International Journal of Innovation and Scientific Research
ISSN 2351-8014 Vol. 53 No. 2 Mar. 2021, pp. 174-179

http://www.ijisr.issr-journals.org/

Bladder extramedullary plasmacytoma: An unusual location revealing multiple myeloma

Zineb El Hamzaoui[1-2], H. Bencharef[1-2], FZ. Alouhmy[1-2], Y. Ghannam[1-3], H. Moudlige[1-3], M. Dakir[1-3], A. Debbagh[1-3], R. Aboutaib[1-3], and B. Oukkache[1-2]

[1]Hematology Laboratory, Ibn Rochd University Hospital of Casablanca, Morocco

[2]Medicine and Pharmacy Faculty, Hassan II University, Casablanca, Morocco

[3]Urology Department, Ibn Rochd University Hospital of Casablanca, Morocco

ABSTRACT: *Background*: Extramedullary plasmacytoma is an immunoproliferative monoclonal disease of the B-cell line that originates from malignant transformed plasma cells. It's a rare variant of plasma cell tumor involving organs outside the bone marrow, found in 13% of cases. Urinary bladder involvement remains a location rarely reported in the literature. Herein, we report a case of bladder extramedullary plasmacytoma revealing multiple myeloma. *Case report*: A 49-year-old man presented to the urology department with an acute obstructive renal failure revealed by renal colic and dysuria gradually evolving over 2 months. The renal ultrasound and the pelvic abdominal CT scan revealed a bilateral ureter hydronephrosis with a locally advanced bladder tumor. The patient underwent surgical resection of the tumor and the histopathology study of surgical specimen showed an infiltration of the urothelial mucosa by abnormal plasma cells. The bone marrow aspirate established the presence of 59% of abnormal plasma cells and rouleaux formation of red blood cells, serum protein electrophoresis showed a monoclonal peak in the area of gamma globulin, and the conventional radiography of the axial skeleton objectifies lytic spine lesions. The diagnosis of a multiple myeloma associated to an extramedullary bladder location was retained. The outcome was unfavorable and the patient died of severe pulmonary embolism before initiating any therapy. *Conclusion*: Secondary extramedullary plasmacytoma is a marker of poor prognosis in both newly diagnosed and relapsed multiple myeloma patients. Bladder location remains a rare entity, the clinical presentation is nonspecific and management constitutes a therapeutic challenge even in the era of new agents.

KEYWORDS: Extramedullary plasmocytoma, bladder, multiple myeloma, plasma cell, acute obstructive renal failure.

1 INTRODUCTION

Extramedullary plasmacytoma is an immunoproliferative monoclonal disease of the B-cell line that originates from malignant transformed plasma cells. It's a rare variant of plasma cell tumor involving organs outside the bone marrow, often secondary to a systemic myelomatosis [1].

Extramedullary locations of multiple myeloma are rare, found in 13% of cases, 6 to 8% in newly diagnosed patients against 10 to 30% in relapsed or refractory patients; it indicates a very aggressive disease with short overall survival and a worse prognosis [2], [3].

These solid lesions most commonly affect the upper respiratory tract, followed by lymphatic tissue, liver, kidneys, skin, and central nervous system (CNS). Urinary bladder involvement remains a location rarely reported in the literature [4], [5], only 10 to 20% of bladder plasmacytomas progress to multiple myeloma [6].

We report a case of bladder plasmacytoma revealing multiple myeloma.

Corresponding Author: Zineb El Hamzaoui

2 CASE REPORT

A 49-year-old man with no significant medical history presented to the urology department with acute obstructive renal failure revealed by renal colic and dysuria gradually evolving over 2 months without any other associated signs.

On physical examination, the patient was in fairly good general state and presented neither distended bladder nor tumor nor pain on the kidney area.

A renal ultrasound and a pelvic abdominal CT scan revealed a bilateral ureterohydronephrosis with bladder thickening and a locally advanced bladder tumor. (Figure 1 and 2)

Blood tests showed a renal failure with a serum creatinine level at 75 mg/l (7-13 mg / l), uricemia at 1.08 g/l (0.13-0.43 g / l) and a glomerular filtration rate (GFR) estimated using the MDRD formula to 8 ml/min/1.73m² (90-120 ml/min/1.73m²), associated to a normochromic normocytic anemia at 9.8g / dl (13-18g / dl). Calcemia was normal, with no other biological abnormalities.

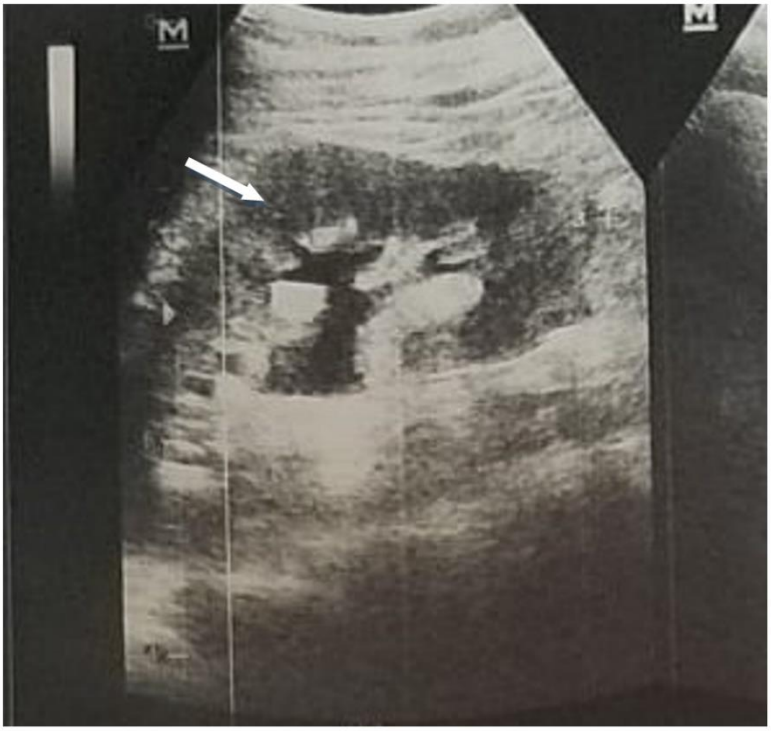

Fig. 1. A renal ultrasound image bladder showing thickening and a locally advanced bladder tumor

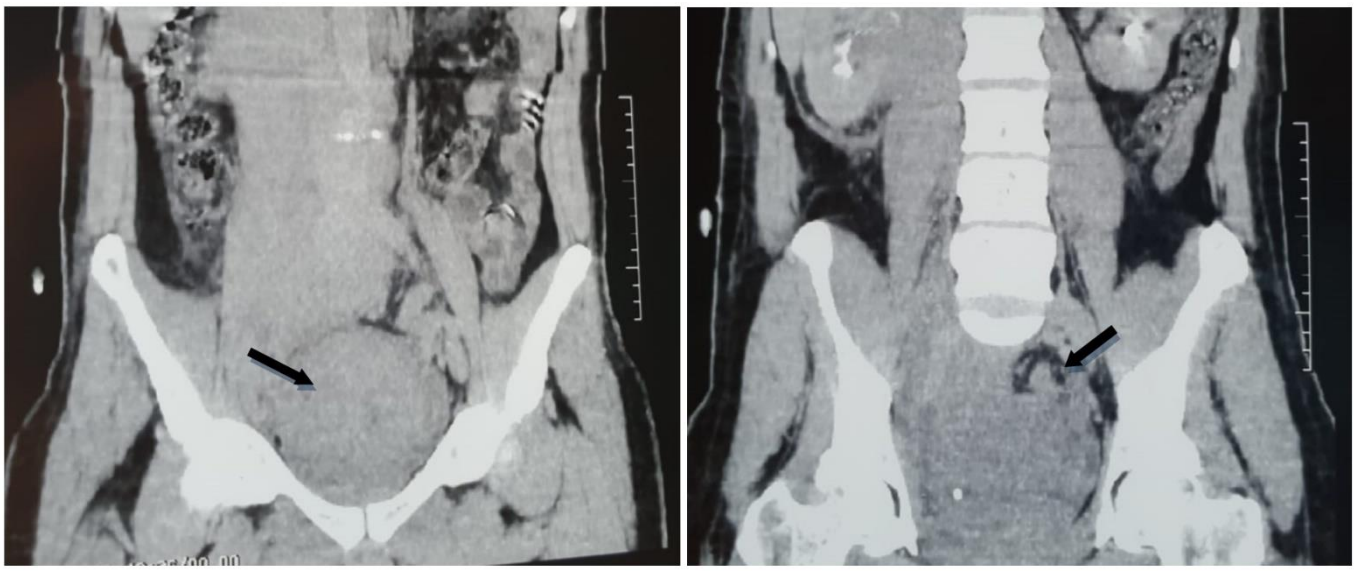

Fig. 2. A frontal section of a pelvic abdominal Computed tomography scan showing bladder thickening and a locally advanced bladder tumor

The patient underwent surgical resection of the tumor and the histopathology study of surgical specimen showed a diffuse infiltration of the urothelial mucosa by sheets of round tumor cells presenting a plasma cell differentiation with a diffuse expression of CD138 and light chains kappa in the immunohistochemistry study.

Additional work up for multiple myeloma has been requested; the bone marrow aspirate established the presence of 59% of abnormal plasma cells and rouleaux formation of red blood cells (figure 3), serum protein electrophoresis showed hypeproteinemia at 97g/l (60-80 g/l) associated to a monoclonal peak in the area of gamma globulin with a level of 44.4g/l (8-13.5 g / l) (figure 4), and the conventional radiography of the axial skeleton objectifies lytic spine lesions. The diagnosis of a multiple myeloma associated to an extramedullary bladder location was retained.

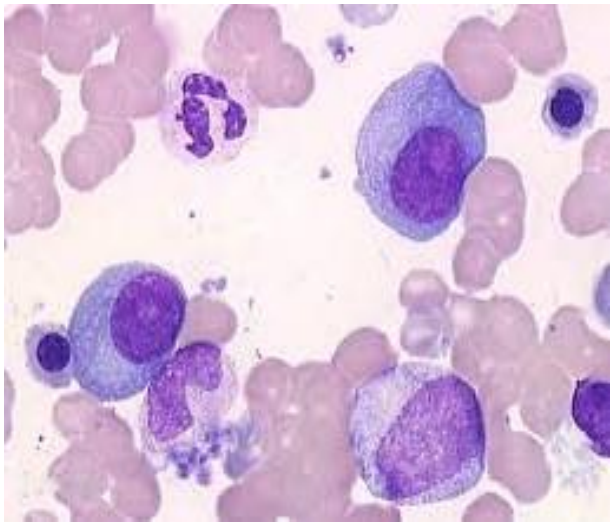

Fig. 3. Bone marrow cytology showing abnormal plasma cells and rouleaux formation of red blood cells

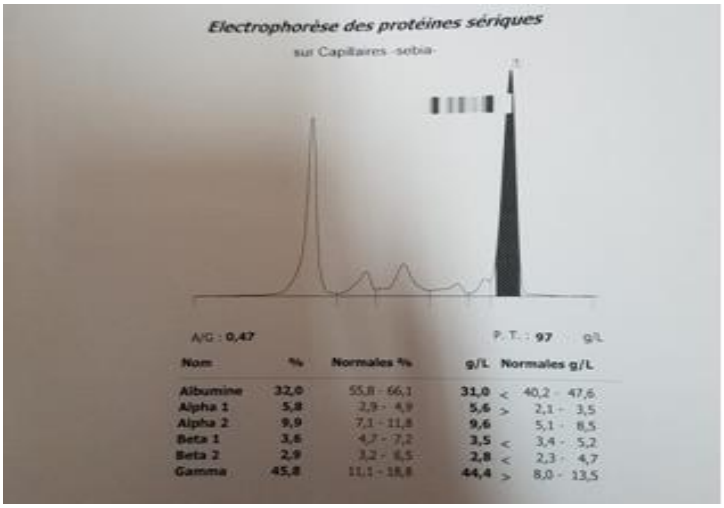

Fig. 4. Serum protein electrophoresis showing a monoclonal peak in the area of gamma globulin

Despite the correction of kidney function following the surgery, the outcome was unfavorable and the patient died of severe pulmonary embolism before the initiation of any therapy.

3 DISCUSSION

Extramedullary plasmocytoma is defined by the presence of plasma cells outside the bone marrow; it has two major subtypes, primary when it's isolated and secondary when it's associated to prior bone-marrow involvement [5], [7].

The importance of diagnosing patients with atypical presentations cannot be understated as approximately 10–20% of multiple myeloma patients do not present lytic lesions on radiography [8], It is also important to note that the incidence of extramedullary myeloma is found to be 6–8% of newly diagnosed multiple myeloma patients [7]. The prevalence increases to 10–30% in relapsed/refractory patients. The disease remains incurable; however improving diagnosis and therapies have led to increasing length of survival, which has in turn increased the prevalence of atypical disease progression or features of relapse, such as extramedullary lesions [9].

According to a literature review reported by Jeff Ames et al [3], collating 2027 cases of extramedullary multiple myeloma over a period of 50 years; the most affected extraosseous anatomical sites are the upper airways (33.8%), followed by soft tissues including the abdomen and retroperitoneum (14.1%), the gastrointestinal tract (10.3%), the central nervous system, head and neck (16%), the genitourinary system (2.4%) and lastly the soft parts of the extremities (1.7%).

Bladder involvement is unusual and therefore poorly described. According to the same review, only 5 cases out of 2027 were found.

The pathophysiological mechanisms underlying the hematogenous spread of plasma cells outside the bone marrow remain unclear, and hypotheses have been suggested by various authors.

According to Manisha et al [10], the primary genetic events endow tumor-initiating abilities in a clone of plasma cells susceptible to progress from precursor states to active multiple myeloma; while acquisition of secondary and terminal genetic events, in collaboration with microenvironment influence, intra and extracellular signaling, epigenetic changes and immune evasion, potentially trigger egress to ecosystems outside the bone marrow (figure 5). Once in circulation, these cells must overcome several challenges in order to survive; including failure to attach to a substrate, hydrodynamic flow, shear stress and immune interactions that can target malignant cells for elimination.

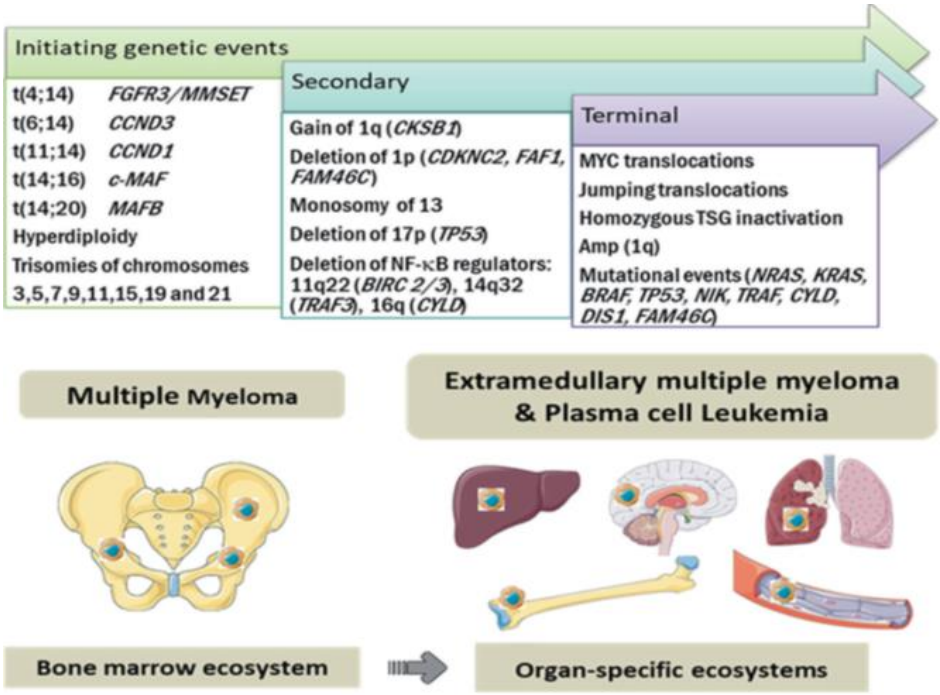

Fig. 5. Model illustrating central drivers in pathogenesis of extramedullary multiple myeloma [10]

Another study by AZAB et al [11] suggests that regional hypoxia of the bone marrow promotes the spread of myeloma cells in the same way that solid tumor metastases.

The molecular pathogenesis underlying the extramedullary spread of plasma cells is only partially understood. Extramedullary myeloma plasma cells are characterized by a decreased expression of the CD56 adhesion molecule and an increased expression of CD44, which is involved in cell proliferation and migration [12], [13]. The increased expression of CXCR4 and its ligand CXCL12 have also been implied to contribute to the dissemination of plasma cells, notably through the activation of an epithelial-mesenchymal transition pattern [14].

Urinary symptoms are nonspecific, hematuria and irritative bladder symptoms are more described than obstructive bladder symptoms notably dysuria [4], [10]. No case of renal colic has been reported, contrary to our case where the obstructive renal failure was revealed by a renal colic.

The diagnosis is based on the histopathology and immunohistochemistry study of the tumor process demonstrating a proliferation of abnormal plasma cells characterized by a similar range of immunophenotypic abnormalities to those encountered in standard myeloma, in particular a low expression of CD19, CD45, and CD27 and an aberrant expression of CD56, CD117, CD27 and CD20 [15], in addition to an increased expression of CD44 isoforms involved in cell proliferation and migration [10].

The simultaneous presence of bone marrow plasma cell infiltration, monoclonal immunoglobulinemia, and bone involvement suggests a secondary extramedullary plasmacytoma revealing multiple myeloma as reported in our case.

Data on the prognostic impact of extrameullary involvement in multiple myeloma are limited and controversial, but their presence at diagnosis indicates a very aggressive disease with short overall survival [2]. Furthermore, in relapse cases, the prognosis is worse with an overall survival less than 6 months [16].

In cases of secondary extramedullary plasmocytoma, radiotherapy or surgery alone is insufficient, and systemic therapy is required. In younger patients, the use of immunomodulatory drugs with induction agents in combination with autologous hematopoietic stem cell transplant results in higher remission rates and overall survival [17].

In our case, the outcome was unfavorable and the patient died of severe pulmonary embolism before the initiation of any therapy.

4 CONCLUSION

Secondary extramedullary plasmacytoma is a marker of poor prognosis in both newly diagnosed and relapsed multiple myeloma patients. Bladder location remains a rare entity, the clinical presentation is nonspecific and management constitutes a therapeutic challenge even in the era of new agents.

ACKNOWLEDGMENTS

Grateful thanks to the urologists' team for their collaboration by providing the clinicals informations for the redaction of this article.

REFERENCES

[1] Shizuhiro Hirata, Koji Yamaguchi, Sachiko Bandai et al Secondary extramedullary plasmacytoma involving the pancreas, J Hepatobiliary Pancreat Surg (2002) 9: 111–115.

[2] Varettoni M, Corso A, Pica G, et al. Incidence, presenting features and outcome of extraosseous disease in multiple myeloma: a longitudinal study on 1003 consecutive patients. Ann Oncol 2010; 21: 325-30.

[3] Jeff Ames, Ahmad Al-Samaraee, Takashi Takahashi et al "Extraosseous Multiple Myeloma: Case Report of Presentation in the Lower Extremity Soft Tissues with Literature Review", Case Reports in Radiology, vol. 2017, Article ID 9159035, 9 pages, 2017.
Available on https://doi.org/10.1155/2017/9159035.

[4] Alvin Lopez, Freddy Mendez, Antonio Puras-Baez. Extramedullary plasmacytoma invading the bladder: case report and review of the literature, May 2003
Doi: 10.1016/S1078-1439 (03) 00076-0.

[5] Lydie OciniNgolet, Norbert LaminiN'soundhat, Eliane Ndounga et al, plasmocytome cutané secondaire révélant un myélome multiple: à propos d'un cas. Pan Afr Med J2016; 24: 44. 10.11604/pamj.2016.24.44.8697.

[6] D. Klifa, J. Verine, O. Mathieu et al. Tumeurs non épithéliales de la vessie. EMC 2008.
Doi: 10.1016/S1762-0953 (08) 46407-5.

[7] C. Touzeau and P. Moreau, "How I treat extramedullary myeloma," Blood, vol. 127, no. 8, pp. 971-976, 2016.

[8] R. Ferraro, A. Agarwal, E. L. Martin-Macintosh, et al. "MR imaging and PET/CT in diagnosis and management of multiple myeloma". RadioGraphics. vol. 35, no. 2, pp. 438–454, 2015.

[9] S. K. Kumar, S. V. Rajkumar, A. Dispenzieri et al., "Improved survival in multiple myeloma and the impact of novel therapies, " Blood, vol. 111, no. 5, pp. 2516–2520, 2008.

[10] Manisha Bhutani, David M Foureau, Shebli Atrash et al. Extramedullary multiple myeloma Leukemia 2020 Jan; 34 (1): 1-20.
Doi: 10.1038/s41375-019-0660-0.

[11] Azab AK, Hu J, Quang P, et al. Hypoxia promotes dissemination of multiple myeloma through acquisition of epithelial to mesenchymal transition-like features. Blood 2012; 119 (24): 5782-5794.

[12] Bladé J, Fernandez de Larrea C, Rosinol L, et al. Soft-tissue plasmacytomas in multiple myeloma: incidence, mechanisms of extramedullary spread, and treatment approach. J Clin Oncol. 2011; 29 (28): 3805-3812.

[13] Dahl IMS, Rasmussen T, Kauric G, Husebekk A. Differential expression of CD56 and CD44 in the evolution of extramedullary myeloma. Br J Haematol. 2002; 116 (2): 273-277.

[14] Roccaro AM, Mishima Y, Sacco A, et al. CXCR4 regulates extra-medullary myeloma through epithelial-mesenchymal-transition-like transcriptional activation. Cell Reports. 2015; 12 (4): 622-635.

[15] Boll M, Parkins E, O'Connor SJ, Rawstron AC, Owen RG. Extramedullary plasmacytoma are characterized by a 'myeloma-like' immunophenotype and genotype and occult bone marrow involvement. Br J Haematol. 2010; 151 (5): 525–527.

[16] Pour L, Sevcikova S, Greslikova H, et al. Soft tissue extramedullary multiple myeloma prognosis is significantly worse in comparison to bonerelated extramedullary relapse. Haematologica. 2014; 99 (2): 360-364.

[17] Lopes Da, Silva R. Extramedullary plasmacytoma of the small intestine: clinical features, diagnosis and treatment. J Dig Dis. 2012; 13: 10–18.
Doi: 10.1111/j.1751-2980.2011.00544.x.