MONOCLONAL GAMMOPATHY IN HIV AND HEPATITIS B CO- INFECTION: A CASE REPORT

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ABSTRACT:

Plasma cell disorders are reported in patients with HIV infection. These disorders range from benign polyclonal hypergammaglobulinemia to indeterminate monoclonal gammopathy of unknown significance (MGUS) to malignant dyscrasias, including multiple myelomas and plasma cell leukemia. Monoclonal gammopathy is also reported with increasing frequency in HBV AND HCV infection. In this case report a 51 year old male diabetic and hypertensive, presented with altered behavior and drowsiness. Laboratory investigations showed thrombocytopenia, elevated total proteins and globulin. HBsAg and HIV were positive. Serum electrophoresis revealed diffuse increase in the gamma region and albumin was reduced. Patient was in hepatic encephalopathy, sepsis and coagulopathy, therefore an invasive procedure could not be done. The patient was managed conservatively in ICU. Patient succumbed to acute decompensated liver failure and sepsis.Long term follow up and treatment protocols should be developed to determine the outcome of patients with this condition and to determine if lymphoma develops as an ultimate event.

Key Words : *HIV, Hepatitis B, Monocolonal Gammopathy of unknown significance, Paraproteinemias.*

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INTRODUCTION:

HIV positive patients present with plasma cell disorders at a younger age than the average age of presentation in general population and the increased presence of other viral infections (hepatitis B or C or Kaposi sarcoma, herpes virus). They may have transient paraproteinemias or have persistent paraproteins, which may or may not be associated with true plasma cell malignancies. In most patients the paraprotein contains high – titer anti HIV activity, which suggests that an antigen – driven process in response to HIV infection may contribute to early development of plasma cell disorders in these patients.

CASE HISTORY

A 51year old man, a known diabetic and hypertensive on treatment, came to the ER with a history of altered behavior and drowsiness for 3 days, constipation for 2 days and dry cough for 10 days. On examination, he was pale, icteric and afebrile. He had a pulse rate of 120/min, BP of 120/80mmhg and RR of 18/min. Abdominal examination did not reveal any signs of abdominal distension, organomegaly, or any localized tenderness. Central nervous system examination revealed flaps, patient was disoriented to time, place and person. Examination of other systems showed no abnormalities.

Laboratory investigations revealed a hemoglobin of 8.9gm/dl, thrombocytopenia, elevated liver enzymes and elevated total proteins with albumin:globulin reversal. Renal function test was normal. Serum ammonia was elevated, peripheral smear showed normocytic normochromic to macrocytic picture with increased rouleax formation. Investigations also revealed coagulopathy. HBsAg was positive and HCV was negative. HIV type 1 was positive by ELISA which was confirmed by Western blot. CD4 count was 113cells/microL (Table 1). Serum electrophoresis showed low albumin with reduction in the Alpha region along with diffuse increase in the gamma region. Beta region was merged with the gamma region (Figure 1; Table2). CT abdomen showed caudate lobe hypertrophy (Figure 2; Table3). The patient was treated with IV antibiotics and anti-hepatic encephalopathy measures.In view of coagulopathy, 4 fresh frozen plasma were transfused. Patient succumbed to acute decompensate liver failure and sepsis.

Table 1: Laboratory Investigations

Parameters	Values
Hb	8.9gm/dl
Leucocyte count	5940cells/cu mm
Platelets	1.25 lakhs/cu mm
ESR	03 mm/hr
PT	28.8 seconds
PTT	50.6 seconds
INR	2.28
Liver Function Test - Total bilirubin	3.43 mg/dl
Direct bilirubin	2.94 mg/dl
SGOT/SGPT	134/101 U/L
Alk. Phosphatase	79 U/L
Total proteins	8.8 gm/dl
Albumin/globulin	1.2/7.6 gm/dl
Serum Ammonia	66 micromol/dl
HBsAg	Positive
HIV 1 (Western Blot & ELISA)	Positive
HCV	Negative
CD4 count	113cells/micro L

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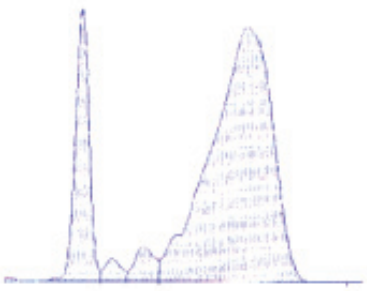

Protein electrophoresis

Total protein : 9.6 g/dl A/G : 0.23

Name	%	g/dl	Normal Ranges %	g/l
ALBUMIN	18.5	1.8	60-71	39-46
ALPHA 1	1.9	0.2	1.4-2.9	0.9-1.9
ALPHA 2	3.4	0.3	7-11	5-7
BETA/GAMMA	76.2	7.3	8-13	5-8
			9-16	6-10

Fig. 1

Table 2: Serum electrophoresis report

Albumin is decreased. There is a decrease in the Alpha region. There is a diffuse increase in the Gamma region Beta region is merged with the Gamma region.

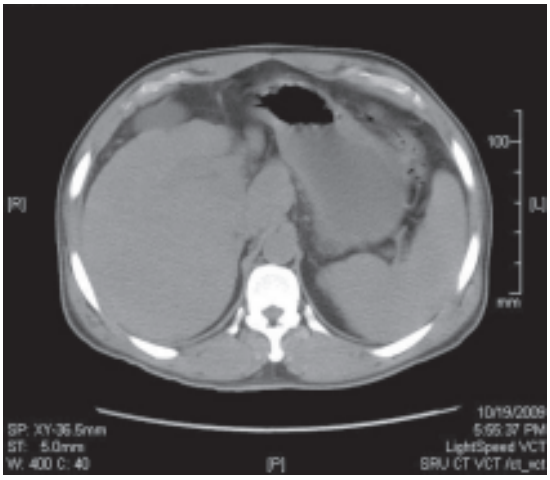

Fig. 2

Table 3: CT Abdomen report

Caudate lobe hypertrophy. Other organs are normal.

DISCUSSION:

The plasma cell disorders are monoclonal neoplasms related to each other by virtue of their development from common progenitors in the B lymphocyte lineage. Multiple myeloma, Waldenström's macroglobulinemia, primary amyloidosis and the heavy chain diseases comprise this group and may be designated by a variety of synonyms such as monoclonal gammopathies, paraproteinemias, plasma cell dyscrasias, and dysproteinemias.

Electrophoretic analysis of components of the serum proteins permits determination of the amount of immunoglobulin in the serum. The immunoglobulins move heterogeneously in an electric field and form a broad peak in the gamma region. The gamma globulin region of the electrophoretic pattern is usually increased in the sera of patients with plasma cell tumors. There is a sharp spike in this region called an M component (M for monoclonal). Less commonly, the M component may appear in the $Beta_2$ or $Alpha_2$ globulin region. The antibody must be present at a concentration of at least 5 g/L (0.5 g/dL) to be detectable by this method. M components may be detected in other lymphoid neoplasms such as chronic lymphocytic leukemia and lymphomas of B or T cell origin; nonlymphoid neoplasms such as chronic myeloid leukemia, breast cancer, and colon cancer; a variety of nonneoplastic conditions such as cirrhosis, sarcoidosis, parasitic diseases, Gaucher disease, and pyoderma gangrenosum; and a number of autoimmune conditions, including rheumatoid arthritis, myasthenia gravis, and cold agglutinin disease.

HIV infected patients can present with a range of plasma cell disorders , including reactive plasmacytosis, paraproteinemia, amyloidosis, light chain deposition disease, plasmacytosis, multiple myelomas, and plasma cell leukemia (1,2). The abnormalities in serum proteins are associated with a younger age, a higher HIV viral load, and a more robust immune system (i.e., a higher CD4 cell count), and hepatitis B and/ or C virus co-infection [1,2,3].

B-cell activation during HIV type1 infection is a specific response to HIV-1 determinants [4,5,6]. This activation which can be either monoclonal or oligoclonal, can result in hypergammaglobulinemia, a common finding in AIDS [7]. In HIV positive cases, it is noted that paraprotein contains high – titer anti HIV activity. The presence of high titer anti- HIV activity in the paraproteins of AIDS patients suggest that an antigen – driven process in response to HIV infection may contribute to early development of plasma cell disorders in these patients. Recent work in plasma cell tumorigenesis has indicated that transformation at a single point in the B lymphocyte lineage can give rise to either lymphoma or myeloma, dependent upon environmental factors such as T cell function, which may be required for directing transformed lymphocytes from lymphoma and towards plasma cell differentiation. This explains why B lineage oncogenesis in AIDS patients favors the development lymphoma over that of myeloma [8].

A subset of these patients go on to develop myeloma, plasmacytoma or lymphoma[1,2]. Myeloma patients with concomitant HIV infection may have an increased risk for intractable hypercalcemia, hyperviscosity, cytopenia, and renal failure [1]. HAART appears to have a favourable impact on the serum monoclonal protein level [2]. Long term follow up with complete blood count, serum and urine protein immunoelectrophoresis, bone marrow studies, skeletal survey and HIV viral load is needed to better define the natural history of MGUS and the link to other possible contributing

factors (eg Epstein - Barr virus (EBV), Kaposi sarcoma, Herpes virus and Hepatitis B and C viruses), which contribute to B cell expansion and, ultimately, to monoclonal paraproteinemia.

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