (thromboplastin) which is the cause for DIC [2]. This underlying disorder, which causes release of mucin, stimulates thrombin generation. Thrombin causes increased conversion of fibrinogen to fibrin, which is deposited widespread to small and midsize vessels causing a worsening of condition and thrombotic occlusion of mid and small sized vessels. Widespread thrombosis leads to consumption and depletion of platelets and clotting factors leading to bleeding tendency. Simultaneously there is abnormal removal of fibrin (impaired fibrinolysis) due to the prostate cancer cells producing urokinase type plasminogen activator that converts plasminogen to plasmin (a fibrinolytic protease enzyme). That is how excessive bleeding complications arises which was seen in this patient. Similar case was reported by Desai et al., [4].

In some patients, this condition may be prolonged and protracted as what was seen here. Most of the patients may be asymptomatic but this patient started to develop acute DIC [5]. In acute DIC, fibrinolysis predominates over coagulation and there is excessive bleeding. Investigational features which can give us a strong clue for DIC are findings seen in tests which identify thrombin and plasmin generation in blood (serum D-dimers, protamine paracoagulation assay for fibrin monomer) and tests for haemostasis that can give information regarding consumption and depletion of coagulation factors (PT, PTT and thrombin time). All the features discussed were reported in this patient. Also acute DIC, thrombocytopenia, elevated fibrin or fibrinogen degradation products, prolonged PT, thrombin time and PTT, and low fibrinogen levels were also reported by Duran et al., [6].

Treatment of DIC requires supportive measures to replenish the depleted coagulation factors, which are consumed due to extensive fibrin deposition. For hormone sensitive prostate cancer,

the treatment would be to suppress testosterone with antiandrogen therapy as reported by Rasool et al., [7]. LHRH agonist with short course of antiandrogen was on board but patients' condition worsened suggesting a hormone resistant prostate cancer in this case. Radiotherapy has been used in some reported cases to ablate the prostate as emergency haemostasis [7]. Success rate is 88% when hypofractionated radiotherapy is used as a local haemostatic agent. Survival as reported by Memorial Sloan-Kettering Cancer Centre, New York with DIC-XFL averages only 4-14 weeks with median survival period of only 4 weeks [8]. The patients' family could be informed earlier regarding the patients' prognosis as his bleeding tendency was resistant to treatment and continued to manifest bleeding tendencies despite radiotherapy and blood products were provided.

There are no particular treatment strategies other than treating the coagulation factors depletion by replenishing it and reducing the activity of the prostate cancer cells with optimal hormonal therapy. There is evidence that treatment with co-administration of tranexamic acid with low molecular weight heparin and high dose of antiandrogen therapy with fosfestrol can control excessive bleeding and prolongs the disease survival [9]. This kind of treatment [4,6] is controversial as a balance between treatment of coagulation and fibrinolysis is difficult to achieve and requires close monitoring with team approach employment.

Ethical consideration:

The case study was approved by hospital's ethics committee and signed informed consent was taken from the patients' relatives.

CONCLUSION

There is no cure for DIC-XFL. It would be more appropriate to inform the family members earlier regarding the patients prognosis. Additionally, there is high clinical index of suspicion when patient with advanced prostate cancer presents with haematuria and deranged coagulation profile. A more aggressive treatment with replenishment of coagulation factors and platelets with optimum hormonal treatment are needed to get better survival and disease progression outcome. A teamwork approach of the urologist, haematologist, oncologist, blood transfusion specialist and a dedicated laboratory team can play a role in getting a balance to treat the coagulation disorder and anti-fibrinolytic treatment.

REFERENCES

[1] Smith JA, Soloway MS, Young MJ. Complications of advanced prostate cancer. Urology. 1999;54(6):8-14.
[2] De la Fouchardiere C, Flechon A, Droz JP. Coagulopathy in prostate cancer. The Neth J Med. 2003;61(11):347-54.
[3] Albiges L, Cottu PH, Cojean-Zelek I, Raymond F, Zerkak D, Aerts J, et al. Haematological complications of prostatic cancer: 2 cases, one revealing the neoplasia. La Revue de Medecine Interne. 2007;28(3):176-78.
[4] Desai M, John B, Evans G, Eddy B. Prostate cancer: beware of disseminated intravascular coagulation. BMJ Case Reports. 2015;2015:bcr2014206814.
[5] Spector JI, Zimbler H. Carcinoma of the prostate presenting as acute disseminated intravascular coagulation. Canadian Medical Association Journal. 1987;136(6):570.
[6] Duran I, Tannock IF. Disseminated intravascular coagulation as the presenting sign of metastatic prostate cancer. J Gen Intern Med. 2006;21(11):C6-C8.
[7] Rasool MT, Manzoor NA, Mustafa SA, Maqbool LM, Afroz F. Hypofractionated radiotherapy as local hemostatic agent in advanced cancer. Indian journal of palliative care. 2011;17(3):219-21.
[8] Hyman DM, Soff GA, Kampel LJ. Disseminated intravascular coagulation with excessive fibrinolysis in prostate cancer: a case series and review of the literature. Oncology. 2011;81(2):119-25.
[9] Wada Y, Uchiba M, Kawano Y, Kai N, Takahashi W, Honda J, et al. Severe bleeding tendency caused by a rare complication of excessive fibrinolysis with disseminated intravascular coagulation in a 51-year-old Japanese man with prostate cancer: a case report. J Med Case Rep. 2012;6(1):378-82.

PARTICULARS OF CONTRIBUTORS:
1. Consultant Urology Surgeon and Senior Medical Lecturer, Urology Unit, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia.
2. Doctor, Urology Unit, Department of Surgery, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia.
3. Professor, Discipline of Social and Administrative Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia.
4. Senior Lecturer, Discipline of Social and Administrative Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia.
5. Masters (Research) Candidate, Discipline of Social and Administrative Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Mohamed Azmi Hassali,
Professor of Social and Administrative Pharmacy, School of Pharmaceutical Sciences,
Universiti Sains Malaysia, 11800 Penang, Malaysia.
E-mail: azmihassali@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Jul 04, 2016**
Date of Peer Review: **Aug 06, 2016**
Date of Acceptance: **Nov 01, 2016**
Date of Publishing: **Jan 01, 2017**