Accumulation of Tc99m-DMSA-3 in the spleen in a case of multiple myeloma with associated amyloidosis

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ABSTRACT

We describe a case of a 58-year-old male with longstanding hypertension and Type 2 diabetes mellitus who developed sudden onset renal impairment. The first clue to the possible presence of amyloidosis in this case was provided by the radionuclide renal cortical scan performed with trivalent dimercapto succinic acid (Tc99m-DMSA-3), which revealed intense tracer uptake in the spleen suggesting amyloid deposit. Further workup to ascertain the cause of amyloidosis led to the diagnosis of multiple myeloma. We conclude that in cases of extra-renal or splenic accumulation of Tc99m-DMSA-3, a diagnosis of amyloidosis should be considered, in an appropriate clinical setting.

KEY WORDS: Amyloidosis, DMSA-3, multiple myeloma, spleen

A kind of starch or cellulose, was first described in the 19th century by Virchow. Amyloidosis constitutes a heterogeneous group of disorders associated with abnormal extracellular deposits of protein that have a characteristic b-sheet fibrillar ultrastructure. Tissue deposition of amyloid protein can lead to several conditions that have protean clinical presentation. Demonstration of amyloid protein in the tissue is the mainstay of diagnosis of amyloidosis, which often requires invasive procedures.[1] Non-invasive diagnostic procedures like radionuclide imaging for amyloid deposits have played a relatively minor role in the diagnosis and management of amyloidosis. We describe a case of a 58-year-old male with longstanding hypertension and Type 2 diabetes mellitus who developed sudden onset renal impairment. Renal cortical scan performed with trivalent dimercapto succinic acid (Tc99m-DMSA-3) provided the first clue to the possible presence of amyloidosis which was revealed by intense tracer uptake in the spleen. We believe this is the first reported case of accumulation of Tc99m-DMSA-3 in amyloid deposit in the English literature.

Case History

A 58-year-old male presented with unexplained weakness, lethargy and swelling of feet since three weeks. He was a known case of essential hypertension and Type 2 diabetes mellitus for the last 15 years and was under regular treatment for the same. Both blood pressure and diabetes mellitus were well controlled by oral medications. On biochemical examination, serum urea was 190 mg/dl and serum creatinine was 3.2 mg%, fasting blood sugar was 92 mg% and serum calcium was 9.8 mg%. Urine examination revealed proteinuria. Clinically, a diagnosis of diabetic nephropathy was considered. Glomerular filtration rate was 47 ml/min (Reference Range 106 ± 27 ml/min) as measured by multiple plasma sample method. Ultrasound of abdomen showed bilateral normal sized kidneys with irregular margin. Renal cortical scan was done with DMSA-3 for evaluation of possible renal scars which revealed poorly visualized, but apparently normal sized kidneys without any obvious scarring. However, surprisingly, an intense DMSA-3 uptake in the spleen was noted [Figure 1]. Splenic uptake of DMSA-3 was considered very unusual. Considering the

![Figure 1: Posterior view of Tc99m-DMSA-3 renal cortical scan showing intense radiotracer uptake in the spleen (shown by arrow). Both the kidneys shows poor radiotracer uptake.](image)
fact that DMSA-3 has considerable chemical and structural similarity with DMSA-5, which sometimes shows accumulation in the areas of amyloid deposit, the possibility of splenic amyloid deposition was considered. Further workup for exclusion of multiple myeloma, which frequently causes systemic amyloidosis in elderly population revealed ‘M’ band in serum and urine electrophoresis and Bence Jones protein in urine by heat coagulation test. Bone marrow biopsy revealed excess plasma cells and renal biopsy revealed classical histological features of amyloid deposition [Figure 2]. Thus a diagnosis of multiple myeloma leading to amyloidosis and renal impairment was finally reached.

**Discussion**

Amyloidosis is a group of clinico-pathological conditions in which there is abnormal extracellular deposit of misfolded protein, which leads to varied clinical presentations depending on the organ involved. The commonest forms of systemic amyloidosis are light-chain (AL) amyloidosis, reactive amyloidosis (AA) secondary to chronic inflammatory diseases and hereditary amyloidosis. Multiple myeloma constitutes an important cause of AL amyloidosis. Kidneys are frequently involved in most forms of systemic amyloidosis. Browning et al. reported renal involvement in 42% patients of light chain amyloidosis. The clinical manifestations of renal amyloidosis are quite varied and usually include non-selective proteinuria, nephrotic syndrome and renal insufficiency. Hypertension is rare, except in longstanding amyloidosis.

Demonstration of amyloid protein in the tissue is the mainstay of diagnosis of amyloidosis. The classical amyloid dyes like congo red and thioflavin T and S, have been used extensively to detect amyloid inclusions in situ. The amyloid deposits can be identified on the basis of their apple-green birefringence under a polarized light microscope after staining with Congo red and the presence of rigid, non-branching fibrils of 7.5 to 10 nm in diameter, on electron microscopy.

Radionuclide investigations typically have played a relatively minor role in the diagnosis of amyloid deposits. Radionuclide imaging of amyloid deposits has been attempted with various tracers such as Tc99m-pyrophosphate or diphosphonates, Ga citrate, Tc99m-DMSA, Tc99m-sulfur colloid or Tc99m-phosphate. All of these appear to have relatively low sensitivity and specificity for amyloidosis. Pentaventmal DMSA exhibits its high background activity in the chest, complicating evaluation of pleuropulmonary and cardiac involvement. Trivalent Dimercapto succinic acid (Tc99m-DMSA-3) is used for imaging the renal cortex. It has considerable chemical and structural similarity with DMSA-5, though there are some differences in biodistribution, as the trivalent form shows more intense renal uptake while the pentavalent form shows avidity for a wide variety of neoplastic tissues. Another method is scintigraphic imaging with radiolabeled serum amyloid P component (SAP) that has lately been developed as a specific non-invasive alternative. The presence of systemic amyloidosis is characterized by accelerated initial clearance of I-SAP from the plasma and increased interstitial exchange rate and extravascular retention. These findings reflect reversible binding of radiolabeled SAP to amyloid deposits and provide clinically useful information for diagnosis, monitoring of therapy and prognosis in patients with systemic amyloidosis. Tc99m-Aprotinin scintigraphy also appears to be a fairly sensitive and specific diagnostic modality to detect amyloid deposits in different organs of the body patients with suspected amyloidosis. Tc99m-Aprotinin scintigraphy is characterized by a fairly high signal-to-noise ratio of amyloid lesions in the head and neck region, chest, and extremities. The well-known, physiological urinary excretion and hepatic uptakes complicate the assessment of the kidneys, urinary tract and liver.

In our case Tc99m-DMSA-3 scan revealed intense Tc99m-DMSA-3 accumulation in the spleen, which raised the suspicion of the presence of systemic amyloidosis in the patient. The relatively less uptake in the kidneys can be explained by the presence of advanced azotemia in our patient. Thus this case becomes unique in terms that increased uptake of DMSA-3 in the spleen contributed significantly in reaching the final diagnosis of multiple myeloma associated systemic amyloidosis.

We conclude that in cases of extra-renal or splenic accumulation of DMSA-3, a diagnosis of amyloidosis should be considered, in an appropriate clinical setting.

**References**


Figure 2: Renal biopsy specimen, with Hematoxylin-Eosin stain showing glomerular, mesangial and capillary wall deposit of amyloid. There is also deposit in the interlobular artery (Arrow) (x10).


