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Case Report

Infliximab-induced hot kidneys on bone scintigraphy

ABSTRACT

^{99m}Technetium-methylene diphosphonate bone scintigraphy is widely used in various clinical settings to detect bone abnormalities. Many reasons may cause abnormal tracer uptake in soft tissues on bone scintigraphy. Here, we present a 70-year-old man diagnosed with rheumatoid arthritis receiving chimeric anti-tumor necrosis factor alpha (TNF-α) therapy (infliximab). In order to evaluate the bone involvement of rheumatic disease, the patient underwent a whole-body bone scan that revealed left side dominant diffuse uptake in both kidneys defined as the "hot kidneys." Since the patient had no other identifiable reason, anti-TNF-α therapy might be responsible for the "hot kidneys" on bone scan. Thus, therapy regiment of the patient changed from the chimeric anti-TNF-α to a human monoclonal TNF inhibitor (golimumab). After 6 months of the change of the therapy, the bone scintigraphy was repeated and revealed that the previous "hot kidneys" finding had disappeared.

Keywords: ^{99m}Technetium-methylene diphosphonate, anti-tumor necrosis factor alpha therapy, bone scintigraphy, hot kidneys

INTRODUCTION

Tumor necrosis factor-alpha (TNF-α) antagonists have been widely used for the treatment of rheumatoid arthritis (RA) patients who have not responded to other antirheumatic drugs.[1] Infliximab (IFX) which is a chimeric monoclonal TNF-α inhibitor, can induce the formation of neutralizing antibodies and may lead to renal dysfunction.[2] Human anti-TNF monoclonal antibodies, such as subcutaneous golimumab (GLM-SC), are less immunogenic than IFX.[3] Here, we present a patient with RA with renal deterioration under IFX therapy, and after a switch from IFX to GLM-SC, improvement of renal functions was observed both on bone scintigraphy and biochemically.

CASE REPORT

A 70-year-old man with RA, who had been treated with for 5 years with IFX (300 mg/8 weeks), was in remission. The patient presented with a complaint of knee pain for a few months. His laboratory examination at admission showed high levels of serum urea (63 mg/dL [normal values (N): 17–44]), creatinine (1.47 mg/dL [N: 0.84–1.25]), C-reactive protein (138 mg/L [N: 0–8]), Antistreptolysin O (ASO) titer by rate nephelometry (41.5 IU/mL [N: 0–200]), and erythrocyte sedimentation rate (98 mm/h [N: 0–20]). Glomerular filtration rate (GFR) was calculated using both the modification of diet in renal disease and Cockroft–Gault formula which showed slightly decreased GFR values as 50.34 mL/min/1.73 m^2 and 42.99 mL/min, respectively. The results of urinalysis were normal (pH, specific gravity, ketones, glucose, protein, blood, nitrite, bilirubin, and leukocytes). Notwithstanding, the patient had no symptoms of urinary tract diseases.

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Moreover, ultrasonography (USG) of the urinary system was obtained as a part of investigative work up and revealed an anechoic simple cortical cyst (30 mm × 24 mm in diameters) in relatively small right kidney and normal left kidney, normal parenchyma echogenicity and thickness, and no pelvicalyceal dilatation in both kidneys. In order to evaluate the bone involvement of rheumatic disease, the clinician referred the patient to the nuclear medicine department. We performed 99mTechnetium-methylene diphosphonate (99mTc-MDP) whole-body bone scintigraphy which exhibited symmetrically increased tracer activities associated with arthritic changes in the joint regions and a diffusely increased tracer accumulation in both kidneys. However, radioactivity uptake was relatively lower in the right kidney which may be attributed to the smaller size of the kidney [Figure 1a]. Moreover, upper abdominal computerized tomography (CT) showed a simple cyst in the upper pole of the right kidney which may explain the relatively lower tracer uptake of the kidney, and a normal left kidney [Figure 2]. Since the patient had no other identifiable reason, anti-TNF-α therapy was accused for the "hot kidneys" appearance on the bone scintigraphy. Accordingly, IFX was stopped, and less immunogenic GLM-SC was started with 50 mg at 4 weeks' intervals since the patient had active RA. After 6 months of GLM-SC therapy, the bone scintigraphy was performed again and showed that the previous "hot kidney" finding had disappeared [Figure 1b]. Therewithal, serum urea and creatinine levels decreased to normal values (30 mg/dL [N: 17–43] and 0.6 mg/dL [N: 0.67–1.17], respectively). Thus, the scintigraphic finding of "hot kidneys" was considered to have been related to the use of IFX therapy.

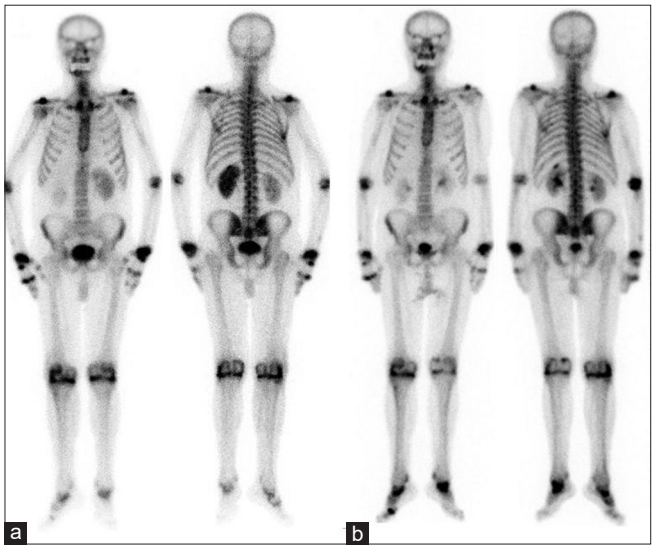

Figure 1: The patient, who was using ınfliximab therapy for 5 years, underwent ^{99m}Technetium-methylene diphosphonate bone scintigraphy which revealed symmetrically increased tracer activity associated with arthritic changes in the joint regions and diffusely increased tracer accumulation in both kidneys which was relatively prominent in the left kidney (a). Six months after switching ınfliximab to subcutaneous golimumab reperformed bone scintigraphy showed increased tracer activity associated with arthritic changes in the joint regions, without hot kidneys appearance (b)

DISCUSSION

TNF-α is a pleiotropic cytokine that plays a central role in the inflammation process of RA. It has been previously reported that TNF-α induces renal damage in patients with RA by decreasing renal perfusion. In addition, migration of immune cells into the kidney leads to cytokine releasing that may result as inflammation and cell death. Thus, anti-TNF drugs are assumed to have protective effects on renal damage. The development of TNF-α inhibitors as disease-modifying antirheumatic drugs has revolutionized RA management. TNF-α is a proinflammatory cytokine and may induce renal damage by decreasing renal perfusion.[4] Anti-TNF-α drugs are prescribed frequently in RA and other inflammatory connective tissue diseases. It is assumed that TNF-α inhibitors likely to be protective against renal damage in patients with RA.[1] However, anti-TNF-α agents may lead to side effects that can be sometimes life-threatening such as infections, malignancies (e.g., lymphoma), anemia, pancytopenia, demyelinating disorders, congestive heart failure, the occurrence of autoantibodies and autoimmunity, and hypersensitivity reactions.[5] IFX is a chimeric monoclonal anti-TNF-α IgG1 antibody which specifically binds to TNF-α. The efficacy of IFX treatment in RA patients was demonstrated in many clinical trials. Nevertheless, in RA patients, chimeric anti-TNF agents may induce autoantibodies and may cause lupus-like immune complex glomerulonephritis or antineutrophil cytoplasmic antibody-related necrotizing and crescentic glomerulonephritis.[2]

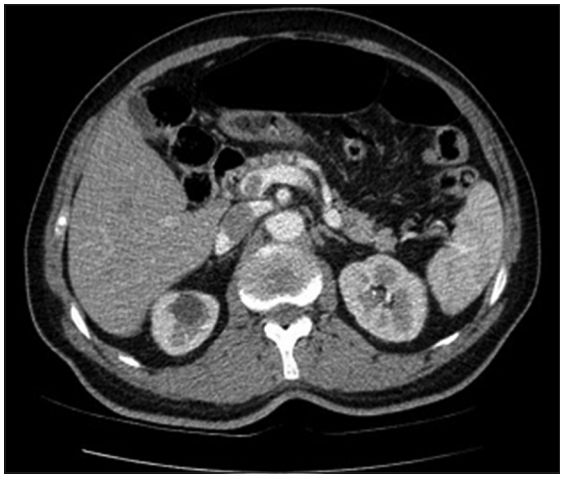

Figure 2: Abdomen computerized tomography shows renal cyst in relatively small right kidney

Diffusely increased radioactive uptake in the kidneys greater than of lumbar vertebrae in the posterior projection of bone scan termed as "hot kidneys."[6] Nephrotoxic drugs (antibiotics, chemotherapeutics, and nonsteroidal anti-inflammatory drugs), iron overload, inflammation, urinary obstruction, hypercalcemia, vascular pathologies, and acute tubular necrosis may lead to diffuse tracer activity on bone scanning.[7-9] In the literature, the reported incidence of high renal uptake of ^{99m}Tc-MDP on bone scintigraphy ranges from 2% to 15%.[8,10] "Hot kidneys" is accepted as an incidental benign and transient condition.[10]

In our patient, we have not observed potential factors that might be harmful to kidneys such as urinary complaints, drug use history, or coexisting problems which may explain the cause of diffusely increased tracer accumulation in both kidneys. Anatomical imaging studies (CT and USG) of the patient had not displayed serious renal pathology.

The switching of therapy from IFX to GLM-SC alleviated the hot kidney appearance and renal biomarkers after 6 months, in this case. Thus, diffusely increased tracer accumulation in both kidneys of our patient could be explained by the long-term use of a chimeric TNF-α inhibitor.

CONCLUSION

"Hot kidneys" related with a treatment of TNF-α inhibitors in a patient with RA is a unique aspect of this case and has not been reported previously. We recommend that patients receiving long-term anti-TNF-α treatment should be closely monitored in terms of renal functions. Bone scintigraphy might be a valuable imaging modality in the follow-up of patients with RA who use a chimeric anti-TNF- α therapy. The chimeric anti-TNF-α drugs might be considered to be changed to a less immunologic TNF inhibitor, a human monoclonal anti-TNF such as GLM-SC, in patients with a hot kidneys appearance on bone scintigraphy.

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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