Plasma cell leukemias (PCL) can be de novo (primary PCL) or arising as leukemic transformation of underlying relapsed or refractory multiple myeloma. The diagnostic criteria of the disease are well described previously [1]. The disease has a very poor prognosis and usually exhibits a rapid and downhill course despite aggressive treatment.

Bortezomib was the first proteasome inhibitor approved for the treatment of multiple myeloma (MM). Recent reports have illustrated a beneficial response from upfront treatment using this agent in PCL [2]. We report our experience with PCL. 5 patients were identified with PCL. One patient had primary PCL while the rest had secondary PCL.

Case Report

Case 1

A 48 year old male of south Asian descent presented with weakness and fatigue. He was admitted to another hospital where he was found to have leukocytosis and anemia. He had circulating plasma cells > 2000/mm3. Patient was transferred to our institute for further management. He had a comprehensive work up including Hepatic, renal and bone profile, serum and urine electrophoresis, immunofixation, bone marrow biopsy and cytogenetic study, LDH, skeletal survey and echocardiography.

Bone marrow showed 93% plasma cells with plasmablasts. CD 138 +, CD 38 +, CD 19-, CD 45-. SPEP showed IgG lambda at 68.7 gm/liter. Bence Jones protein was positive with IgG lambda and free lambda light chain. Beta 2 microglobulin was elevated at 4.5. Cytogenetic study showed a normal male karyotype (FISH was not performed).

He was induced with Doxil, Dexamethasone, Bortezomib and thalidomide (DVD-T). After 3 cycles his SPEP/IFE showed a monoclonal spike of 4.3 gm/liter (>90% response) however the bone marrow still showed 50% residual disease. Patient continued on for another 3 cycles of the same regimen and reassessed. SPEP and IFE showed residual M protein at 3.4 gm/liter. Beta 2 microglobulin had decreased to 2.3. Bone marrow showed residual 2% plasma cells. Patient was subsequently referred for HSCT to an outside institute.

Case 2

A 49 year old was diagnosed in January 2010 with chronic phase CML. She achieved a major molecular remission on Imatinib 400 daily and stayed on it till January 2014 when she presented with fatigue and bone pain at her local hospital. She was found to have severe anemia (hemoglobin 6.4), acute renal failure. After supportive care she was referred for further work up. She was found to have an elevated total protein, elevated IgG with a monoclonal spike and free lambda light chain > 1000 mg per ml. Patient refused bone marrow biopsy. Flow cytometry data was consistent with PCL. Induction was given with RVd with rapid improvement in renal function. She subsequently went to Singapore where another 4 cycles of RVd were given with a partial response. Subsequently she received 2 cycles of VCd and then went for stem cell transplant with Melphalan 140 mg/m2, Restaging 6 weeks later showed only PR. Patient was started on Lenalidomide 10 mg. She was seen again in December 2014 with pancytopenia. She had circulating plasma cells and elevated monoclonal spike and free lambda light chains > 2300 mg per ml. Patient rapidly worsened and expired.

Case 3

A 59 year female was admitted to ICU with sepsis, acute renal failure and hypercalcemia. She had an elevated total protein and circulating plasma cells. After stabilization she was diagnosed with salmon Durie stage 3 B IgA MM with circulating plasma cells (ISS staging not done) with normal female karyotype and absence of (t 4;14), (t11;14). Patient was treated with 3 cycles of VMP with partial response (PR). Patient transformed into PCL before starting the 4th cycle of VMP. She was admitted with urosepsis and progressive deterioration of her condition and expired.

Case 4

A 60 year male was diagnosed with salmon Durie stage 3 A, ISS 2 MM with normal male karyotype FISH negative for P53, t4;14 and t 11;14. Induction with Bortezomib, pegylated Adriamycin and low dose dexamethasone was given. Patient had progressive disease within 6 months of finishing therapy and was given salvage therapy with Thalidomide and dexamethasone and therapeutic anti-coagulation with warfarin. After 6 cycles he achieved a vGPR. He was unable to tolerate therapeutic dose of thalidomide and dose was reduced to 100 mg daily. He subsequently converted to CR after 6 months of low dose thalidomide. He maintained the remission rate for 3 years when he developed slowly progressive anemia and increasing M spike. He was admitted with acute onset shortness of breath and rapidly increasing WBC and LDH and decreasing platelets. Bone marrow biopsy confirmed PCL. He was given salvage with RVd x 1 cycle. He had no response to therapy and died within 4 weeks of transformation to PCL.

Case 5

A 77 year old male presented with renal failure and was diagnosed with IgG lambda MM Salmon Durie stage 3 B and ISS stage 3. He was induced with Bortezomib and dexamethasone. Patient achieved a PR after 6 cycles. He refused further Bortezomib and was given Lenalidomide and dexamethasone (Rd) for 2 cycles. He had evidence
of biochemical progression and Bortezomib was added (RVd). Patient continued for a total of 16 cycles. He was subsequently placed on Rd again for 8 months. He was then given salvage with VMP without any benefit. Patient was lost to followup for 6 months. In the interim he went for a second opinion to Germany where he was started on Pomalidomide however he developed PCL. He was placed on palliative care and expired after 8 weeks.

**Discussion**

PCL is the most aggressive presentation of the plasma cell neoplasm. Previously treatment had been based on either melphalan or polychemotherapy (VAD). Results were dismal with median survival of 6-7 months. Recently reports have suggested the use of novel agents like IMiDs as well as bortezomib in PCL may prolong survival. Our experience although limited to 6 patients tends to support the theory that PCL has to be treated with the novel agents upfront. In our experience secondary PCL did poorly even with the novel agents.

Bortezomib and IMiD based regimens can be easily given in clinic setting with appropriate supportive care. Eligible patients can then be consolidated with autologous HSCT [3]. Subsequently patients may require consolidation for 2-4 cycles followed by maintenance. This line of management can only be tested and validated in a large inter-group trial because of the rarity of the disease.

**References**