**Monoclonal Gammopathy of Undetermined Significance in a Case of Type 2 Diabetes Mellitus**

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**Abstract**

**Background**: A case of Non-insulin dependent diabetes mellitus (NIDDM) in the clinical setting presented with proteinuria, hypoalbuminemia, paraproteinemia, deranged renal functions and possibility of Multiple Myeloma in bone scan. The diagnostic challenge was resolved by bone marrow aspiration and serum protein electrophoresis. This case demonstrates the differential diagnoses of paraproteinemia in clinical scenario of NIDDM which include diabetic nephropathy, multiple myeloma and Monoclonal gammopathy of undetermined significance (MGUS).

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*Received: 09 June 2021*

*Revised: 26 July 2021*

*Accepted: 11 August 2021*

*Published: 22 October 2021*

**Keywords**:- Diabetes mellitus, Monoclonal gammopathy, Non-insulin dependent diabetes mellitus.

**INTRODUCTION**

NIDDM is a complex disease that involves the interplay of genetic, environmental factors and a pro-inflammatory states. Hyperglycemic state in diabetes has been implicated in myelomagenesis and has been linked with plasma cell disorders (MGUS, multiple myeloma).[[1](#One)] MGUS is an asymptomatic, premalignant clonal plasma cell (PC) disorder characterised by the presence of monoclonal immunoglobulin (Ig) M protein in blood &/or urine. It is typically detected as an incidental finding when electrophoresis & immunofixation of serum &/or urine or serum flow cytometry assay are performed during workup of unexplained weakness, anemia, hypercalcemia, renal insufficiency, proteinuria & nephrotic syndrome. It has high propensity to progress to more serious PC disorders such as multiple myeloma, Waldenstrom Macroglobulinemia or immunoglobulin amyloid light chain (AL) amyloidosis. We wish to evaluate the association between NIDDM and MGUS through this study.

**CASE REPORT**

A case of a 56-year-old male who was a known case of hypertension and NIDDM. He presented with low back-ache and on routine follow up was found to have raised levels of blood urea, serum creatinine, serum uric acid and serum calcium. Abdominal ultrasonography revealed bilateral chronic renal parenchymal disease. Hence the treatment was started on the lines of chronic kidney disease. Bone scan showed the possibility of renal osteodystrophy or multiple myeloma due to deranged renal functions. No lytic lesions were found but microfractures were noted. Multiple investigations were performed to rule out multiple myeloma. Complete hemogram revealed no anaemia. Raised values of serum beta 2 microglobulin, kappa and lambda free light chains. Serum protein electrophoresis showed hypoalbuminemia and monoclonal gammopathy (M spike) in globulin region. Immunofixation electrophoresis was done and identified M spike as IgG and Lambda. Since M spike was low (<1%), bone marrow aspiration was done which showed 6% plasma cells. Multiple myeloma was ruled out keeping in view the International Myeloma Working Group (IMWG) diagnostic criteria and the patient was diagnosed with MGUS. A diagnosis of MGUS was made in case of NIDDM with Chronic Kidney Disease with deranged renal functions and microfractures on bone scan.



**Figure 1:** Serum protein electrophoresis of the patient showing ‘M’ spike in gammaglobulin region.

**DISCUSSION**

Diabetes is a chronic disease associated with diffuse complications and increased risk of premature death. It is the leading cause of chronic kidney disease and is associated with increased cardiovascular morbidity and mortality. The earliest change caused by diabetic nephropathy is hyperfiltration with proteinuria. During the synthesis of immunoglobulins by plasma cells, light chains(LCs) are produced more than heavy chains.[[2](#Two)] These polyclonal LCs are removed by the kidney.[[3](#Three)] Previous studies have indicated that kappa and lambda chains excretion is higher in diabetics with normoalbuminuria than controls.[[4](#Four)] Groop et al similarly found increased kappa LCs excretion in normoalbuminuric diabetic patients and suggested that increased excretion of kappa chains may be an early sign of Diabetic Nephropathy.[[5](#Five)]

In our patient, bone scan suggested the possibility of multiple myeloma. Age, male gender, NIDDM and obesity have been considered to be important mediators of the complex process of myelomagenesis.[[6](#Six)] NIDDM is thought to influence myelomagenesis through hyperglycemia and insulin dependent and –independent mechanisms.[[1](#One)] Considering this correlation, we hypothesised that the excretion of light chains and bone scan findings might be related to multiple myeloma. The diagnosis of multiple myeloma was ruled out as the International Myeloma Working Group criteria was not fulfilled. Instead all the criteria of MGUS were fulfilled i.e. serum monoclonal protein (Non IgM type <3gm/dl, clonal bone marrow plasma cells <10% and no myeloma related end organ damage). MGUS is a disorder characterised by elevated abnormal serum protein levels are observed because of increased monoclonal immunoglobulins.[[7](#Seven)] It probably results from chronic antigenic stimulation, leading to abnormal B cell clonal expansion, accumulation of this proliferating B cell or plasma cell clone within bone marrow, and resulting in increased monoclonal immunoglobulin production.[[8](#Eight)] This is a disorder whose frequency increases with age.[[9](#Nine)] MGUS is often discovered incidentally through routine blood tests as it is asymptomatic. Studies have found no association between diabetes duration, glucose levels and MGUS. But the patient should be monitored closely, as reports reveal that patients can develop multiple myeloma, macroglobulinemia or lymphoma.[[10](#Ten)] Our patient has been kept under follow-up.

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Source of Support: Nil, Conﬂict of Interest: None declared