Paraneoplastic Hyperfibrinolysis: Detection of Occult Prostate Cancer with 18F-Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography

Abstract

Hyperfibrinolysis caused by abnormal over-activation of the fibrinolytic system can be associated with occult cancer. We present an interesting case of a 48-year-old man with paraneoplastic hyperfibrinolysis, where ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography-computed tomography (PET-CT) was able to detect occult prostate-specific antigen-negative metastatic prostate cancer as the underlying etiology. This shows that while ^{18}F-FDG PET-CT has overall poor sensitivity for prostate cancer, it can be useful in certain clinical situations.

Keywords: *^{18}F-fluorodeoxyglucose, hyperfibrinolysis, hypofibrinogenemia, positron emission tomography-computed tomography, prostate cancer*

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A 48-year-old man presented at our hospital with sudden onset multifocal muscle pains and cutaneous ecchymosis. There was no history of trauma. He had known comorbidities of hypertension and chronic kidney disease (Stage III). He was on a renal diet with fluid restriction, was not on dialysis and antiplatelet. Physical examination revealed tender lumpy swellings in the thighs, back, and shoulders, along with few cutaneous ecchymosis. Ultrasound examination showed multiple intramuscular hematomas. Blood examination revealed moderate anemia (hemoglobin: 8.3 g/dL, normal 12.0–15.0), moderate thrombocytopenia (82,000/µl, normal 1.5–4.0 lacs), raised serum creatinine (2.1 mg/dL, normal 0.6–1.1), and raised serum lactate dehydrogenase (380 IU/L, normal 140–280). Coagulation studies showed prolonged thrombin time (27 s, normal 14–19), with normal prothrombin time (PT) (14.0 s, normal 14.2) and activated thromboplastin time (APTT) (36 s, normal 30–40), low fibrinogen (96 mg/dL, normal 200–400), raised D-dimer (450 ng/ml, normal <250), and fibrin degradation product (48 mg/L, normal <10). Liver function tests were normal. With suspicion of paraneoplastic coagulopathy, multiple tumor markers were assayed. Prostate-specific antigen (PSA) was normal (2.6 ng/mL, normal <4), while carcinoembryonic antigen, cancer antigen-19.9, α-fetoprotein, and β-human chorionic gonadotropin were all normal. A noncontrast ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography-computed tomography (PET-CT) was then performed to localize occult malignancy if any [Figure 1a-g]. Maximum intensity projection whole-body PET image (a) showed multiple foci of increased ^{18}F-FDG uptake in the body (*broken arrows*, *arrows*). On transaxial CT (b) and PET-CT (c) images of the pelvis focal ^{18}F-FDG uptake was seen in the peripheral zone of prostate (*bold arrow*, SUV max 5.8), raising suspicion of primary prostatic malignancy. Also noted were extensive skeletal sclerotic lesions, including in the pelvic bones (d and e), showing increased ^{18}F-FDG uptake (*broken arrows*; SUV max 6.5). Some ^{18}F-FDG-avid pelvic nodes were also seen. Many hematomas were seen in the muscles. One in the right rectus femoris muscle is seen in coronal (f) and sagittal (g) PET-CT images of the thigh with peripheral increased ^{18}F-FDG uptake (*arrow*, SUV max 4.6), suggesting organizing hematoma. Based on PET-CT findings a diagnosis of metastatic prostate cancer was made. Transrectal ultrasound-guided biopsy from

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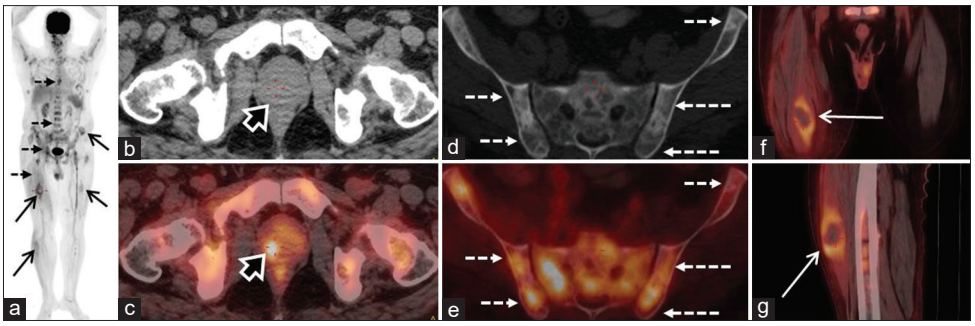

Figure 1: Maximum intensity projection whole-body positron emission tomography image (a) showed multiple foci of increased ^{18}F-fluorodeoxyglucose uptake in the bones (broken arrows) and muscles (arrows). Transaxial computed tomography (b) and positron emission tomography-computed tomography (c) images of the pelvis showed focal ^{18}F-fluorodeoxyglucose uptake in the right postero-lateral peripheral zone of prostate (bold arrow). Transaxial computed technology (d) and positron emission tomography-computed tomography (e) images also showed ^{18}F-fluorodeoxyglucose-avid extensive skeletal sclerotic lesions in the pelvic bones (broken arrows). Coronal (f) and sagittal (g) positron emission tomography-computed tomography images of thigh showing organizing hematoma in the right rectus femoris muscle with peripheral ^{18}F-fluorodeoxyglucose uptake (arrow)

the prostate was performed which showed high-grade adenocarcinoma (Gleason score 5 + 4). The patient was then managed with fresh frozen plasma transfusion, hormonal therapy, and spinal palliative radiotherapy. The patient improved clinically and was discharged in stable condition. He was doing fine till follow-up at 4 months.

Hyperfibrinolysis is characterized by abnormal over-activation of the fibrinolytic system, thereby causing excessive degradation of coagulation factors, including fibrinogen and bleeding.[1] It can be a paraneoplastic disorder, most commonly associated with prostate cancer and promyelocytic leukemia.[2,3] In that setting, hyperfibrinolysis is caused by the production of urokinase-type plasminogen activator and tissue-type plasminogen activator by tumor cells. Furthermore, some tumor cells can overexpress urokinase plasminogen activator receptor on the cell membrane, which favors over activation of the fibrinolytic cascade.[4] In prostate cancer disseminated intravascular coagulation is the most frequent coagulation disorder (30%–40%), whereas primary hyperfibrinolysis is rare (0.4%–1.6%).[5] These two entities can be differentiated by normal PT and APTT in the latter. While PSA is a sensitive marker for prostate cancer, a subset of patients can have normal PSA values even with high-grade cancers, as was seen in the present case. Such cancers are commonly hormone-refractory and have a poorer prognosis.[6] While ^{18}F-FDG PET-CT has overall low sensitivity for prostate cancer,[7] it continues to be useful in certain clinical scenarios.[8,9] In the present case, ^{18}F-FDG PET-CT was able to detect the occult PSA negative metastatic prostate cancer as the underlying etiology for acquired hyperfibrinolysis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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