MULTIPLE MYELOMA COMPLICATED WITH TAKOTSUBO CARDIOMYOPATHY: CASE REPORT

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MULTIPLE MYELOMA COMPLICATED WITH TAKOTSUBO CARDIOMYOPATHY: CASE REPORT (Abstract): Multiple myeloma (MM) is characterized by clonal proliferation caused by the expansion of monoclonal plasma cells, in which, due to immunoglobulin deposition (M protein/amyloid), renal dysfunction or another organ involvement like cardiac amyloidosis can be periodically encountered. We present the clinical case of a 61-year-old man admitted to our clinic with acute low back pain in the lumbar region. One month earlier, the patient was diagnosed with Takotsubo cardiomyopathy. The lumbosacral spine x-ray showed lumbar vertebral compression fractures and skull x-ray revealed various well-circumscribed lytic bone lesions. The typical M-peak (M band of IgG-kappa monoclonal gammopathy was found) was indicated by serum immunofixation. Keywords: TAKOTSUBO SYNDROME, MYOCARDIAL INFARCTION, MULTIPLE MYELOMA, CARDIAC AMYLOIDOSIS, CHEMOTHERAPY.

Multiple myeloma (MM), also known as plasma cell myeloma, is a cancer of plasma cells which was historically defined by end-organ damage, especially hypercalcemia, renal failure, anemia, and bone lesions (CRAB features) that can be associated with the neoplastic process (1). The following three new criteria are used in the diagnosis of MM: greater than 60% clonal plasma cells on bone marrow biopsy, serum free light chain (sFLC) ratio of > 1 (the involved sFLC must be > 100 mg/l), and more than one unequivocal focal lesion on cutting-edge imaging (low dose whole body computed tomography, magnetic resonance imaging, or 18-F-fluorodeoxyglucose-positron emission tomography) (2). Takotsubo cardiomyopathy, also known as “broken heart syndrome”, is a transient cardiac syndrome that involves left apical akinesis without obstructive atherosclerotic coronary artery disease. It is believed that this syndrome is triggered by an episode of emotional stress; it frequently occurs in female patients, 12% of patients with an uncertain diagnosis of acute coronary syndromes undergoing cardiac catheterization. Currently, few data in the literature advocate that multiple myeloma can be complicated with Takotsubo cardiomyopathy before the
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initiation of chemotherapy (3-11).

**CASE REPORT**

A 61-year-old man was admitted to University Hospital in Amman, Jordan, with low back pain which lasted for about four weeks. One month earlier, the patient had been admitted to another hospital where he was diagnosed with Broken Heart Disease (Takotsubo cardiomyopathy) and hyperchromic macrocytic anemia. He had been smoking for 40 years— one packet a day—but he did not consume alcohol. He had positive family history of cardiovascular diseases (CVD) but no personal history of other CVD or cardiometabolic syndrome.

At admission, the physical examination showed normal weight (BMI of 24 kg/m²), resting blood pressure (BP) of 120/70 mmHg and heart rate of 85 beats per minute; his respiratory rate was 18 breaths/min, and he was afebrile.

Blood test results showed hyperchromic macrocytic anemia (RBCs = 2.73*10^6/mm³, Hb = 11.2 gm/dL, MCV = 122.3 fl, MCH = 40.8 pg). Erythrocyte sedimentation rate, a non-specific indicator of inflammation (normal range for men < 50 years: 0-15 mm/hour) was highly increased (136 mm/h). As to the lipid profile, an important cardiovascular risk factor, the levels of all components: Triglycerides, Total Cholesterol, LDL-Cholesterol, and HDL-Cholesterol were within normal range. However, total protein level was too high = 9.5 g/dL, globulin = 6.4 g/dL and albumin level was too low = 3.1 g/dL. The fasting blood sugar (FBS) and glycated hemoglobin (HbA1c) presented a satisfying short-term and long-term control of blood sugar levels. The renal function, which is evaluated by creatinine and urea levels, was normal, and so were the liver function and the hydro-electrolytic balance. At admission the biological markers of myocardial necrosis-CPK, CK-MB and Troponin T were within normal range. Serum immunofixation showed the typical M-peak (M band of IgG-Kappa monoclonal gammopathy was detected), FLC Kappa = 1500 mg/dL, FLC Lambda = 12.2 mg/dL, and Kappa/Lambda ratio = 122.9. The calcium level was normal. The liver enzyme levels and kidney function were normal, too.

The patient underwent resting electrocardiography (ECG) which showed ST elevation in anterior precordial leads (V1-V5). Fully developed Pardee’s waves were seen in precordial leads V2-V3-V4-V5. Sinus tachycardia was about 90 beats per minute; however, the heart rhythm was regular. The normal electrical heart axis (QRS axis) was preserved. Consequently, the patient displayed only electrical signs of lesion and necrosis, specific for supra acute myocardial infarction; however, there were no disturbances of electrical function (fig. 1).

**Fig. 1.** Electrocardiogram at rest revealed STEMI
The patient underwent chest radiography which showed cardiomegaly with a cardiothoracic ratio of 69.3% and bilateral pulmonary congestion (fig. 2).

The 2D transthoracic Doppler echocardiography demonstrated apical akinesis of the anterior wall. Coronarography showed normal left main artery (LM), left circumflex coronary artery (LCX) and anteroapical akinesis of the left ventricle wall (fig. 3).

Disseminated multiple myeloma has two common radiological appearances, although it should be noted that initially radiographs may be normal despite the presence of symptoms. The two main diffuse patterns are: numerous, well-circumscribed lytic bone lesions (more common), and punched out lucencies, raindrop skull, endosteal scalloping (fig. 4).

**Fig. 2.** Chest X-Ray- cardiomegaly with a cardiothoracic ratio of 69.3% and bilateral pulmonary congestion

**Fig. 3.** Coronarography with normal LM, LCX, LAD and anteroapical akinesis of LV

**Fig. 4.** Skull x-ray with numerous, well-circumscribed, lytic bone lesions and punched out lucencies
DISCUSSION

Multiple myeloma (MM), also known as myelomatosis, is a rare type of hematological malignancy which accounts for approximately 10% of all hematological malignancies. Osteolytic bone destruction, anemia, recurrent infections and renal impairment are caused by the neoplastic proliferation which is defined as an uncontrolled reproduction of plasma cells in the bone marrow (12).

The diagnostic criteria for MM were updated in 2014 by the International Myeloma Working Group (IMWG) to add specific biomarkers which can be used to make the diagnosis of the disease in patients who did not present CRAB features. Moreover, MM bone disease can be diagnosed by using cutting-edge imaging methods such as computed tomography (CT) and positron emission tomography-CT (PET-CT) Bone pain and bone fractures, anemia, increased susceptibility to infections, hypercalcemia, neurological manifestations, hyper viscosity syndrome, renal failure and progressive osteolytic vertebral fractures are among the most frequently encountered characteristics of MM (13-14).

Approximately 15-20% of the patients suffering from MM secrete monoclonal light chains only, without the expression of the normal immunoglobulin heavy chain, and this constitutes light-chain multiple myeloma. “CRAB” is the abbreviation for high calcium, abnormal kidney function, anemia, and bone lesions. All initial treatments are started when myeloma is symptomatic. MGUS and smoldering myeloma should be carefully followed-up. Bence Jones proteinuria is a disorder characterized by the excretion of monoclonal light-chain protein. MM, which is usually confined to the bone marrow, sometimes infiltrates into other tissues; this phenomenon is known as extramedullary plasmacytoma (EMP). MM is defined as the monoclonal proliferation of bone marrow plasma cells producing multiple bone lesions and overproduction of a monoclonal protein (M-protein) that could amass in tissues (amyloidosis) (15).

In our case the serum immunofixation showed the typical M-peak (M band of IgG-Kappa monoclonal gammopathy was detected) that is specific for the diagnosis of MM.

Takotsubo cardiomyopathy (TCM) is a transient cardiac syndrome that involves the left ventricular (LV) apex akinesis and mimics acute coronary syndrome; this condition is triggered by emotional or physical stress and usually resolves completely (16). Even though TCM is usually reversible, it can be associated with significant morbidity, such as cardiac arrhythmia. The repolarization abnormalities characteristic to TCM can be associated with characteristic T-wave anomalies and QT prolongation that place patients at increased risk for ventricular arrhythmia, as well as for torsade de pointes. Life threatening arrhythmias such as VT and SCA are prevailing among men, while TTC has been agreed upon to be a disease mainly of females.

TTC may lead to severe heart failure and hemodynamic instability, even if most patients with Takotsubo cardiomyopathy (TTC) have benign clinical course and prognosis. TTC mimics the clinical characteristics of acute anterior wall myocardial infarction (AMI). Generally, clinicians often have difficulties in making the diagnosis whenever cardiac catheterization and angiography are contraindicated or causes adverse effects. In addition, differential diagnosis is also crucial since electrocardiogram findings in patients with Takotsubo
cardiomyopathy and acute coronary syndrome are similar, consisting among others in ST-segment elevation, T-wave inversion, QT-prolongation. Normally, apical involvement with hypercontraction of basal left ventricle (apical type) is prevalent; however, abnormal types affecting basal, mid-ventricular, and right ventricular myocardium have been depicted as well. Patients suffering from acute coronary syndrome die while hospitalized and this is usually caused by hidden conditions (17).

CONCLUSIONS
This case underlines the importance of suspecting a TTC in all patients with myocardial infarction and normal coronaryography, mainly if they do not have any cardiovascular disease or symptom at the onset of a major cardiovascular event.

This disease should be suspected more frequently in all patients even though it is rarer in male patients especially if they develop myocardial infarction in the absence of any cardiovascular disease.

REFERENCES