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Case Report
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A Patient with Chronic Lymphocytic Leukemia, Chronic Myeloid Leukemia and Multiple Myeloma

Donatella V, Annalisa S, Giorgio R, Carmelo T, Al Sayyad S, Mauro C, Francesco T, Giuseppina C, Carmela F, Giuseppe I, Francesco M, Maria Grazia MCD, Oliva Bianca Maria BIE, Cristina G, Veronica L, Francesca L, Angela P, Bruno M, Massimo R, Domenico Q and Bruno M*

Department of Hematology, Great Metropolitan Hospital, Bianchi-Melacrino-Morelli, Italy

Abstract

Hematological malignancies represent an important part of all blood disorders. Many hematological cancers feature chronic course, requiring repeated cycles of treatment and determining long-term sequelae. In the last few years, there have been remarkable developments in the diagnosis and treatment of these cancers, and their prognoses markedly improved.

This article is descriptive in nature. It shows how the pattern of VMP therapy (velcade, dexamethasone and melphalan and revlimid) alternating with imatinib controlled myeloma and chronic myeloid leukemia. Great efficacy of adding daratumumab and dexamethasone to lenalidomide treatment. This is a case report of a male adult of 78 years of age with monoclonal gammopathy progressing to multiple myeloma, chronic lymphocytic leukemia that did not require treatment, and chronic myeloid leukemia.

Keywords: Chronic Lymphocytic leukemia; Chronic Myeloid leukemia; Multiple myeloma; Malignancies; Hemoglobin

Introduction

Hematological malignancies represent an important part of all blood disorders. Many hematological cancers feature chronic course, requiring repeated cycles of treatment and determining long-term sequela. In the last few years, there have been remarkable developments in the diagnosis and treatment of these cancers, and their prognoses markedly improved.

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Chronic Lymphocytic Leukemia (CLL) is an indolent lymphoproliferative disorder characterized by progressive accumulation of B cells in blood, bone marrow, and lymphatic tissues. Initial stages must not be treated (guideli00000003nes, NCNN 2023).

Chronic Myeloid Leukemia (CML) is a clonal myeloproliferative disorder characterized by myeloid cells at various stage of maturation in the peripheral blood, and such a pathogenetic mechanism stem from the presence of an aberrant tyrosine kinase protein; namely, the product of the mutant BCR-ABL1 gene. The chimeric gene results from a reciprocal translocation [t(9,22)(q34;q11)] that places the ABL gene from chromosome 9 next to the BCR gene on chromosome 22, demonstrable as the Philadelphia chromosome (Ph).

Due to the new generation tyrosine kinase inhibitors the survival of a patient with CML is comparable to that of a normal person.

Multiple Myeloma (MM) is characterized by the accumulation of clonal plasma cells in the bone marrow. The malignancy is characterized by skeletal lesions, anemia, hypercalcemia, and renal failure. According to the United States Surveillance, Epidemiology and End Results (SEER), the incidence of MM is 6.1/100.000 people per year and increases to 30.4/100.000 people per year in those older than 65 years. At present the disease is curable thanks to the availability of new drugs

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Correspondence:
Vincelli Donatella, Department of Hematology, Great Metropolitan Hospital, Azienda Ospedaliera Bianchi-Melacrino-Morelli, 89124 Reggio Calabria, Italy

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defined as target therapy.

Case Presentation

Our patient is a 78-year-old man. In 2014, the patient was diagnosed with CLL and Monoclonal Gammopathy of Undetermined Significance (MGUS). Below we have summarized key information.

- Hemoglobin 13.5 g/dl, White Blood Cells 35.520/mm^3, Lymphocytes 58%, Neutrophils 42%, Platelets 203.000/mm^3
- Normal hepatic and renal function
- Calcium 8.7 mg/dl
- Immunoglobulins: IgG 1678 mg/dl, IgA 68 mg/dl, IgM 60 mg/dl
- Serum Immunoelectrophoresis: IgG kappa, Bence Jones kappa
- Total protein 7.5 g/dl, Beta-1 6.5%, Beta-2 24.1%

Fluorescence analysis was performer by the flow-cytometer BD FACSCanto II with 8 colors and 2 physical parameters.

A panel with the following monoclonal antibodies was used for the study of MM consisted of: CD38, CD138, CD56, CD19, CD117, CD45, CyIgK, CyIgL.

Medullary aspirate has shown low cellularity (13×10^9/L), marked lymphocytosis and hypoplasia of the erythroid series (2%) Flow-Cytometric examination showed pathological plasma cells equal to 60% of the total population: CD38+ CD138+ CD56+ CD117+ CD19- CD45-.

FISH: Identified two copies for each locus (6q21) and MYC (8q24), ATM (11q22) and GLI (12q13), DLEU (13q14) and p53 (17p13);

Karyotype: 46, XY

Skeleton X-ray: rarefaction of the ostospongiotic structure adjacent to the femoral prosthetic stem in the trochanteric district.

The whole-body TC has identified small adenopathy's less than one centimeter in bilateral retrocaval region, in paratracheal region and in the Barety region, adenopathy's of 18 mm and 15 mm of diameters at bilateral axillary level, normal spleen outcomes of previous TURP surgery for prostate adenocarcinoma, diverticulosis of the sigmoid tract, adenopathy of 22 cm in the left obturator iliac region; presence of left hip prosthesis.

As for the bone marrow biopsy, the results have been 90% cellularity, hypercellular bone marrow with expansion of granulopoiesis maturing with precursors to localization by low-grade plasmacytoma, interstitial and in first-stage anatomopathological aggregates. Presence of very modest lymphoid component B, no CLL;

Echocardiogram: had shown good cardiac function, FE 60%.

Findings

A watch and wait approach have been put in place until April 2015, when we observed the presence of myelocytes and metamyelocytes in peripheral blood and an increased spleen (18 cm).

We have, therefore, determined the stage of the diseases with instrumental and laboratory tests. The following tests have been performed:

- Blood Count; Hemoglobin 12 g/dl; White Blood Cells 24.800/mm^3; Neutrophils 72%; Lymphocytes 10%; Monocytes 2%; Basophils 2%; Eosinophils 4%; Platelets 108.000/ mm^3;
- BCR-ABL: 60%;
- Bone Marrow Biopsy: 98% cellularity, hypocellulose bone marrow with expansion of granulopoiesis, a picture that appears suggestive for a myeloproliferative disease (Chronic Myeloid Leukemia). It is associated with a modest lymphoid B component and a monotypic plasma cellular portion quantitatively classified into a Monoclonal Gammopathy with Uncertain Biological Significance (MGUS).
- FISH: Pathological presence of double fusion signal of the ABL1 and BCR loci in 209 of 271 interphase nuclei examined (77%).
- Abdominal ultrasound: Spleen 16 cm.
- 6/6/2015 Whole body MRI

Diffuse hyperintensity areas in STIR corresponding to sternum, home, and lumbosacral spine.

These tests confirmed the diagnosis of CML, with Sokal Score: 1.34 H; EUTOS Score: 60 L, Hasford Score 1488.5.

In July 2015, the patient started cancer treatment with Imatinib, 400 mg/die. The suspension of treatment with Imatinib was evaluated on the basis of the good response to treatment and the progressive increase of the Serum M-Protein (SPEP). In fact, the patient underwent further hematological re-evaluation that confirmed the evolution of Gammopathy in Multiple Myeloma according to following exams:

Blood Count; Hemoglobin 9.1 g/dL, White Blood Cells 6410/ mm^3, Platelets 166.000/mm^3, Neutrophils 57%, Lymphocytes 35%, Monocytes 8%.0

- Creatinine 1.1 mg/dl;
- Calcium 10.5 mg/dl;
- Total Protein: 8.6 g/dl, Gamma 48.02%, SPEP 4 g/dl;
- Immunoglobulin dose: IgG 3536 mg/dl, IgA 29 mg/dl, IgM 23 mg/dl;
- Karyotype: male with t (9; 22) and Philadelphia Chromosome formation in 25% of the analyzed metaphases;
- BCR-ABL: 14.3230727%;
- Bone Marrow Aspirate: Plasma cells 15%;
- Bone Marrow Biopsy: Intermediate-interstitial plasmacytoma and in first stage anatomopathological aggregates. There are lymphoid components with small lymphocytes equal to 10% of the cellularity to phenotype of Chronic Lymphatic Leukemia/ Lymphoma with small lymphocytes, plasma cells 15% to 18%.

In consideration of the onset of severe painful bone symptomatology, the patient has performed the following instrumental investigations.

MRI whole body: Hyperintensity at the level of the seventh right rib; -PET: Osteolytic lesions of the tenth side arch right rib, right iliac bone, left iliac region, third right tibia diaphyseal.

-RX right hemithorax: Osteolytic area at the level of the seventh

right rib.

Therefore, in consideration of the seriousness of the clinical picture characterized by bone localizations, we have first prescribed anti-MM first line treatment with Bortezomib, Dexamethasone and Melphalan (total 9 cycles, last one on 03/06/2016).

It should be noted that in June 2016, due to sudden pain in his left leg, he performed a radiography that showed many osteolytic areas of 45 mm on third distal femur, third proximal and intermediate tibia, third proximal and third distal of fibula. The urological evaluation showed nothing in the prostate and the PSA values were normal. A second PET documented a further Multiple Myeloma progression due to new bone localizations and a left tibia biopsy showed localization disease.

On 07/06/2016 the patient started a treatment with Lenalidomide for 15 days, interspersed by Imatinib. This treatment maintained the disease stable.

In September 2017 he developed diplopia, the following RM showed the presence of abnormal tissue harbored by right cavernous sinus with involvement of Sella, sphenoid sinus, clivus. The overall complex clinical and radiological picture was interdisciplinary assessed and a biopsy through the nose was deemed a viable option in order to formulate histological diagnosis at this specific site (Lymphoma, Myeloma, other). In October 2018, the patient underwent surgery.

Through endonasal endoscopic approach the Sellar and right Parasellar region were easily reached; lesion emerged in the sphenoid sinus from the right cavernous space and through the mucosa of the clival recess of the sphenoid sinus; thus, enough material was obtained with mini-invasive technique. Patient recovered well and rapidly. The histological diagnosis turned out to be – with a little surprise– just inflammatory tissue.

In the same period, a right gluteus phlegmon was suspected. Therefore, the patient was treated with surgical dressing. As phlegmon was persisting, in December 2018 a needle aspirate of the gluteus was performed and it confirmed the presence of inflammatory tissue. As blood tests revealed increase of paraprotein levels, bone marrow biopsy was required and it showed the presence of 15% plasma cells. Bone marrow biopsy resulted negative for myeloma and lymphoma diseases. Luteal skin biopsy revealed plasmacytoma.

BCR-ABL dosage was 213, 87%, SPEP was increased at 5 gr/dl, immunoglobulin dosage was 4440 mg/dl, Creatinine and serum calcium were normal.

After 2 months the patient's condition deteriorated: A deviation of the oral fissure caused by 7th cranial nerve involvement was observed. Given the presence of pathological tissue in the brain, the patient received 18 sessions of radiotherapy.

He was then hospitalized on 26/04/2019, because of disease progression.

In April 2019, TAC abdomen and pelvis has been carried out: Solid and dis-homogeneous pathological tissue with lumpy margins is found which occupies part of the right upper abdomen and the ipsilateral pelvic excavation.

It implies body of L1 up to the last sacral vertebrae, with axial diameters greater than 20 cm × 15 cm. The lesion seems to originate from the right psoas muscle and then moves downwards and posterolaterally, causing infiltration and extensive erosion of the right iliac wing and the ipsilateral hemisacrum, of part of some adjacent vertebral bodies and of their posterior arch (L3, L4 and L5). The common iliac and right internal iliac arteries are located in the context of the lesion described.

The pathological tissue then borders on the soft dorsal subcutaneous tissue of the right lumbo-sacral region, also incorporating the muscles at this level until it comes into contact with the skin posterolaterally. Diffuse areas of osteolysis with a repetitive appearance in the various bone segments examined.

Multiple lymph node swellings in the groin with a diameter greater than about 35 mm.

Important to highlight that the volume's mass in the gluteus is considerably increased and it is responsible for consistent pain that prevents him to walk autonomously. For this reason, he required morphine-like therapy.

A bone marrow re-evaluation has been performed and it has documented the presence of plasma cells equal to 80% of the global cellularity. The cytogenetic study confirmed the presence of a complex karyotype. And the biopsy of the gluteal tissue documented at localization of Multiple Myeloma.

After 4 cycles of PAD (chemotherapy), and after he obtained a stability of disease, the patient received therapy with Daratumumab, Lenalidomide and Dexamethasone of which he performed a total of 12 cycles with excellent clinical hematologic response.

Conclusion

In this case report we have demonstrated the efficacy of a treatment with VMP, Dara-RD, and Imatinib for LMC and MM.