



## Primary Plasma Cell Leukaemia in a Young HIV Infected Male, Associated with Epstein-barr Virus

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### Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

### Article Information

#### Editor(s):

(1) Dr. Alberto Olaya Vargas, National Institute of Pediatric, Universidad Nacional Autonoma de México, México.

#### Reviewers:

(1) S. Danish Kadir, University of Rajshahi, Bangladesh.

(2) Zhen Sun, Memorial Sloan Kettering Cancer Center, USA.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/54395>

Case Report

Received 10 December 2019

Accepted 18 February 2020

Published 07 March 2020

### ABSTRACT

**Background:** Primary Plasma Cell Leukaemia (PPCL) in young patients has been evaluated in very few studies in the English literature. The aim of this study is to describe a case of PPCL in a young HIV infected male associated with EBV. This is first such case in Indian literature. This is an interesting study that reported a rare case where primary plasma cell leukaemia is observed in a young HIV infected male, which will be valuable case for future studies. Thorough clinical examinations were done and reported in detail.

**Methods:** A 35 years old male presented with abdominal pain, backache and asthenia. A thorough workup was done including clinical examination, CBP, KFT, LFT, serology (HIV, HBsAg), Serum electrophoresis, radiology and bone marrow examination. A systematic literature review was conducted by searching the Pub Med and National Centre for Biotechnology Information database.

**Results:** Patient had hepatosplenomegaly and icterus. Peripheral smear revealed atypical plasma cells (53%). Serum protein electrophoresis showed a monoclonal IgG-K paraprotein at a concentration of 4.56 (45 g/l) (Ref- 0.10-0.40). Patient had hypoalbuminemia and raised liver enzymes. The serology test for HIV was reactive for HIV-I and II. Bone marrow examination showed

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hypercellularity with near replacement of the normal marrow elements by sheets of mature plasma cells and a few immature plasma cells. Plasma cells were EBER positive. Based on the overall findings, a diagnosis of PPCL was made and subsequently, the patient was referred for chemotherapy.

**Conclusion:** To our knowledge PPCL in HIV infected young male associated with EBV has not been previously reported in the Indian literature. Given the rare incidence of this entity in the general population, it is very unlikely that they occurred by chance. Further research is needed to determine what would be the optimal management options of such patients.

**Keywords:** Primary plasma cell leukaemia; HIV; EBER.

## ABBREVIATIONS

PPCL	: Primary Plasma Cell Leukaemia
EBV	: Epstein Barr Virus
HIV	: Human Immunodeficiency Virus
CBP	: Complete Blood Picture
LFT	: Liver Function Test
KFT	: Kidney Function Test
HBSAG	: Hepatitis B Surface Antigen
EBER	: Epstein Barr Encoding Region
PCS	: Plasma Cells
MM	: Multiple Myeloma
PCL	: Plasma Cell Leukaemia
SR.	: Serum
G/L	: Gram/ Litre
MG/DL	: Miligram/ Decilitre
LDH	: Lactate dehydrogenase
IU/L	: International Units/ Litre
SGOT	: Serum Glutamic Oxaloacetic Transaminase
AIDS	: Acquired Immune Deficiency Syndrome
KS	: Kaposi Sarcoma
NHL	: Non-Hodgkin Lymphoma
HHV8	: Human Herpes Virus 8
HPV	: Human Papilloma Virus
IL-6	: Interleukin-6
KSHV	: Kaposi Sarcoma Herpes Virus

## 1. INTRODUCTION

Monoclonal gammopathies comprise a wide range of entities characterized by the proliferation of a clonal population of terminally differentiated B cells and plasma cells (PCs) [1]. When the number of circulating PCs is significant, the term Plasma cell leukaemia (PCL) is used.

Plasma Cell Leukaemia (PCL) is a rare variant of Multiple myeloma (MM) accounting for less than 5% of all malignant plasma cell disorders [2,3]. These are characterized by presence of more than 20% plasma cells in the peripheral blood at the onset of illness, with the absolute plasma cell count above  $2.0 \times 10^9/L$  [4]. PCL can be of two

types. The primary form occurs in individuals without a preceding MM, with de novo presentation in leukemic phase and usually with a rapid clinical progression and a short survival; whereas, the secondary form evolves as a terminal event in 1-2% of MM [2].

Primary PCL (PPCL) accounts for about 60% and secondary PCL (SPCL) for 40% of cases [5]. Plasma cell Leukaemia (PCL) and Neoplasia of plasma cells (NPC) affect persons of advanced age and has a torpid course. PPCL is a distinct clinicopathological entity with several biologic features different from MM in its clinical features, aggressive course with a poor response to standard MM chemotherapy and overall prognosis. There are only few cases of primary plasma cell leukaemia diagnosed at young age, available in literature [6,7,8]. Neoplasia of plasma cells in young HIV infected patients have been discussed, since 1983 [9].

Here, we report a case of Primary Plasma cell leukaemia in a young patient associated with HIV infection which is extremely rare. To the best of our knowledge, this is the first such case in the Indian literature and the third case reported in the English literature.

## 2. MATERIALS AND METHODS

A 35 years old male presented with abdominal pain, backache and asthenia. A thorough workup was done including clinical examination, CBP, KFT, LFT, serology (HIV, HBsAg), Serum electrophoresis, radiology and bone marrow examination. A systematic literature review was conducted by searching the Pub Med and National Centre for Biotechnology Information database using the keyword search Primary plasma cell leukaemia in HIV patient. All cases published hitherto were included. Excluded were reports published in a language other than English and without an English-language abstract. This yielded a total of 3 publications (Table 1).

**Table 1. Reported cases of primary plasma cell leukaemia associated with HIV**

Case no.	REF.	Age/ Sex	C/L	Duration of symptoms	Phy. exam	HIV status		Disease progression	Course	RX.
1	Heuberger L [12] (September 1997)	54/M	Asthenia, Anorexia, Fever, Abdominal Pain	10 Days	Hepatospleomegaly	3 YRS.	HIV-1	Hypercalcemia, sepsis, CNS involvement, multiorgan failure	Died within 48 Hrs.	STEROIDS
2	Jung Christoph P [17] (Nov 2003)	41/M	Fever, WT. Loss, Anaemia. K/C/O Kaposi sarcoma AND Multicentriccastleman's disease (KS with MCD)	N.A.	Giant Splenomegaly (Splenectomy done). Thrombocytopenia, shock. severe systemic inflammatory response syndrome	N.A.	HIV+ associated with HHV-8	KS with MCD	Na	2 cycles of doxorubicin and etoposide, bleomycin
3	Present case (2010)	35/M	Abdominal Pain, Backache, Asthenia	10 Days	Hepatosplenomegaly left pleural effusion.	At the time of diagnosis	HIV-1 associated EBV +	Sepsis, internal haemorrhage, DIC	Died within 48 hrs.	VAAD along with HAART.

NA - Not available/ known

### 3. RESULTS AND DISCUSSION

A 35 years old man was admitted for abdominal pain, backache, asthenia lasting for 10 days. On physical examination: Hepatosplenomegaly, icterus and left sided pulmonary crepitations and effusion were detected.

The outside haematological findings were as follows:

Haemoglobin was 6 g/L, Leukocyte count- $49 \times 10^9/L$ , with neutrophils-34%, lymphocytes-10%, monocytes-03% and atypical plasma cells (53%) with occasional binucleate cells with basophilic cytoplasm and eccentric nucleus and clumped chromatin (Figs.1 and 2).

Sr. protein electrophoresis showed a monoclonal IgG-K paraprotein at a concentration of 4.56 (45 g/l) (Ref- 0.10-0.40). "M-Band" was present. No free light chains were detected in urine. Sr. Calcium was 8.3 g/dl (N- 8.2-10.2 g/l). Blood urea was raised to 84 mg/dl and Sr. creatinine was also mildly elevated to 2.4 mg/dl. LDH was 780 IU/L (N- 250-450 IU/L) and Sr. Uric acid 16.6 mg/dl (N 2.5 to 7.0 mg/dl). Hypoalbuminaemia was noted (2.2 mg/dl); however S.G.O.T. was elevated to 130 IU/L. The patient had abnormal prothrombin time – 31.2 seconds and activated partial thromboplastin time of 74.2 seconds. The serology test for HIV was reactive for HIV-I and II. HBsAg was negative.

#### 3.1 Radiological Examination did not Reveal any Lytic Lesion

Bone marrow examination showed hypercellularity with near replacement of the

normal marrow elements by sheets of mature plasma cells and a few immature plasma cells were seen (Fig. 3). There was paucity of erythroid, myeloid and megakaryocytic precursors. EBER positive plasma cells seen (Fig. 4).

No chromosomal studies and flow cytometric analysis were performed on the plasma cells as the patient was not affording.

Based on the overall findings, a diagnosis of PPCL was made and subsequently, the patient was referred for chemotherapy.

A palliative chemotherapy comprising of Vincristine, Adriamycin and Dexamethasone along with antiretroviral treatment was planned. But despite of the supportive treatment, the patient had rapid multisystem failure with sepsis, internal haemorrhage and Disseminated intravascular coagulopathy and died within 48 hours.

The association of Cancer and AIDS is well described, Kaposi sarcoma (KS) and Non-Hodgkin lymphoma (NHL) occur at an exceptionally high incidence. The other cancers associated with Acquired immunodeficiency syndrome are Hodgkin Lymphoma, Multiple myeloma and cancers of the cervix, anal canal, skin, lung, liver and testis [10]. Due to the dysregulation of immune system; about 34% of AIDS victims suffer from cancer in the developed countries while the incidence of cancer in HIV infected Indian population is surprising low to 3-4%, [11] as Kaposi Sarcoma is rare in Indian patients having AIDS.

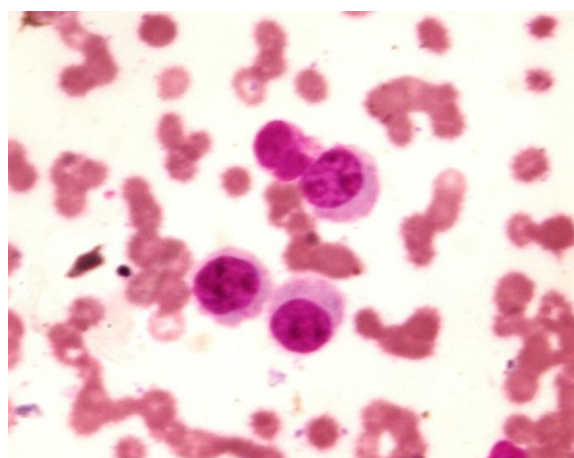
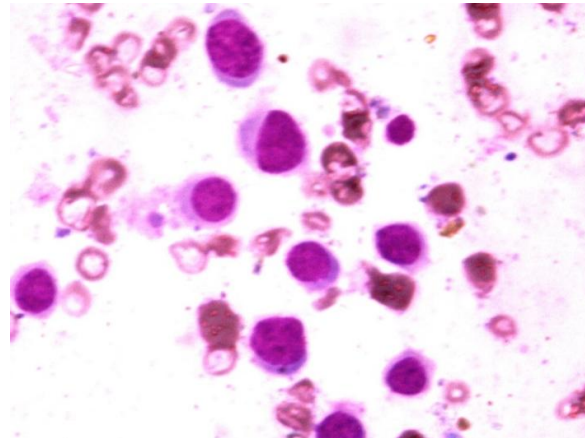
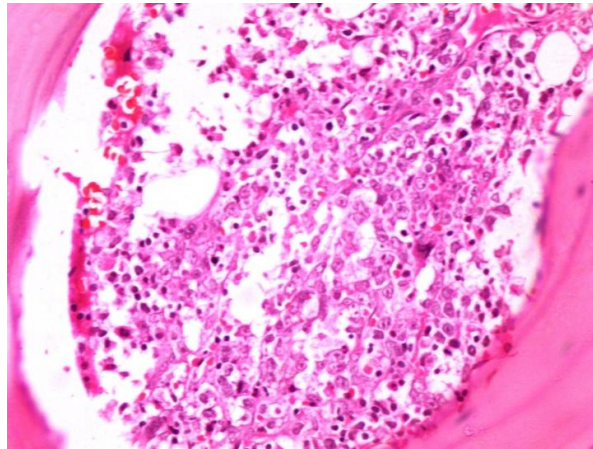


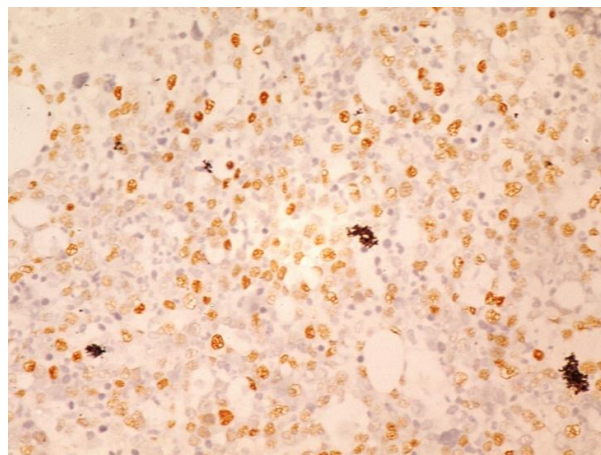
Fig. 1. Leishman stained peripheral smear showing plasma cells with basophilic cytoplasm, eccentric nuclei and clumped chromatin (40X)



**Fig. 2. Leishman stained peripheral smear showing many plasma cells with basophilic cytoplasm, eccentric nuclei and clumped chromatin (40X)**



**Fig. 3. H&E stained sections from the bone marrow showing hypercellularity with near replacement of the normal marrow elements by sheets of mature plasma cells and a few immature plasma cells (40X)**



**Fig. 4. EBER positive plasma cells (10X)**

It is evident from different studies that HIV infection does not induce malignant tumour directly as the genome of HIV is not found in cancers associated with AIDS. It is the immunodeficiency (CD4 < 200) that permits the various other viruses to bring malignant transformation in the target organs. e.g.: HHV8 in Kaposi Sarcoma, primary effusion lymphoma & multicentric Castleman's disease, EBV in Non-Hodgkin lymphoma & Hodgkin lymphoma and HPV in cervical & anal cancers [11].

HIV infected patients can present with a range of plasma cell disorder including Reactive plasmacytosis, Paraproteinemia, Amyloidosis, Light chain deposition disease, Plasmacytosis, MM and PCL [7]. The association of plasma cell leukaemia with retrovirus is noted and clearly understood. However, factors considered responsible for progression to MM or PCL may include stimulation of growth factors, inactivation of tumour suppressor genes, altered expression of adhesion molecule with deterioration of immune regulation, activation of oncogenes via c-myc, stimulation by cytokine like IL-6 and chronic viral infections [12].

The pathophysiologic studies suggest a chronic antigen driven response to the circulating viral antigen, directed against the p24 and this may contribute to early development of plasma cell disorders in these patients. Epstein Barr virus (EBV), Kaposi sarcoma Herpes Virus (KSHV) and Human herpes virus-8 (HHV-8) are detected in the myeloma plasma cells of HIV positive patients. HHV-8 in HIV positive patients via the induction of IL-6 by bone marrow stromal dendritic cells play a major role in perpetuating the differentiation of native B cells into plasmablasts or lymphoproliferative lesion [13,14,15].

PPCL can present as primary or secondary PCL. In literature, the median age for PCL ranged between 53 and 57 years (about 10 years younger than the median age in myeloma). The youngest age reported was 21 years old male [7]. Neoplasms of plasma cells associated with HIV do occur with a mean age of 33 years, whereas, only 2.2% myeloma in younger than 40 years of age and 0.3% in patients less than 30 years were noted [16].

Only two cases of plasma cell leukaemia co-existing with HIV infection have been reported in literature [12,17]. Reported cases of Plasma cell leukaemia associated with HIV are summarized

in the Table 1. The patients were 54 and 41 years old males respectively. Our case is 35 years male. PPCL in younger patients less than 40 years should imply the suspicion for evaluation of immune status.

Patients of PPCL with concomitant HIV infection are often younger with abrupt onset, and have multiple extra-medullary disease, ascites, anaemia, hypercalcaemia, renal failure and elevated LDH while they don't have osteolytic lesions. They have unusual aggressive manifestations as compared to secondary PCL leading to a poor response rate and a mean survival with chemotherapy ranging from 2 to 12 months [15,7].

#### 4. CONCLUSION

To conclude, PPCL in HIV infected young are extremely rare, aggressive disease with poor prognosis and should be treated with high dose chemotherapy in combination with autologous bone marrow transplant to improve the survival [6,7,8]. This is an interesting study which will be valuable case for future studies. To the best of our knowledge, this is the first such case in the Indian literature and the third case reported in the English literature.

#### CONSENT AND ETHICAL APPROVAL

As per international standard or university standard guideline Patient's consent and ethical approval has been collected and preserved by the authors.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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