Plasma Cell Leukaemia a Rare Cause of Disproportionate Anaemia in a Patient Presenting as CKD

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Abstract
The anaemia in patient of chronic kidney disease is commonly related to secondary erythropoietin deficiency. When the severity of anaemia is disproportionate and associated with other haematological abnormalities like thrombocytopenia, then primary haematological disorder and secondary renal involvement must be considered. Renal involvement is common in haematologic disorder like Multiple Myeloma. The diagnosis of haematological disorder may be missed. This is a case of chronic kidney disease with disproportionate severe anaemia with bleeding diathesis which ultimately turned out to be plasma cell leukaemia.

Introduction
The anaemia of chronic kidney disease has been widely studied. The anaemia becomes more prevalent as renal function declines. It is more common in end stage renal disease (ESRD). The various studies have reported the correlation between varying levels of kidney function and the severity of anaemia.

The anaemia in patient of chronic kidney disease is almost always related to secondary erythropoietin deficiency. Thus it is common practice to assess the iron status and load the patient with iron and erythropoietin. But when the severity of anaemia is disproportionate and associated with other haematological abnormalities like thrombocytopenia leading to bleeding diathesis, then primary haematological disorder and secondary renal involvement must be thought of.

Renal involvement is common in haematologic disorder like multiple myeloma. Otherwise the diagnosis of haematological disorder may be missed. Here we present the case of chronic kidney disease with disproportionate severe anaemia with bleeding diathesis which ultimately turned out to be plasma cell leukaemia.

Case report
A 35 year old female was admitted with complaints of fever and cough since 6 months, per-vaginal bleeding since 1 month, bleeding from gums, burning micturition and vomiting since 7 days. There was no history of generalised swelling, or swelling over face or feet. 4 months back she was hospitalised with same complaints. At that time her investigations revealed haemoglobin of 3.7 gm/dl, TLC 7000/cu.ml, Polymorphs 63%, Lymphocytes 32%, Eosinophils 3%, Monocyte 2%. PS revealed normochromic to microcytic, moderate hypochromic and platelets were low. The renal function test revealed blood urea 51 mg/dl, serum creatinine 6.7 mg/dl, urine albumin was 4 +, 24 hour Proteinuria was 7.5 gm/24 hour and urine output was around 1.2 lit/day. She was suspected as case of sputum negative pulmonary tuberculosis with chronic
kidney disease stage IV. She received antitubercular treatment for 6 months and was given supportive treatment for renal dysfunction. Patient also had dysfunctional uterine bleeding with history of passing clots since last 1 year. Her past menstrual cycles were normal.

On general examination patient was moderately built and poorly nourished. Her vitals were normal. Severe pallor was present. Respiratory system examination was suggestive of right upper lobe pulmonary fibrosis. No other systemic abnormality was detected.

On investigation haemoglobin was 2.6 gm%, total leucocytes count- 8300 cells /mm³, platelets were 0.92lac/mm³ and the peripheral smear showed microcytic hypochromic RBCS and presence of plasmacytoid cells. The differential leucocyte count was as follows Neutrophils- 48%, Lymphocytes-22%, Platelets were on lower side.

USG abdomen showed Normal size kidneys with bilateral renal parenchymal disease; with loss of cortico-medullary differentiation (right kidney measured-10.4 x 4.3 cm left kidney measured- 10.1 x 4.4 cm). Computed tomography of thorax was suggestive of right upper lobe fibrosis with tractional bronchiectasis with multiple nodules. X -ray of bone did not show any lytic lesions. Serum calcium was 8.5 mg/dl, serum phosphate was 4.0 mg/dl and Serum lactate dehydrogenase was 500 IU/L. KFT however was deranged (BU-58mg/dl, SC- 6.0 mg/dl, GFR 8.4 ml/min/1.73m² by MDRD formula, urine albumin- 4+, 24 hour urine- 6.4 gm/24 hour). Serum electrophoresis showed M band (Figure 1) however urinary Bence Jones proteins were negative. Urinary electrophoresis showed no evidence of M band. Beta-2 microglobulin levels were-38163ng/ml which is 36 times more than normal.

The bone marrow aspiration study were done to evaluate the patient further, bone marrow aspiration showed multinucleated and binucleated plasma cells > 50% of cell population and bone marrow biopsy and imprint study showed erythroid series suppressed, myeloid series suppressed with normal mature cell, intratrabecular spaces shows few binucleate and multinucleated plasma cells suggestive of plasma cell leukaemia. Now when peripheral smear was repeated it showed that the plasmacytoid cells were more than 30% of cell population. The Figure 2 is showing the picture of bone marrow aspiration study.

**Discussion**

This patient was diagnosed as case of chronic kidney disease with severe iron deficiency anaemia with bleeding tendencies, thrombocytopenia. The anaemia and bleeding tendencies were disproportionate to her CKD. The erythropoietin deficiencies as cause of iron deficiency anaemia and platelet function abnormality associated with CKD was unable to explain her disproportionate anaemia and bleeding tendencies.
This disproportion between CKD and anaemia made us further investigate the case. The presence of plasma cell in peripheral smear is reactive process. The reactive process is usually secondary to bacterial or viral infections like parvovirus B19, hepatitis, dengue fever, or EBV, autoimmune phenomenon such as rheumatoid arthritis, Systemic Lupus Erythematosus, Sjogren syndrome. The other possibilities for disproportionate anemia per say were associated sickle cell disease, thrombotic thrombocytopenia, aplastic anaemia, erythropoietin resistance, multiple myeloma or other leukaemias. The bone marrow aspiration study with repeat peripheral smear clinched the diagnosis.

Plasma cell leukaemia (PCL) is rare plasma cell dyscrasia with incidence of 2-4% of plasma cell dyscrasias. By definition > 20% plasma cell in peripheral blood with an absolute plasma cell count >2 x 10^9/L only one can be considered positive for diagnosis. Two types primary (De novo) and secondary, evolving from an existing case of myeloma. Primary differ from secondary by late age of onset and underlying multiple myeloma (MM). Although there is overlap between PCL and MM, plasma cells more frequently express CD20 antigen in PCL and they often lack CD56 antigen which is anchoring protein, that helps in adhesion of plasma cells to bone marrow. Another protein CD28 is also frequently expressed by secondary PCL cells. PCL plasma cells have higher proliferative rates and more complex karyotypes than myeloma. Loss on 13q, monosomy 13 and loss on chromosome 16 exists in more than 80% pts of PCL. In addition PCL patients have unique losses of 2q and 6p. Over expression of PRAD1/cyclin D1 which plays important role in control of cell cycle has been observed in PCL.5 The Table 1 will enumerate some of differences between PCL and multiple myeloma. The renal involvement in case of multiple myeloma consists of deposition in mesangium and in severe cases deposition around perivascular region and sometimes in basement membrane.

The table 1 shows the difference between multiple myeloma and plasma cell leukemia.

**Treatment**: The response to therapy in primary and secondary PCL is same and poor. The regimens used in treatment of PCL are VMCP-Vincristine, Melphalan, Cyclophosphamide and Prednisolone VBAP- Vincristine, BCNU, Adriamycin and Prednisolone VAD-Vincristine, Adriamycin and dexamethasone.

The response rate for secondary PCL is low but can be increased with adding thalidomide to the therapy. With above regimens the median survival rate is 18-20 months. With autologous bone marrow transplantation survival rate of 36 months could be achieved.

**Table 1: Difference between Multiple myeloma and Plasma cell leukaemia**

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<tr>
<th></th>
<th>Multiple myeloma</th>
<th>Plasma cell leukaemia</th>
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<tbody>
<tr>
<td>% of Plasma cell dyscrasia</td>
<td>30-40% PCD</td>
<td>2-4% of PCD</td>
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<tr>
<td>Age of onset</td>
<td>Late age of onset</td>
<td>Early age of presentation</td>
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<tr>
<td>Bone marrow and peripheral smear picture</td>
<td>Bone marrow plasma cells &gt; 20%, peripheral blood shows &lt; 10% plasma cells, plasma cells express CD56</td>
<td>Peripheral blood plasma cells &gt; 20%, Plasma cells express CD56</td>
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<tr>
<td>Extramedullary manifestations</td>
<td>Extra medullary manifestations less common</td>
<td>Extra medullary manifestations like anaemia, thrombocytopenia and renal involvement more common</td>
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<tr>
<td>Proliferative capacity</td>
<td>Plasma cell proliferative capacity is less</td>
<td>Plasma cell proliferative capacity is more</td>
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<tr>
<td>Lytic lesions</td>
<td>Lytic lesions must for diagnosis</td>
<td>Lytic lesions and organomegaly very rare</td>
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<td>LDH and beta 2 microglobulin level</td>
<td>Less increased</td>
<td>LDH and beta 2 microglobulin are more increased</td>
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References

5. Wintrobe's Clinical Hematology 12th edition page no 2414