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ORIGINAL ARTICLE

Frequency and pattern of bone metastases in renal and urinary bladder carcinomas on skeletal scintigraphy

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Abstract

Objective The study was designed to determine the frequency and patterns of bone metastases in renal and urinary bladder carcinomas on skeletal scintigraphy.

Methods This retrospective cross sectional study included 76 sequential patients with renal and urinary bladder carcinomas referred for a ^{99m}Tc-MDP whole-body bone scan to the Nuclear Medical Centre, AFIP Rawalpindi, from Jan 2011 to Jan 2013. Focal increased radiotracer uptake seen on the bone scans was identified as an osteoblastic or 'hot' lesion, whereas a photon-deficient area was labelled as an osteolytic or 'cold' lesion.

Results Out of 76 patients, renal cell carcinoma was the commonest at 64%, followed by urothelial carcinoma at 27%, transitional cell carcinoma at 5% and clear-cell carcinoma 4%. Three-fourths (75%) of the patients were male and a quarter (25%) female with a mean age of 60 years. 52.6% were negative for skeletal metastases and 47.4% positive. Commonly involved sites in decreasing frequency included the lumbar vertebrae (61%), dorsal vertebrae (25%), the ribs (25%), pelvic bones (22%), sternum (5%), proximal femoral and humeral halves (5%), scapula (2%) and skull (2%). Lytic lesions were present in 11% of the cases.

Conclusion Skeletal metastases were found in 47.4% of the cases of renal/urinary bladder carcinomas with the lumbar spine being the commonest site involved. In addition to typical 'hot' osteoblastic lesions, 'cold' osteolytic lesions were also present in a small with significant number of cases, which appear deceptive and warrant a meticulous survey of bone scan images in patients with renal and bladder cancers.

***Key words**: ^{99m}Tc-MPD, Bone scan, renal cell carcinoma, urinary bladder cancer*

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Introduction

Renal cell carcinoma (RCC) and urothelial cell carcinoma (UCC) of renal pelvis are two of the commonest types of kidney cancers. RCC is the commonest solid lesion in kidney comprising approximately 90% of all kidney malignancies. In patients with advanced RCC, bone is the second most common site of

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distant metastatic spread following lungs [1]. The peak incidence occurs between 60-70 years and there is 1.5:1.0 dominance of men over women. In developing countries, the incidence and mortality rates (age standardized rates-per 100,000) in males are 2.5 and 1.3, and in females 1.4 and 0.8 respectively [2]. Risk factors include smoking, obesity, and hypertension [3]. However, there is a controversy over obesity as some published reports indicate a better prognosis for obese patients with renal cell cancer [4]. After first starting therapy, the prevalence of skeletal metastases seems to increase, indicating the possibility of bones being a poorly controlled site of spread. Almost 30% of patients present with metastatic disease with approximately 40% patients relapsing with disseminated disease later on [1].

Cancer of the urinary bladder is predominantly a disease of older men with its incidence increasing with age (median age: 69–70 years). Smoking, living in urban areas and working in the dye, rubber, or leather industries increases the risk. In developing countries, the incidence and mortality rates (per 100,000) are 5.4 and 2.6 in males, and 1.4 and 0.7 in females respectively [2]. Transitional cell carcinoma accounts for 95% of all bladder cancers; the other cell types include squamous cell cancer, mixed transitional cell carcinoma, adenocarcinoma and undifferentiated tumours. Rare histologies include lymphoma, carcinosarcoma, sarcomas, pheochromocytoma and metastases [5]. Cancer of urinary bladder, particularly transitional cell carcinoma, spreads through the lymphatics as well as the blood stream. Favoured sites for metastases include the liver, lungs, skeleton and adrenal glands [6]. Metastases to bones at presentation, as compared to renal carcinomas, are less frequent and skeletal scintigraphy is indicated if specific symptoms or signs suggest such a possibility [7].

Metastatic bone disease causes significant morbidity through skeletal-related events (SREs), which comprise of pathological fractures, spinal cord compression and/or hypercalcaemia of malignancy. The SREs incur a significant financial toll on healthcare in addition to increased morbidity and mortality [1]. Given this background, the study thus aimed at determining the frequency and type of skeletal metastases (osteoblastic and/or osteoclastic). The study additionally aimed at documenting the specific sites in the skeleton prone to metastatic involvement by these malignancies.

Patients and Methods

The study included a total of 76 cases of renal and urinary bladder carcinomas. 75% of the patients were male and 25% female with an age age range of 2-87 years with a mean age of 60 years. Relevant clinical history was taken and clinical examination of the patient conducted prior to radiotracer injection to decide upon the type of scan required such as a standard delayed whole-body bone scan or 2/3-phase bone scanning with additional blood pool and blood flow acquisition. Complaints related to benign causes like osteoarthritis and degenerative changes were documented in addition to those attributed to iatrogenic/ traumatic aetiologies. ^{99m}Tc-MDP (Tc-99m Methylene Diphosphonate) in a dose of 740 MBq (20 mCi) was injected intravenously. The patient was encouraged to maintain good hydration and void frequently to minimize the radiation dose and increase the bone-to-background ratio in the projected images. After a period of 2-3 hours the patient was asked to void again and a whole-body bone scan was acquired on the gamma camera (Siemens E-Cam® or Scintronix®) fitted with LEAP (low-energy all-purpose) collimator at a table speed of 10 cm/min. Extra spot views at 1000-k counts per minute were obtained when required and SPECT imaging was performed if deemed necessary for accurate lesion localization especially in spine. Increased focal/local radiotracer uptake was labeled as an active bone lesion (osteoblastic), whereas a photon-deficient lesion was labeled as a cold or lytic lesion (osteoclastic). Skeletal radiotracer uptake attributed to benign, iatrogenic and traumatic aetiologies was excluded from the study.

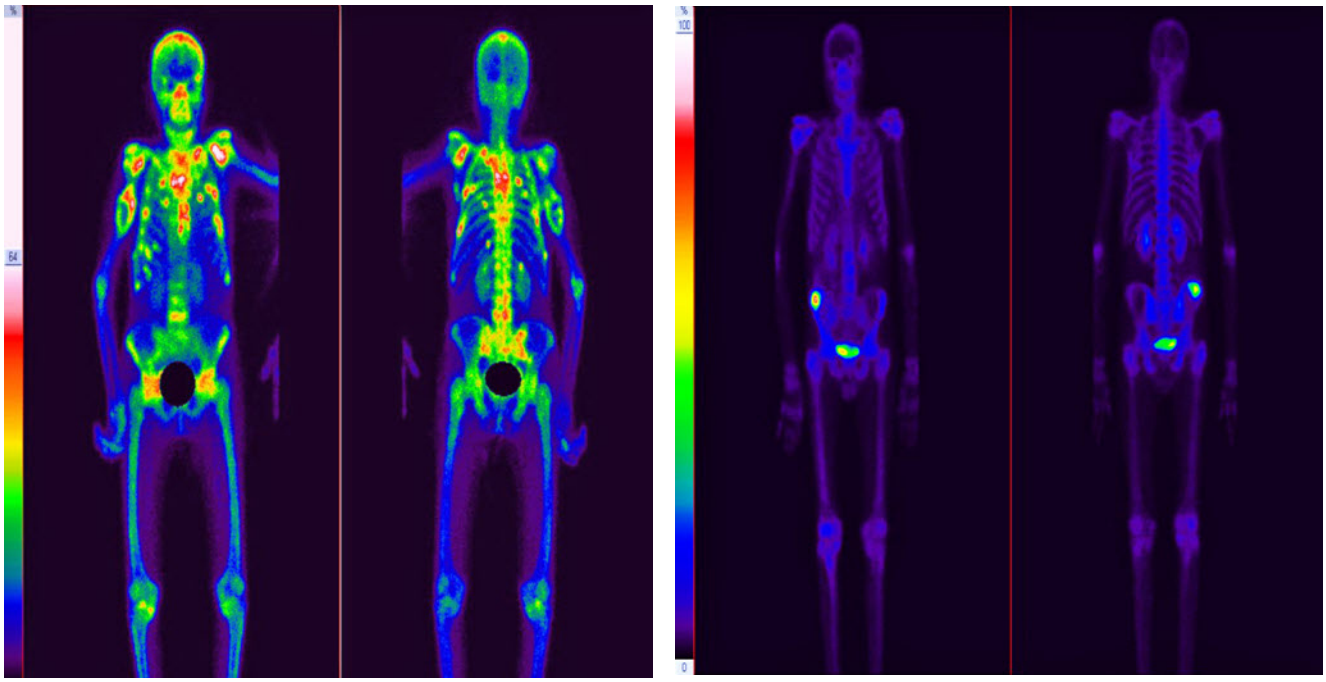

Figure 1 *Example bone scan of a patient with multifocal osteoblastic metastatic lesions (left) and that of a patient with a solitary bone metastasis (right)*

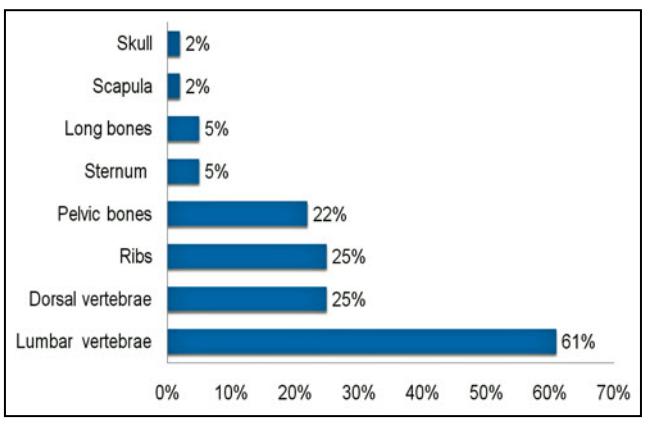

Figure 2 *Osteoblastic (sclerotic) lesions: site and frequency*

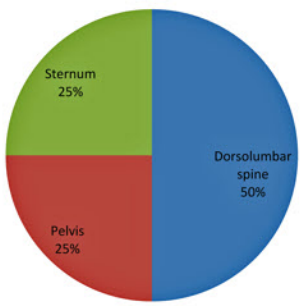

Figure 3 *Site distribution of osteoclastic (lytic) lesions*

Results

Out of 76 patients, renal cell carcinoma was the commonest at 64% followed by urothelial carcinoma at 27%, transitional cell carcinoma at 5% and clear-cell carcinoma at 4%. Out of the study population, 52.6% cases were negative for skeletal metastases and 47.4% positive. The commonly involved sites for osteoblastic (sclerotic) metastatic lesions were lumbar vertebrae in 61%, dorsal vertebrae in 25%, ribs in 25%, pelvic bones in 22%, sternum in 5%, proximal femoral and humeral halves in 5%, scapula in 2% and skull in 2% of the patients. Figure 1 shows the example bone scan of a patient with multiple and a solitary active metastases. Figure 2 shows the sites and frequency distribution of the osteoblastic lesions documented on the bone scans.

Osteclastic (lytic) metastatic lesions were present in 11% cases diagnosed positive for skeletal metastases. The cold/lytic metastatic skeletal sites were seen to involve the dorsolumbar spine in 2%, pelvis and sternum each in 1% of the cases (see Figure 3). Figure 4 showing an example of a solitary cold or osteoclastic lesion.

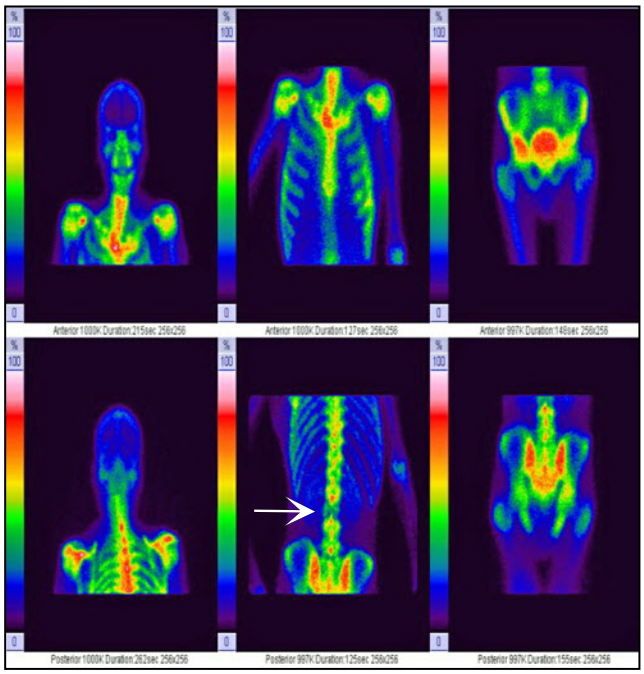

Figure 4 *Bone Solitary osteoclastic bone metastasis involving the spine (arrow)*

Discussion

Renal cell carcinoma (RCC) and urothelial cell carcinoma (UCC) of the renal pelvis, reflect the cell type from which they develop and have a different prognosis and management plan [8]. Almost 25-30% of patients with RCC have metastases at presentation [9]. Locally advanced disease may be present in ~20% of patients with RCC on presentation [10]. Post-nephrectomy recurrent or metastatic disease in earlier stages of RCC occur in 50% of patients [11] with ~85% of recurrences occurring within 3 years after initial resection, but may recur up to several decades later. The median time to diagnosis of recurrence ranges from 15 to 32 months for pT2 and pT3 tumours [12].

An important risk factor for developing distant metastases post-nephrectomy is stage of primary tumour. Relapse risk is stage dependent: a higher rate and shorter time to relapse is noted in patients with pT3 and pT4 renal tumors, compared with those at lower stages [13]. Therefore, staging is the single most important factor in ascertaining prognosis. Recurrence occurring after a prolonged disease-free interval is associated with a better prognosis [14].

Prognosis is also effected by the metastatic site involved and the overall disease volume. Patients with only pulmonary metastases, have a better survival rate than patients with other sites of metastases. Liver metastases in particular, are associated with a poor prognosis, whereas skeletal metastases appear to have an intermediate prognosis. Involvement of regional lymph nodes is associated with a higher incidence of metastatic disease and poorer response to immunotherapy [15]. Metastasic disease may occur in following sites in descending order: lung (50–60%), bone (30–40%), liver (30–40%) and adrenal gland, contralateral kidney, retroperitoneum and brain (5% each) [12].

Skeletal metastatic sites typically have large lesions preponderant in the axial skeleton which are expansile in appearance on plain radiograph. CT depicts bone destruction in presence or absence of enhancing soft-tissue mass. Skeletal scintigraphy (more commonly known as the bone scan) shows variable uptake in positive cases. Majority of skeletal metastases are symptomatic and selected use of skeletal scintigraphy, in presence or absence of elevated serum alkaline phosphatase, is advocated because of advantage of whole-body skeletal survey [12, 14]. However, routine imaging in all asymptomatic patients with RCC may result in a low yield of skeletal metastases, but nevertheless, remains vital for staging in indicated cases [16].

Local recurrence post nephrectomy appears as solid enhancing masses with central necrosis on CT and may involve underlying psoas or quadratus lumborum muscle. Incidence of local recurrence is variable and ranges from 1.8-27%. Assessing local recurrence by ^{18}F-FDG PET (Flourine-18 fluorodeoxyglucose positron emission tomography) can clearly differentiate tumour recurrence from fibrosis or necrosis thereby altering subsequent management, and is thus far more superior than all other imaging modalities in such scenarios [17].

Carcinoma of the urinary bladder usually occurs in older males and its incidence increases with age (median age: 69–70 years). Risk factors include smoking; working in the dye, rubber or leather industries; and urban living. In developing countries, the incidence and mortality rates (per 100,000) in males are 5.4 and 2.6, and in females 1.4 and 0.7 respectively [2]. Transitional cell carcinoma accounts for 95% of all bladder cancers [5].

Painless haematuria is generally the initial presentation. Although urine cytology may be helpful, cystoscopy and biopsy are required for definitive diagnosis. Urinary bladder carcinoma may be encountered as an incidental mass on routine imaging or staging and follow-up after therapy. An incidentally noted mass in bladder has a broad differential diagnosis, which includes benign aetiologies such as hematoma, calculus, benign (papilloma, hamartoma, leiomyoma) or malignant neoplasms, etc. [6].

Ultrasonography is not routinely used in staging urinary bladder carcinoma. If tumour is found incidentally, it often appears as a hypoechoic polypoid or plaque-like lesion that may project into bladder [18]. CT is the primary imaging modality for cancer of the urinary bladder, whereas MRI, especially with gadolinium enhancement, might add useful information [19]. The tumour can metastasize via lymphatic or haematogenous route. Lymphatic spread occurs to perivesical, obturator, internal and external iliac nodes [20]. Urinary bladder carcinoma, particularly transitional cell carcinoma, spreads through the blood stream as well. Favoured sites for metastases include the liver, lungs, skeleton and adrenal glands [21]. Although MRI is more sensitive in picking up micrometastases, whole-body MRI, at this point in time, remains costly and less widely available. In contrast, skeletal scintigraphy has the ability of conducting whole-body skeletal survey cost effectively and is widely available. Combination of bone scan with MRI might yield better localization however [22].

Conclusion

The patterns and the incidence of skeletal metastases in our study is in line with that reported in the literature. We found skeletal metastases in 47.4% cases of renal and urinary bladder carcinomas with lumbar spine being the commonest site for bone metastases. In addition to the typical osteoblastic (hot) metastatic lesions, a meticulous prospective review of the scan to search for the osteoclastic (cold) lesions is important as these lytic lesions represent a more aggressive skeletal response and may help preclude devastating SRE.

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