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Case Report

Bilateral Synchronous Testicular Plasmacytoma as Extramedullary Relapse in High-Risk Multiple Myeloma Patient

Gonzalez de la Calle V[1], Alonso S[1], Del Carmen S[2], Dávila J[1], Antúnez P[2], Gomez Veiga F[3], Lopez-Godino O[1], Puig N[1], Gutiérrez N[1], Lopez-Corral L[1], Ocio EM[1], Caballero MD[1] and Mateos MV[1]*

[1]Hematology Department, University Hospital of Salamanca-IBSAL, Spain

[2]Pathology Department, University Hospital of Salamanca-IBSAL, Spain

[3]Urology Department, University Hospital of Salamanca-IBSAL, Spain

***Corresponding author:** Mateos MV, Hematology Department, University Hospital of Salamanca, Paseo de San Vicente 88-182, 37007, Spain, Fax: 34 923 29 11 00; Email: mvmateos@usal.es

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Abstract

Testicular Plasmacytoma is a very rare neoplasm, even more bilateral and synchronous forms. We report a young multiple myeloma patient, with a high risk disease early relapsing after autologous stem cell transplantation presenting bilateral and synchronous testicular plasmacytoma. In this case, implementation of PET/CT pre-allogeneic stem cell transplantation allows detecting an early and asymptomatic testicular relapse. After combination of orchidectomy, radiotherapy, chemotherapy and allogeneic stem cell transplantation, the patient is currently disease-free and alive.

Keywords: Testicular Plasmacytoma; Extramedullary disease; Multiple myeloma

Case Presentation

A 43 year-old man with no significant medical history, in September 2011, anaemia (Hb: 8.8 g/dl) and hyperproteinemia (13.6 g/dL), were detected both in a medical check-up. The patient was asymptomatic and physical examination was unremarkable, 1.75 m tall, with a BMI of 23 kg/m2. Serum protein electrophoresis and immunofixation assay demonstrated the presence of Ig G-κ monoclonal protein (7.87 g/dL). The required work-up confirmed the diagnosis of Multiple Myeloma (MM) Ig G-Kappa, ISS-2. Anaemia was the only end-organ damage sign. Bone marrow aspiration showed 70% infiltration by Plasma Cells (PC), all of them aberrant. FISH analysis showed *t (4;14)* and del gen RB *(13q14)*.

Induction therapy with chemotherapy VBCMP (vincristine, BCNU, cyclophosphamide, melphalan, and prednisone) was initiated, but in the absence of response, VTD [1] (bortezomib-thalidomide-dexamethasone) was administered. After five VTD cycles, Very Good Partial Response (VGPR) was achieved followed by tandem Autologous Stem Cell Transplantation (ASCT) with Mel 200 and BuMel as conditioning regimens due to the presence of high-risk features. The M-protein remained persistent (0.24 g/dL) on day 100 after second ASCT. The patient received 4 VRD consolidation cycles (bortezomib-lenalidomide-dexamethasone) achieving Immunophenotypic complete response, followed by prednisone/interferon as maintenance.

Eleven months from second ASCT, biochemical relapse was detected. Considering that we were dealing a young MM patient early relapsing after ASCT and with high risk features, together with the availability of an HLA-identical sibling donor, we planned to give one cycle of VRD to maintain the disease under control and to immediately proceed to allogeneic Stem Cell Transplantation (allo-SCT) with reduced-intensity conditioning. Although the patient remained asymptomatic with negative examination findings, a symmetrical 18F-Fluoro-2-Deoxyglucose (FDG) uptake in the testes was identified on the PET/CT (Figure 1) performed as part of the standard work-up prior allo-SCT. Several hypoechoic nodules with hypervascularity were identified by ultrasound scan (Figure 2) and fine-needle aspiration showed infiltration by plasma cells. Immunohistochemical analysis revealed positivity for CD138 with restriction for Kappa light chain, and flow cytometry analysis confirmed also the presence of aberrant plasma cells (90%). Serum M-protein was 0.15 g/dL, with no evidence of plasma cells in peripheral blood or spinal fluid. Bone marrow aspirate showed only 2% of plasma cells, most of them (85%) aberrant by flow cytometry and identical to those identified in the testicular biopsy (Figure 3). Therefore, an asymptomatic bilateral and synchronous testicular extramedullary relapse was diagnosed.

In the absence of therapeutic guidelines, we proposed bilateral orchiectomy and local radiotherapy (200cGy, 15 sessions), plus systemic chemotherapy (D-PACE: dexamethasone, cisplatin,

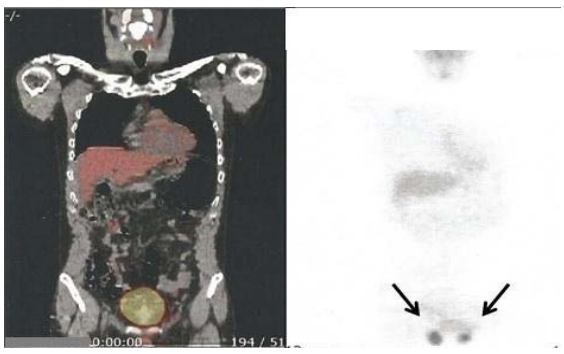

Figure 1: PET/CT image. Bilateral FDG uptake in the testes.

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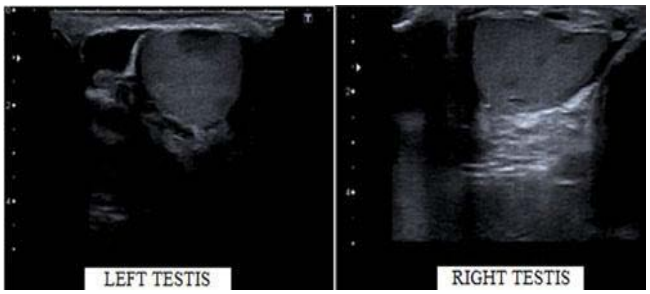

Figure 2: Testicular ultrasound images. Ultrasound scan showed normal testes size and several hypo echoic nodules in both testes (up to 11 mm in left testis and 6 mm in right testis). Doppler ultrasonography revealed hyper vascularity of the nodules.

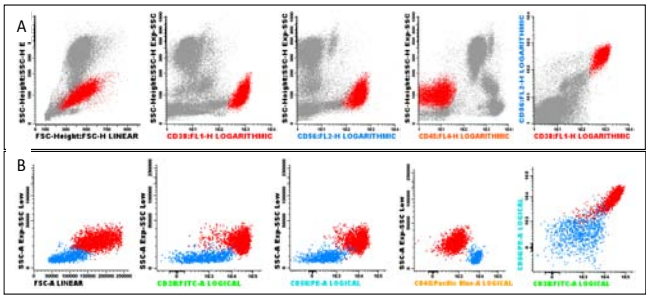

Figure 3: Immunophenotypic studies performed by multiparameter flow cytometry. (A) These dot plots illustrate immunophenotype of aberrant plasma cells, marked in red, in bone marrow at diagnosis (CD138+, CD38+, CD56+, CD19-, CD45-). (B)These dot plots show immunophenotype of aPC, marked in red, in testicular sample obtained by Fine needle aspiration. Lymphocytes are marked in blue. We point out the same immunophenotype of aPC at diagnosis and at the time of relapse both in bone marrow and testicular sample.

doxorubicin, cyclophosphamide and etoposide). Pathology confirmed bilateral synchronous testicular plasmacytoma (Figure 4 and 5). The patient subsequently received allo-peripheral blood SCT using myeloablative conditioning (total body irradiation plus cyclophosphamide). No significant transplant-related complications emerged, with the exception of intestinal acute Graft-Versus-Host Disease (GVHD) (grade Ia) treated with topical steroids. On day + 100 after allo-SCT, serum M-protein (0.1 g/dL) and 1 % of BM CP (77% aPC) are still present, although complete chimerism is achieved and PET/CT remains negative. Our goal is to maintain the lowest immunosuppression levels as possible to achieve graft-versus-tumour effect.

Discussion

MM is a neoplastic plasma cell disorder characterized by the proliferation of clonal plasma cells in the bone marrow with monoclonal immunoglobulin production [2]. When clonal PC arises in tissues other than bone are called Extramedullary Plasmacytomas (EMP). EMP constitute 3-5% of all plasma cell neoplasms [3]. The incidence of EMP is up to 18% at MM diagnosis and higher at relapse [4]. The commonest involved sites are the upper respiratory and the gastrointestinal tracts, whereas testicular involvement is very rare [5] (0.03-0.1% of all primary and secondary testicular tumors) [6]. Differential diagnosis with spermatocytic seminoma and testicular lymphoma [7] has to be made. In our patient, normal serum tumor

Figure 4: Gross Appearance of Testes. Solid and whitish area of replacement of the testicular parenchyma and a foci of hemorrage.

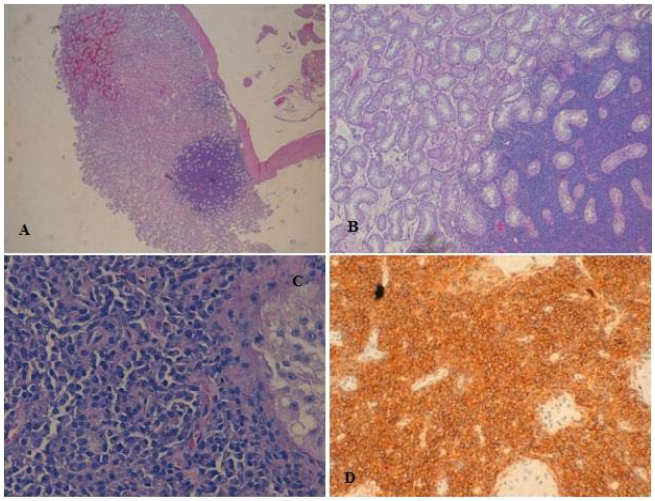

Figure 5: Pathology images. (A): HEMATOXILIN-EOSIN PANORAMIC VIEW OF TESTIS. Testicular parenchyma distorted by a nodule of blue small cells. (B): HEMATOXYLIN-EOSIN 4X MAGNIFICATION. Sheets of lymphoplasmacytic cells showing intertubular growth, respecting seminiferous tubules. (C): HEMATOXYLIN-EOSIN 40X MAGNIFICATION. Tumor cells with eccentrically placed nuclei, dispersed chromatin and basophilic cytoplasm. (D): CD38 INMUNOSTAIN 20X MAGNIFICATION. Cytoplasmic reactivity for CD38 in neoplastic cells.

markers discarded this diagnosis and the testicular fine-needle aspiration was performed.

Less than 80 cases of testicular plasmacytomas are published, even more exceptionally is the bilateral and synchronous involvement. To our knowledge, 3 cases [8-10] of bilateral and synchronous testicular plasmacytomas have been published. Painless scrotal swelling is usually present, but in our patient the testicular involvement was completely asymptomatic. PET/CT is included in our work-up before allo-SCT and we detected the testicular involvement. Otherwise, it may be that we have misunderstood a relapse after allo-SCT. No prospective studies have ever been conducted to evaluate the efficacy of therapy, and there is not any standard treatment. Orchiectomy alone or in combination with radiotherapy and chemotherapy have been used, even SCT [11] in selected cases. Although the impact of the disease is unknown, however extramedullary disease has been associated with a poor prognosis [12,13].

The role of Positron Emission Tomography-Computed Tomography (PET/TC) [14] is very relevant in the diagnosis of plasmacytomas, particularly in this patient, because this technique

allowed detecting an asymptomatic testicular relapse. PET/CT has also a role in the assessment of response, because it is able to distinguish between active and inactive disease, and several studies are evaluating this role.

Although allogeneic SCT is a potentially curative option in MM, the introduction of new drugs together with the transplant-related mortality/morbidity and the high relapse risk make its use controversial [15]. It should be reconsidered with new agents, reduced intensity conditioning and selected patients (those with early relapse after optimal induction and ASCT and poor prognostic features like our patient) in the context of clinical trials. In our local experience [16], the transplant related mortality was of only 14%, with 41% of the patients alive at 5 years after allo-SCT.

Conclusion

We report a young multiple myeloma patient, with a high risk disease and a testicular extramedullary relapse after tandem ASCT. In this case, implementation of PET/CT pre-alloSCT allowed detecting an early and asymptomatic extramedullary relapse. The singularity of this case is that synchronous and bilateral testicular involvement in MM is extremely rare. Treatment strategy should combine surgery, local radiotherapy, chemotherapy and, in selected patients, allo-SCT. Even though, we need more prospective studies to evaluate the role of PET/CT in MM, this patient shows that MM is not only a disease within bone marrow and extramedullary assessment is useful in selected patients, and it will be part of standard management in the near future.

References

1. Rosinol L, Oriol A, Teruel AI, Hernandez D, Lopez-Jimenez J, de la Rubia J, et al. Superiority of bortezomib, thalidomide, and dexamethasone (VTD) as induction pretransplantation therapy in multiple myeloma: a randomized phase 3 PETHEMA/GEM study. Blood. 2012; 120: 1589-1596.

2. Palumbo A, Anderson K. Multiple myeloma. N Engl J Med. 2011; 364: 1046-1060.

3. Swerdlow S, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, et al. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Lyon: IARC Press. 2008.

4. Blade J, Fernandez de Larrea C, Rosinol L, Cibeira MT, Jimenez R, Powles R. Soft-tissue plasmacytomas in multiple myeloma: incidence, mechanisms of extramedullary spread, and treatment approach. J Clin Oncol. 2011; 29: 3805-3812.

5. Pow Sang M, Astigueta JC, Abad M, Sanchez J, Leon J. Testicular plasmacytoma as presentation of multiple myeloma: case report and review of the literature. Arch Esp Urol. 2013; 66: 242-248.

6. Anghel G, Petti N, Remotti D, Ruscio C, Blandino F, Majolino I. Testicular plasmacytoma: report of a case and review of the literature. Am J Hematol. 2002; 71: 98-104.

7. Raspollini MR. Histologic variants of seminoma mimicking lymphatic malignancies of the testis: a literature review with a reportof case series focusing on problems in differential diagnosis. Appl Immunohistochem Mol Morphol. 2014; 22: 348-357.

8. Pham TH, Shetty SD, Stone CH, De Peralta-Venturina M, Menon M. Bilateral synchronous testicular plasmacytoma. J Urol. 2000; 164: 781.

9. Castagna M, Gaeta P, Cecchi M, Pagni GL, Pingitore R. Bilateral synchronous testicular involvement in multiple myeloma. Case report and review of the literature. Tumori. 1997; 83: 768-771.

10. Garrido Abad P, Coloma Del Peso A, Bocardo Fajardo G, Jimenez Galvez M, Herranz Fernández LM, Arellano Ganan R, et al. Secondary bilateral testicular plasmacytoma. Case report and review of the literature. Actas Urol Esp. 2008; 32: 1039-1042.

11. Rosenberg S, Shapur N, Gofrit O, Or R. Plasmacytoma of the testis in a patient with previous multiple myeloma: is the testis a sanctuary site? J Clin Oncol. 2010; 28: 456-458.

12. Billecke L, Murga Penas EM, May AM, Engelhardt M, Nagler A, Leiba M, et al. Cytogenetics of extramedullary manifestations in multiple myeloma. Br J Haematol. 2013; 161: 87-94.

13. Paiva B, Chandia M, Vidriales MB, Colado E, Caballero-Velazquez T, Escalante F, et al. Multiparameter flow cytometry for staging of solitary bone plasmacytoma: new criteria for risk of progression to myeloma. Blood. 2014; 124: 1300-1303.

14. Zamagni E, Cavo M. The role of imaging techniques in the management of multiple myeloma. Br J Haematol. 2012; 159: 499-513.

15. Rosinol L, Perez-Simon JA, Sureda A, de la Rubia J, de Arriba F, Lahuerta JJ, et al. A prospective PETHEMA study of tandem autologous transplantation versus autograft followed by reduced-intensity conditioning allogeneic transplantation in newly diagnosed multiple myeloma. Blood. 2008; 112: 3591-3593.

16. Lopez-Godino O, et al. Long-term follow-up of Allogeneic Hematopoietic Stem Cell Transplantation for multiple myeloma patients. In: Physicians Poster Sessions. 40th Annual Meeting of European Society of Blood and Marrow Transplantation; 2014.

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