

## CASE REPORT

## Secondary plasma cell leukemia

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### Abstract

Plasma cell leukemia (PCL) is a rare disease and is the least common variant of multiple myeloma accounting for 2–3% of all plasma cell dyscrasias. We report a patient who was diagnosed with multiple myeloma, 12 months earlier; he was treated with VBCMP, VCMP regime, and after 12 months he presented of high grade fever, weakness, palpitations, loss of appetite, bone pains, dyspnea. Initial evaluation revealed plasmacytosis with blood plasma cell count of 13 860/mm<sup>3</sup>. His hemoglobin (Hb) was 8.4 mg/dL, platelets were 45 000/mm<sup>3</sup> and total leukocyte count (TLC) was 23 100/mm<sup>3</sup> (60% plasma cells). Bone marrow examination revealed 90% plasmablastic cells. Serum LDH was high at 3117 U/L and serum calcium was also elevated at 9.1 mg/dL. A diagnosis of PCL was made and the patient was started on treatment with VAD regime along with supportive care. Patient condition deteriorated very quickly, despite treatment and he died on the third day. A detailed report of this case and a review of PCL is presented here.

**Keywords:** plasma cell leukemia, multiple myeloma, plasmablastic cells.

### Introduction

Plasma cell leukemia (PCL) is a rare and aggressive plasma cell dyscrasia [1]. The 2008 *WHO* classification recognizes plasma cell leukemia (PCL) as a variant of plasma cell myeloma, characterized by the expansion of a clone of immunoglobulin-secreting terminally differentiated mature B-cells. Plasma cell leukemia (PCL) can develop either *de novo* or in patients with pre-existing multiple myeloma [2]. In an analysis of the *Surveillance, Epidemiology, and End Results* (SEER) database, there were 49 106 patients with multiple myeloma; 291 had plasma cell leukemia (0.5%) [3]. The diagnostic criteria for PCL include the presence of a circulating clonal plasma cell count of more than 2000/μL (if the total white blood cell count is >10 000/μL) or the presence of more than 20% circulating plasma cells. PCL can be secondary PCL (sPCL) if arising from a known diagnosis of plasma cell myeloma or primary PCL (pPCL) if no prior history of plasma cell myeloma can be ascertained. sPCL was felt to arise late in the course of plasma cell myeloma and those patients have been described to have a worse prognosis than those with pPCL. A recent report indicates that the median time to transformation to secondary PCL from plasma cell myeloma is approximately 21 months. Patients with PCL have a very poor prognosis with median survival measured in months. Patients with PCL tend to present with aggressive clinical features, such as extramedullary disease, bone marrow failure, advanced stage disease and expression of distinct immunophenotypic markers, such as lack of CD56 and presence of CD20. PCL is an

extremely aggressive disease with no standard treatment regime so far due to the rarity of the disease. Melphalan/Prednisolone (MP), infusional Vincristine, Doxorubicin and Dexamethasone (VAD) or Thalidomide/Dexamethasone (TD) regimes have been tried but the outcome has been dismal [4–6]. Prognosis is generally very poor with a median survival of 2–8 months [4, 6]. The impact of newer agents, such as Bortezomib and Lenalidomide, in conjunction with autologous and allogeneic stem cell transplantation is uncertain, but emerging data suggest that use of these modalities may help improve the poor prognosis of patients with PCL.

### Patient, Methods and Results

D.I. patient, 61-year-old, accused of approximately four weeks back pain with radiation to right leg, sharp motion and pain relief, and that does not respond antialgic and to muscle relaxants medication. Seven days prior to admission was install progressive bilateral paresthesia, predominantly in the right lower limb. Objective: tactile and painful hypoesthesia the level T12–L1, with hyperreflexia in the legs.

Laboratory: common in normal analysis. Cervical Lumbar MRI – multiple osteolytic lesions in cervical and thoracic spine. Tissue mass in the T3–T4, 3.5/2 cm, with cord compression. The surgical intervention was performed seven days later, with decompression laminectomy; histopathology and immunohistochemistry of the excised tumor formation showed myeloma cell infiltration highlighting intense CD38 positive, CD79a positive and focal EMA positive kappa chains. After surgery is performed corticosteroids and radiotherapy

(8 cGy in two sessions) with gradual recovery of sensation and mobility.

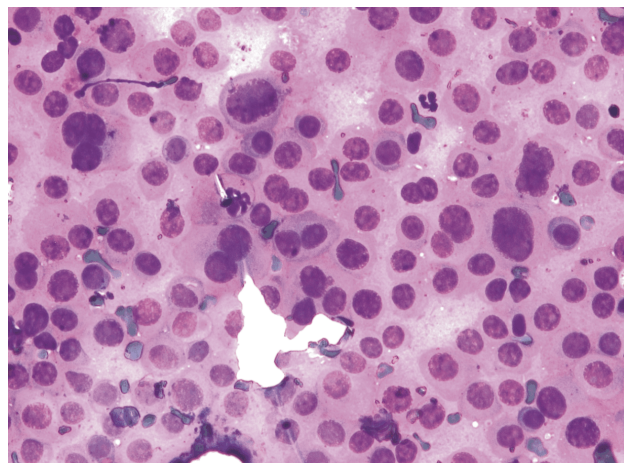
Hematology exam showed: ESR 66 mm, HLG 13 g/dL Hb, Ht 38%, blood counts L 8970/mm<sup>3</sup>, T 272 000/mm<sup>3</sup>, the differential leukocyte counts was normal. The biochemical profile was: serum creatinine 0.74 mg%, urea 49 mg/dL, glucose 131 mg/dL, ALAT 22 U/L, ASAT 57 U/L,  $\gamma$ -GT 86 U/L, BT 0.62 mg/dL, LDH 188 U/L, serum  $\beta$ 2 microglobulin 2077  $\mu$ g/L, serum albumin 3 g/L, CRP 0.7 mg/L. Serum protein electrophoresis: 6.5 g/dL with 2.9 g/dL  $\alpha$ 1, 0.4 g/dL  $\alpha$ 2, 1.2 g/dL

$\beta$  and 0.7 g/dL, range 1.3 g/dL. IgG 1380 mg/dL, IgA 58 mg/dL, IgM 16 mg/dL, urinary protein/24 h 746 mg, serum IgG kappa monoclonal, vitamin B<sub>12</sub> 240 pg/mL, folic acid 3.3 ng/mL, serum iron 98  $\mu$ g/dL, serum ferritin 370 ng/mL.

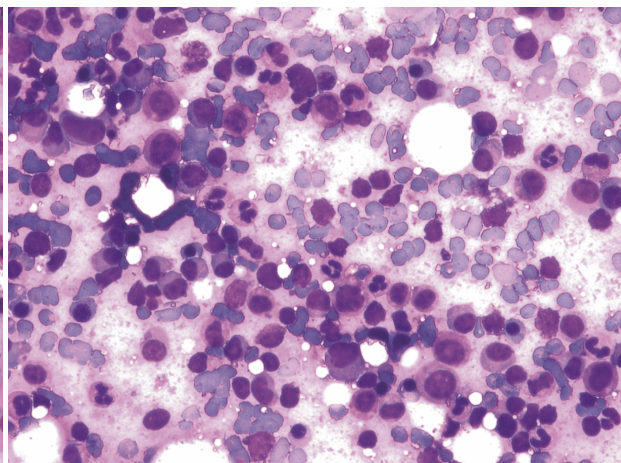
Serology: HIV negative, anti-HBc positive, negative HCV.

Echocardiogram: 72% FE.

Bone marrow highlights 20% myeloma cell infiltrated (Figures 1 and 2), with CD19-, CD56+, CD45-, CD28-, CD27-, CD20-, CD117- immunophenotype.



**Figure 1 – The appearance of bone marrow at diagnosis. There can be noticed the presence of a plasma cells infiltration in approximately 20%, cells with eccentric round nucleus and condensed chromatin, some of them multinucleated, basophilic cytoplasm. MGG stain, ob. 20 $\times$ .**



**Figure 2 – The appearance of bone marrow at diagnosis. There can be noticed a bone marrow infiltration with plasma cells in 20%, fat bubbles. MGG stain, ob. 20 $\times$ .**

Cytogenetic: IGH-FGFR3 to 50% of cells examined, 13q14 to 70% of cells, p53 in 30% of cells.

Diagnosis: IgG kappa multiple myeloma IIIA. T3–T4 cord compression.

Treatment: The emergency treatment was decompression laminectomy, then chemotherapy with VBCMP (Vincristin + Bortezomib + Cyclophosphamid + Melphalan + Prednisone) regime, Lamivudine (B-virus

reactivation prophylaxis) + Aranesp + Zometa, then VMCP (Vincristin+ Cyclophosphamid + Melphalan + Prednisone) regime, monthly, Zometa from December 2010 to February 2011.

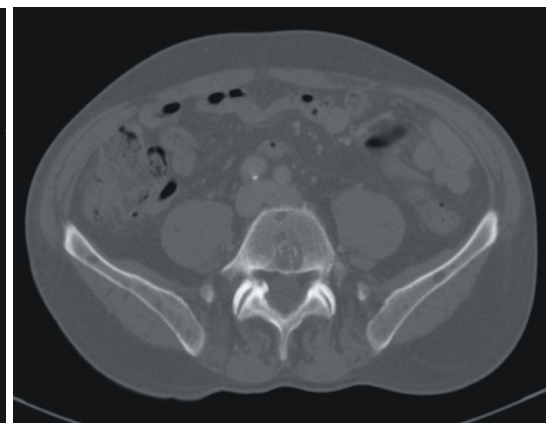
Computed tomography scan (CT scan) revealed many osteolytic lesions (December 2010), in the thoracic and lumbar vertebrae, and also in the basin bones, like it shows in Figures 3–5.



**Figure 3 – Multiple osteolytic lesions in the lumbar spine.**



**Figure 4 – Multiple osteolytic lesions in the thoracic spine of sizes up to 1.5 cm.**



**Figure 5 – Multiple osteolytic lesions in the pelvic bones.**

In March 2011, is presented with fever, dyspnea, easy temporo-spatially disoriented, pale, asthenic, significant weight loss, symptoms installed about two weeks and accentuated in the last week.

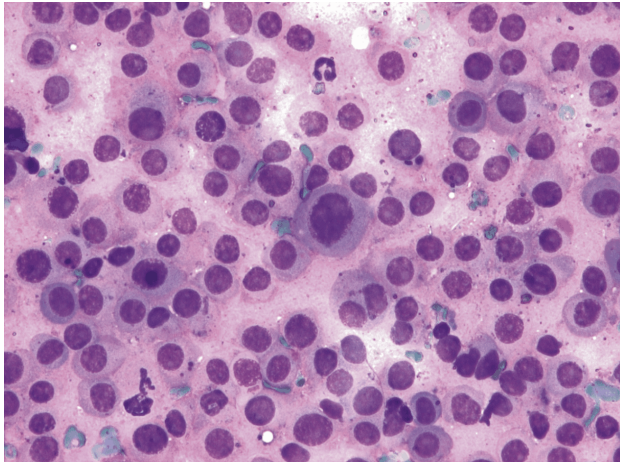
Clinical examination: underweight, pale skin, pain in the lumbar spine, bilateral basilar subcrepitan rales, blood pressure 140/80 mmHg.

Laboratory: ESR 50 mm/h, hemoglobin 8.4 mg/dL,

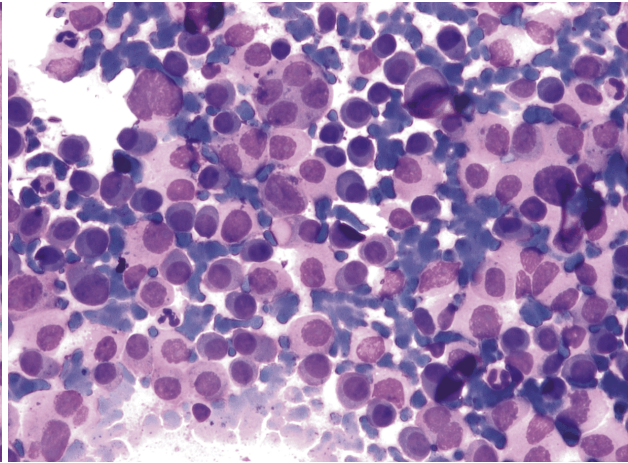


leukocytes  $23\,100/\text{mm}^3$ , platelets  $45\,000/\text{mm}^3$  60% cells with round nucleus with loose chromatin nucleoli sketch centrally located or slightly eccentric, with abundant cytoplasm, basophilia. CRP 5.06 mg/dL; EF: total protein 5 g/dL,  $\gamma$ -globulins 17.3% serum calcium 9.1 mg/dL, LDH 3280 U/L; bone marrow: 90% atypical

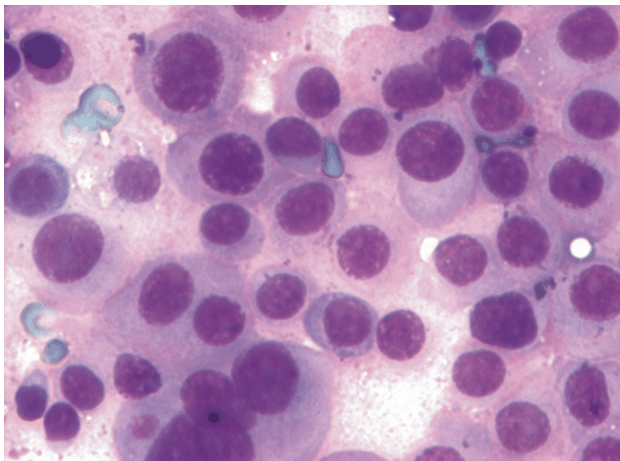
plasma cells and multinucleated unite with unequal nuclei of varying sizes (Figures 6 and 7), some aspect of pro plasma cells and plasmablastic cells (immature plasma cells) (Figures 8 and 9). Frequent mitoses were found.



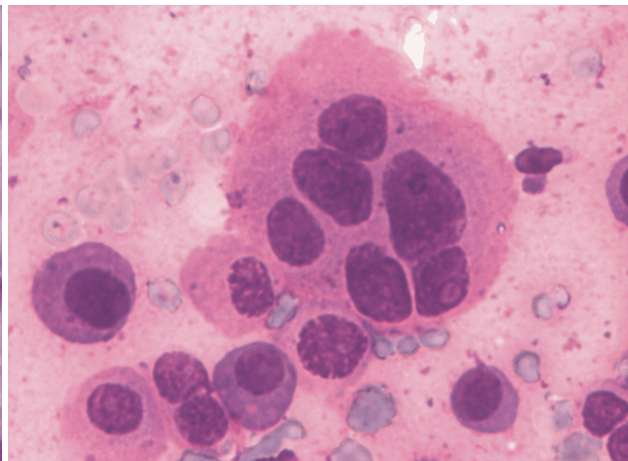
**Figure 6** – Bone marrow morphological examination reveals the presence of an infiltrate in 90% with plasma cells, some of them being large, most of them young, with basophilic cytoplasm and visible nucleoli. MGG stain, ob. 20 $\times$ .



**Figure 7** – The same appearance of the bone marrow. There can be noticed the presence of young multinucleated cells, with three, four nuclei and visible nucleoli. MGG stain, ob. 20 $\times$ .



**Figure 8** – Young multinucleated giant cells with large nucleoli and plasmablast appearance. MGG stain, ob. 40 $\times$ .



**Figure 9** – Giant cell with six nuclei and large nucleoli, together with other cells having plasmablast appearance. MGG stain, ob. 40 $\times$ .

Patient was therefore diagnosed as having secondary plasma cell leukemia (PCL). He was immediately started on intravenous hydration with sodium chloride, steroids, Zyloric, Furosemide and other supportive care. After 24 hours, rigorous intravenous hydration was continued along with blood products, intravenous steroids, Allopurinol, VAD regime were also started. Condition of the patient worsened on day two, and, despite this treatment, the patient died on third day after diagnosis.

## Discussion

Rarity of PCL can be assessed from the fact that at M.D. Anderson Cancer Center, 27 patients with PCL were seen in 20 years period. Overall, incidence of PCL is less than one case per million population [7, 8]. This

is also the reason for lack of prospective data on treatment regimes and treatment outcome in large trials in this disease. In our unit, this was the second case of PCL since 1997. Our patient presented with the typical clinical features of weakness, fever, bone pains and mental confusion. In addition to these, he also had bad prognostic factors of cytogenetics abnormalities and high serum LDH. These are the known bad prognostic signs in the already aggressive disease [7, 8]. Our patient was diagnosed with a high risk multiple myeloma, as it shows the cytogenetics analysis. The evolution was unfavorable, plasma cell leukemia occurring rapidly in our case, after 12 months from diagnosis. Response of PCL to treatment is not good. Median survival of 2–8 months is reported with M+P (Melphalan and Prednisolone) regime or VBAP (Vincristine, Carmustine, Adriamycin and Prednisolone) regime [9]. VAD (infu-

sional Vincristine, Adriamycin and Dexamethasone) regime used in multiple myeloma has shown some good responses in early stage PCL, although most of these studies are based on case reports [10]. Case reports regarding long-term survival after autologous bone marrow transplant or stem cell transplant also exist but again there is no long-term, prospective data on a larger number of patients. The role of novel agents in the treatment of plasma cell leukemia remains undefined. In a study of five patients with plasma cell leukemia, Thalidomide did not result in a response in any [11]. However, in another study, four Thalidomide-treated patients with plasma cell leukemia had a median reduction in M-protein of 80%, one achieving a very good partial response [12]. Lenalidomide has been reported to be effective for the treatment of plasma cell leukemia as a single agent and in combination with Melphalan and Prednisone [13, 14]. In summary, PCL is an aggressive and rare variant of multiple myeloma with poor outcome. No large trials are available on treatment of this disease but VAD regime and bone marrow/stem cell transplant has shown some long-term survivals in individual cases.

## ✉ Conclusions

This paper presents a patient diagnosed with multiple myeloma with high risk of evolution to secondary plasma cell leukemia. Despite aggressive treatment, evolution was unfavorable, transformation occurred in 12 months from diagnosis, with rapid evolution to death.

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