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CASE REPORT

Increased renal parenchymal retention of ^{99m}Tc-MDP (hot kidneys) in two patients of Hepatocellular Cancer: one with and other without osseous metastases

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ABSTRACT

Background: Hepatocellular cancer (HCC) is the fifth-leading cancer in men worldwide. Here we present two HCC patients who showed high diffuse renal parenchymal retention of ^{99m}Tc MDP on bone scan.

Cases presentation: Bone scan with ^{99m}Tc MDP was performed on two known HCC patients, which showed skeletal metastases in one and absent in the other case. Their kidneys showed high renal parenchymal retention of tracer with kidneys looking much HOT than adjacent bones. The differential diagnosis of hot kidneys include nephrocalcinosis, hypercalcemia, hyperparathyroidism, chemotherapy, sickle cell disease, acute renal injury, recent radiotherapy and aluminum breakthrough of ^{99}Mo-^{99m}Tc generator. Our patients did not fit in any of these. Hot kidneys in patient with liver cirrhosis have been reported due to hepatorenal syndrome. Although chronic liver parenchymal disease was present in the background of HCC, but our patients were not having hepatorenal syndrome (normal renal function tests). Quality control of generator and MDP vials used showed absence of any aluminum breakthrough and labeling efficiency was greater than 95% respectively. So, the exact cause of hot kidneys in these cases cannot be ascertained and some altered metabolism in liver and hemodynamic changes in body due to HCC might be the cause.

Conclusion: High diffuse renal parenchymal retention of ^{99m}Tc MDP might be seen on bone scan in HCC cases. Its clinical significance is unknown and needs further research to find out its exact mechanism and cause.

Keywords: Hot Kidney, renal parenchymal retention of MDP, hepatocellular CA, HCC, case report.

Background

Hepatocellular cancer (HCC) is the fifth-leading cancer in men worldwide, and the seventh leading cancer in women, representing about 7% of the total number of cancers diagnosed. Globally, liver cancer is the third-leading cause of cancer death, after lung and stomach [1]. It arises most frequently in patients with cirrhosis, especially in those having hepatitis B and hepatitis C [2]. Incidence of hepatocellular carcinoma (HCC) is on rise in Pakistan because of high incidence of hepatitis C. Its mortality is very high and in spite of well established surveillance programs in patients with chronic liver disease, most tumors are diagnosed in intermediate to advanced stage [3,4]. Pattern of distribution of metastases from HCC has also changed, and skeletal metastases from HCC are now more frequently being observed than mentioned in text books [4,5]. In bone scan performed after 03 hours after i/v injection of ^{99m}Tc-MDP, kidneys are usually faintly visualized in nuclear medicine practice. Increased diffuse cortical renal parenchymal retention has been observed in patients due to different causes in literature. Hot kidney

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sign has also been reported in patient with cirrhosis, and hepatorenal syndrome has been reported as its probable cause [5–10]. In the present case report we present two cases of HCC in the background of chronic liver parenchymal disease with normal renal function tests, in which kidneys were hot on bone scans due to high renal parenchymal retention. Informed written consent was obtained from both patients for this case report.

Case presentation

Case 1:

A 50 year old woman was diagnosed with hepatocellular cancer. She was a known case of chronic liver parenchymal disease due to hepatitis C for the last 04 years. On ultrasonography, a focal solid lesion was seen in the right lobe of liver along with mild spleomegaly and moderate ascites. Her Serum Alpha Fetoprotein [349 IU/ml (normal limits 0.49-9.84 IU/ml)] was markedly raised. Dynamic CT showed a solid mass in right lobe of liver, which enhances vividly during late arterial phase and then washes out rapidly, becoming indistinct or hypoattenuating in the portal venous phase compared with rest of the liver. These features were pathognomonic for the diagnosis of HCC. Both kidneys were normal on USG and CT abdomen. After 15 days of diagnosis of HCC, patient underwent Transarterial chemoembolization (TACE) at Shifa International hospital Islamabad. No chemotherapy was given. After one month of TACE patient complained of severe aches and pains in the body and patient was referred to Punjab Institute of Nuclear Medicine (PINUM) for skeletal metastatic survey. Whole body bone scan was performed 3 hours after 20 mCi i/v injection of ^{99m}Tc-MDP on GE Dual Head SPECT/CT Gamma camera (Hawkeye 2) equipped with low energy high resolution (LEHR) collimator by using 20 cm/min scan speed and 256 × 1024 matrix size. At the time of bone scan, her serum creatinine was 0.9 mg/dl (normal limit 0.6-1.3 mg/dl), urea was 28 mg/dl (normal limit 10-50 mg/dl) and calcium was 9.8 mg/dl (normal limit 8.5-10.5 mg/dl) while serum alkaline phosphatase was 337 IU/L (normal limit 80-306 IU/L). Bone scan of this patient is shown in Fig. 1.

Skeletal metastases in multiple vertebrae were seen on bone scan. Both kidneys looked very hot than those seen on bone scan in routine. There was marked renal parenchymal retention of radiotracer with absence of any pelvicalyceal hold up. Both kidneys looked hotter than adjacent spine and sacroiliac joints.

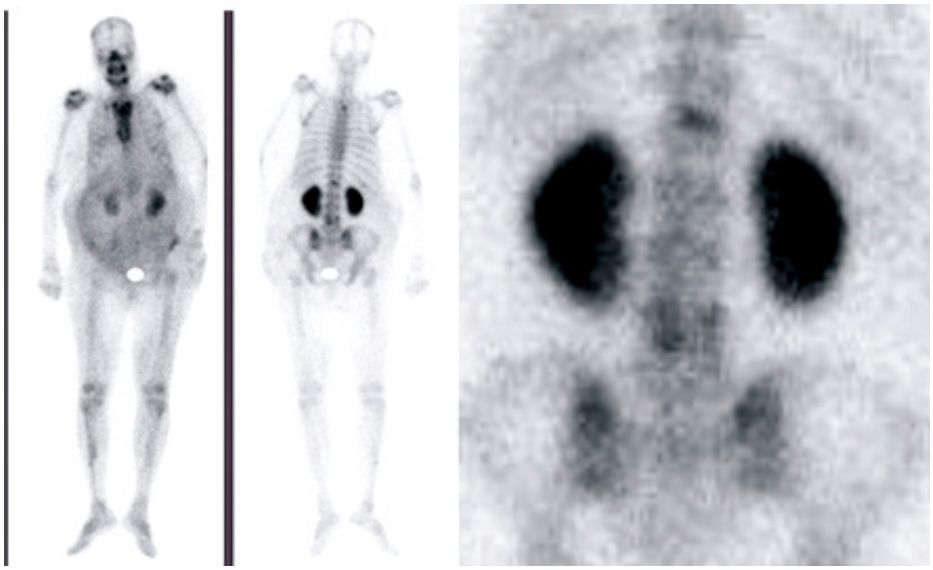

Figure 1: *^{99m}Tc-MDP Bone Scan showing marked bilateral renal parenchymal retention (hot kidneys) and presence of skeletal metastases.*

Case 2:

A 45 year old female was a known case of chronic liver parenchymal disease due to hepatitis B for the last 2 years. Ultrasonography showed cirrhosis of liver with marked splenomegaly, portal hypertension and moderate ascites. A focal solid lesion was seen in the left lobe of liver. Her Serum Alpha Fetoprotein was 286 IU/ml (normal limit 0.49-9.84 IU/ml). Her serum creatinine was 1.0 mg/dl (normal limit 0.6-1.3 mg/dl), urea was 32 mg/dl (normal limits 10-50 mg/dl), calcium was 9.1 mg/dl (normal limit 8.5-10.5 mg/dl) and serum alkaline phosphatase was 452 IU/L (normal limit 80-306 IU/L). Dynamic CT showed a solid mass in left lobe of liver, with early enhancement and rapid wash out of contrast becoming indistinct compared to the rest of the liver, confirming HCC. Both kidneys were normal on USG and CT abdomen. No chemotherapy was given. Patient was referred to PINUM for bone scan due to aches and pains in the body raising the suspicion of skeletal metastases, Whole body bone scan was performed 3 hours after 18 mCi i/v injection of

^{99m}Tc-MDP on GE Dual Head SPECT CT Gamma camera (Hawkeye 2) equipped with low energy high resolution (LEHR) collimator by using 20 cm/min scan speed and 256 × 1024 matrix size, which is shown in Fig. 2.

No skeletal metastases were seen on bone scan, however kidneys were showing marked increased renal parenchymal retention of radiotracer and looked very hot than the adjacent bones and joints. Due to very high diffuse cortical renal uptake in this patient's bone scan, all the bones were faintly visualized, most likely due to color scale/window adjustment for display. However, possibility of osteoporosis/osteopenia could not be totally ruled out.

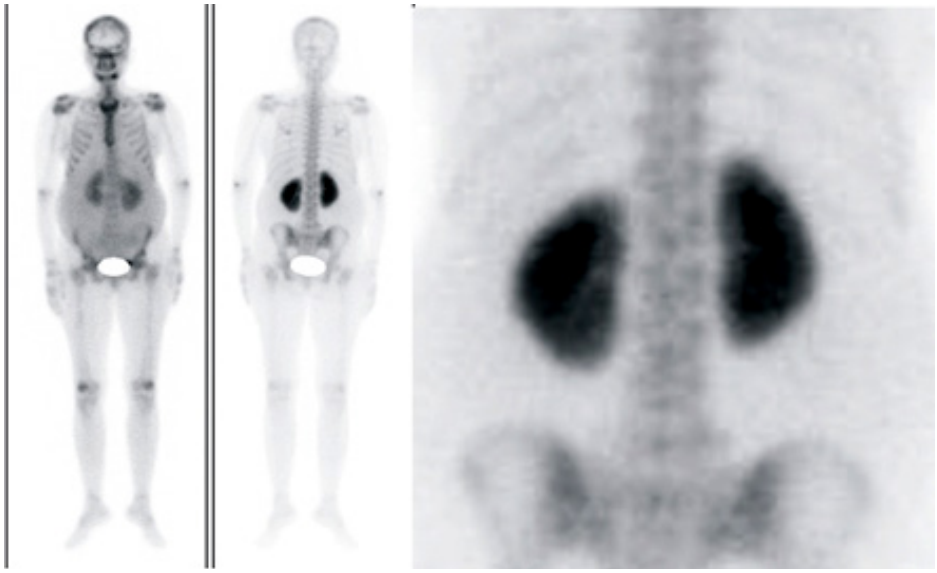

Figure 2: *^{99m}Tc-MDP bone scan showing marked bilateral renal parenchymal retention (hot kidneys) and absence of skeletal metastases.*

Discussion

Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver, which is strongly associated with cirrhosis secondary to alcohol intake and viral etiologies. The incidence of HCC is rising, and it is largely attributed to a rise in hepatitis C infection [11]. Bone scan is routinely used for skeletal metastatic survey in patients with known malignancy. Renal clearance is the main rout of excretion of ^{99m}Tc-MDP and kidneys excrete more than 50% of this injected radiopharmaceutical. At the time of scanning, kidneys are faintly visualized on bone scan images which are acquired after 3 hours of i/v injection of ^{99m}Tc-MDP. If there is renal outflow obstruction, pelvicalyceal hold up of tracer in obstructed kidney is evident on bone scan. In the above-mentioned cases, kidneys were hot bilaterally showing intense bilateral diffuse cortical renal uptake of the radioactive tracer on bone scan with absence of any hold up in pelvicalcyeal system. Renal function tests, USG and CT demonstrated normal kidneys. This finding on bone scan had been termed as "hot kidneys", and few researchers had reported it as an incidental benign and transient condition, while others documented it due to renal injury/insult. The incidence of diffuse cortical renal uptake on bone scintigraphy had been reported to be less than 1 percent [6]. Hot kidneys on bone scan had been reported in patients with hypercalcemia, hyperparathyroidism, chemotherapy, iron over load (sickle cell disease), acute renal injury due to ATN and NSAIDS, recent radiotherapy, use of antineoplastic drugs and secondary to aluminum breakthrough of ^{99}Mo-^{99m}Tc generator [7–12]. The exact mechanism leading to abnormal diffuse renal cortical tracer uptake had not been established. The pathogenesis of uptake of bone scanning agents in extra osseous areas is multi-factorial; one of the primary underlying factors is high calcium metabolism in the soft-tissue [13]. Other proposed mechanisms include renal injury of any kind that acts by adversely affecting the renal secretory and glomerular functions or by the increase of intracellular calcium in ischemic kidneys [9,14]. The overload of iron, by altering the distribution of bone seeking agents and decreasing the renal excretion, had also been proposed to cause diffuse cortical renal uptake on bone scan in thalassemia patients [15]. Hot kidney sign had been seen on bone scan in patients with cirrhosis, and renal injury due to hepatorenal syndrome had been proposed as its cause. Patients with hepatorenal syndrome are characterized by severe cirrhosis, glomerular hypofiltration and low arterial pressure. Renal failure is a common major complication in patients with advanced cirrhosis and generally indicates a poor prognosis when combined

with liver failure [9]. Erhamamci S et al found that in 50% of liver transplant candidates with end stage chronic liver disease showed increased diffuse cortical renal uptake were having high BUN values. They found that patients with severe degree of ^{99m}Tc-MDP diffuse cortical renal uptake had higher serum BUN and creatinine values compared with patients without ^{99m}Tc-MDP high diffuse cortical renal uptake. In addition, they documented that a significant difference also exists in serum creatinine values between patients with mild and severe degree of diffuse renal cortical uptake. They concluded that in patients with normal serum creatinine, increased diffuse cortical renal uptake of bone seeking agent may be correlated with a higher risk of subsequent deterioration in renal function and increased diffuse cortical renal uptake on bone scan might be an early marker of renal dysfunction or a predictor of hepatorenal syndrome [16].

Both cases under discussion did not reveal any chronic disease other than that of CLD and chemotherapy was not yet started. Both were clinically stable, they were neither on NSAID nor having hepatorenal syndrome. So, the effects of chemotherapeutics, antibiotics, NSAIDS, as well as the chronic diseases causing iron overload were excluded. These cases were normotensive and normocalcemic which made the diagnosis of metabolic and vascular pathologies unlikely. Although one of the patients had cirrhosis, however normal renal function tests and hemodynamic stable status rule out the presence of hepatorenal syndrome as the cause of hot kidneys. Normal quality control of the ^{99}Mo-^{99m}Tc generator elute ruled out the possibility of aluminum breakthrough as its cause. Exact cause of hot kidneys in these cases of HCC is not known. Some altered metabolism in liver and hemodynamic changes in body due to CLD and/or HCC might be the cause. Further research work is needed to find out its exact pathophysiology and cause of hot kidneys in such cases.

Conclusion

High diffuse renal parenchymal retention of ^{99m}Tc-MDP might be seen on bone scan in HCC cases. Its clinical significance is unknown and needs further research to find out its exact mechanism and the cause.

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List of Abbreviations

^{99m}Tc	Technetium ^{99m}
CLD	Chronic liver parenchymal disease
CT	Computed tomography
HCC	Hepatocellular carcinoma
MDP	Methyl Diphosphonate
SPECT	Single photon emission computer tomography
TACE	Transarterial chemoembolization
USG	Ultrasonography

Conflict of Interests
None

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None

Consent for publication
Informed consent was obtained from both patients to publish this case.

Ethical approval
Ethical approval is not required at our institution for publishing a case report in a medical journal.

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Authors' contribution
MSA was the main author who wrote this case report. MBI found this case and proposed its publication as case report. MI helped in writing the manuscript. MSA reviewed it. All the authors approved the final version of the manuscript.

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Summary of the case

Patient (gender, age)	1	Female, Case 1 age 50 years, case2 age 40 years
Final Diagnosis	2	Hepatocellular Carcinoma (HCC)
Symptoms	3	Generalized pains due to mass in Liver diagnosed as Hepatocellular Carcinoma
Medications (Generic)	4	N/A
Clinical Procedure	5	Tc-^{99m} MDP Bone Scan
Specialty	6	Nuclear Medicine
Objective	7	To document diffuse renal parenchymal retention of Tc-^{99m} MDP in HCC cases.
Background	8	Hepatocellular Carcinoma, Bone scan, Diffuse parenchymal retention of MDP, Hot Kidneys
Case Report	9	Increased renal parenchymal retention of Technetium-99m MDP (Hot Kidneys) in two patients of hepatocellular cancer: One with and other without osseous metastases
Conclusions	10	High diffuse renal parenchymal retention of 99mTc-MDP might be seen on bone scan in HCC cases. Its clinical significance is unknown and needs further research to find out its exact mechanism and cause.
MeSH Keywords	11	Hot Kidney, Renal parenchymal retention of MDP, Hepatocellular Ca, HCC, case report