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Multiple myeloma with secondary cutaneous plasmacytomas: case report

Mieloma múltiplo com plasmocitomas cutânea secundária: relato de caso

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| Abstract

Multiple myeloma is a neoplasm characterized by abnormal and monoclonal proliferation of plasmacytes in the bone marrow. About 5-10% of patients develop skin lesions, which can be classified into nonspecific or specific. The specific impairment is rare and called secondary plasmacytoma of the skin. Typically, it manifests in the form of erythematous plaques or nodules in the cephalic segment, upper limbs, or trunk. It may be directly related to an underlying bone lesion or the hematogenous dissemination.

We describe the case of a 50-year-old female patient diagnosed with Lambda light chain multiple myeloma, Durie and Salmon stage III A and high risk IPSS. Despite being on chemotherapeutic treatment, she developed after 11 months of disease onset, medullary compression by plasmacytomas at the C5-C6-T1 level, manifested with paresis of the upper limbs and plegia of the lower limbs. In association, she developed erythematous nodules on the scalp. The histopathological analysis of the skin lesion revealed dense infiltrate of plasmacytes with nuclear hyperchromasia, forming mantles in the dermis and hypodermis. The immunohistochemistry indicated compatible profile with plasmacytoma and the cranial x-ray showed osteolytic lesions, which established the diagnosis of secondary cutaneous plasmacytoma by extension of bone lesion. After 5 months of skin affection, the patient died.

We concluded that skin affection tends to occur in patients with multiple myeloma in late stages of the disease and shows a high tumor load, thereby leading to the association with a worse prognosis, with survival of few months.

| Keywords

Multiple myeloma, skin, plasmacytoma

| Resumo

O mieloma múltiplo é uma neoplasia, que se caracteriza pela proliferação anormal e monoclonal de plasmócitos na medula óssea. Cerca de 5 a 10 % dos pacientes desenvolvem lesões cutâneas, que podem ser classificadas em inespecíficas ou específicas. O comprometimento específico é raro e denomina-se plasmocitoma cutâneo secundário. Normalmente se manifesta sob a forma de placas ou nódulos eritematosos no segmento cefálico, membros superiores ou tronco. Pode estar relacionado à extensão direta de uma lesão óssea subjacente ou à disseminação hematogênica.

Descrevemos o caso de uma paciente de 50 anos, diagnosticada com mieloma múltiplo secretor de cadeia leve lambda, Durie e Salmon III A e IPSS

| Palavras-chave

Mieloma múltiplo, pele, plasmocitoma

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de alto risco. Apesar de estar em tratamento quimioterápico, após 11 meses do início do quadro desenvolveu compressão medular a nível C5-C6-T1 por plasmocitomas, manifestando-se com paresia de membros superiores e plegia de membros inferiores. Associado desenvolveu nódulos eritematosos no couro cabeludo. A análise histopatológica da lesão cutânea revelou denso infiltrado de plasmócitos com hipercromasia nuclear, na derme e hipoderme. A imuno-histoquímica indicou perfil compatível com plasmocitoma e a radiografia de crânio demonstrou lesões osteolíticas, estabelecendo-se o diagnóstico de plasmocitoma cutâneo secundário por extensão de lesão óssea. Após 5 meses do acometimento cutâneo, a paciente evoluiu a óbito.

Concluímos que o comprometimento cutâneo em pacientes com mieloma múltiplo tende a ocorrer em estágios tardios da doença e demonstra uma alta carga tumoral, assim associa-se a um pior prognóstico, com sobrevida de poucos meses.

| Introduction

Multiple myeloma is a hematologic neoplasm characterized by abnormal and monoclonal proliferation of plasmocytes in the bone marrow. The type of monoclonal protein produced by these plasmocytes is variable, and it may be an immunoglobulin or an immunoglobulin fragment, detected at the serum and/or urine. The most common type is the IgG (52%), followed by IgA (21%), Kappa or Lambda light chain (16%), IgD (2%), biclonal (2%), and IgM (0.5%). The non-secretory form represents 6.5% of cases.[1,2]

Among the hematologic neoplasms, multiple myeloma accounts for 13% of all cases.[3] In the United States, approximately 20,000 new cases are diagnosed each year, with higher incidence amongst males.[4]

About 5 to 10% of patients develop a skin lesion, which may be classified as nonspecific (amyloidosis, plane xanthomas, subcorneal pustular dermatosis, leukocytoclastic vasculitis, Sweet's syndrome, pyoderma gangrenosum, necrobiotic xanthogranuloma, and scleromyxedema) or specific (secondary cutaneous plasmacytoma).[6,7]

Here, we describe an uncommon case of secondary cutaneous plasmacytomas by extension from an underlying bone lesion, in a patient with Lambda light chain secretory multiple myeloma. We evidence the prognostic meaning of this lesion, justifying the importance of its inclusion in the differential diagnosis.

| Case Report

50-year-old patient, female, caucasian, looked for the Orthopaedics Service due to lower back pain and significant weight loss in six months. During diagnostic investigation, the following tests were taken: alkaline phosphatase: 136 U/L; calcium: 10.7 mg/dL; creatinine: 0.66 mg/dL; urea: 34 mg/dL; hemoglobin: 12.8mg/dL; albumin: 2,4 g/dL: beta-2 microglobulin:5,5 g/dL; and lower spine computed tomography: lytic lesions in L1, L2, L3, L4, L5 and S1.

Biopsy of the patient's spine was taken, and it showed slightly differentiated plasmocyte neoplasia and anaplasic plasmocytoma with light Lambda chain restriction, as confirmed by immunohistochemistry (CD20 and cytokeratin AE1 / AE3 negative; CD138, CD79a, MUM1 and CD56 positive; and Lambda positive in most neoplastic cells).

From that point on, the patient began to be assisted by the Hematology Service. Her serum protein electrophoresis did not evidence a monoclonal peak, but the *urine immunofixation* showed monoclonal Lambda protein and her bone marrow examination showed 25% dysplasic plasmocytes. Thus, the patient was diagnosed with light Lambda chain secreting multiple myeloma, Durie and Salmon stage III A and high risk IPSS.

Despite being on chemotherapeutic treatment with cyclophosphamide, thalidomide and dexamethasone, after 11 months of symptoms onset, the patient developed paresis of the upper limbs and plegia of the lower limbs, due to spinal cord compression at C5-C6-T1. It was observed that after one month of this neurological complication, she developed erythematous nodules on the scalp. The most significant lesion was located in the right parietal region, with 2.5 cm in its wider diameter (figure 1). The histopathological analysis of this lesion revealed dense infiltrate of plasmacytes with nuclear hyperchromasia, forming mantles; the process accompanies the hair follicles and involves vessels in the dermis and hypodermis, with the epidermis being preserved (figures 2 and 3). The immunohistochemistry showed positive profile for CD138 (diffuse) and Lambda (focal).

By associating these findings with the presence of osteolytic lesions in the skull, as observed upon x-rays (fig-

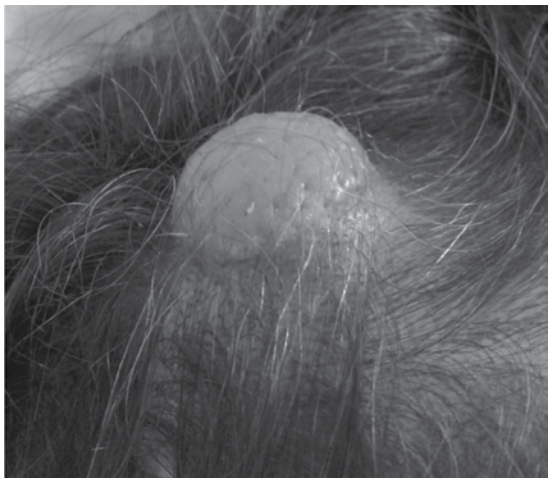

Figure 1. Erythematous nodule in the right parietal region, with 2.5 cm in its wider diameter.

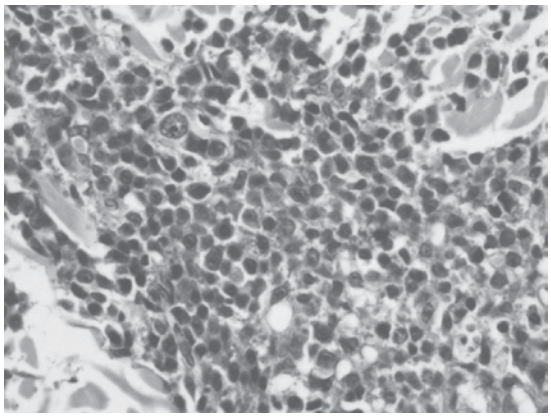

Figure 3. Dense infiltrate of plasmocytes with nuclear hyperchromasia in the dermis (H.E., 400X).

ure 4), we corroborated the secondary cutaneous plasmacytoma diagnosis by extension from a bone lesion. Five months after the skin impairment, the patient died.

| Discussion

Extra-bone plasmacytomas account for 3-5% of plasmacytic neoplasms only, with 80% of them occurring in the pharynx, facial sinuses, or larynx.[8] Therefore, secondary cutaneous plasmacytoma is an uncommon form of the disease. It is most commonly associated with multiple myeloma with monoclonal peak of IgG (54%), with only 4% of cases being associated with the secretory form of light chains, as it is our case.[8] This lesion may appear anywhere in the body; however, 49.5% occur on the thorax and 20% on the head and neck regions, typically in the form of multiple nodules or erythematous-violaceous plaques.[5,7,8]

There are two classic subtypes, with the most commonly seen being by direct extension from an underlying lesion, which is similar to our case. The other subtype is due to hematogenic dissemination.[2,5,7]

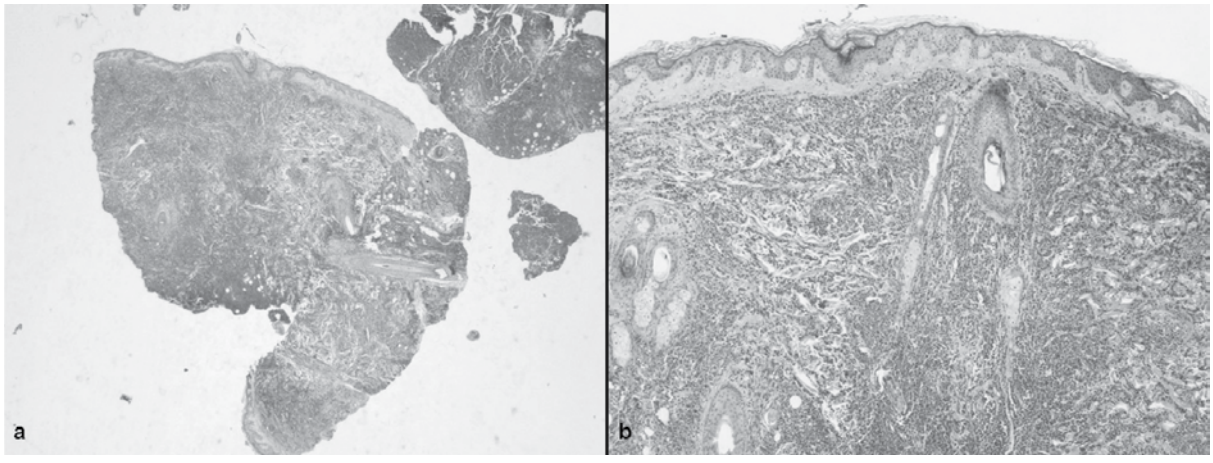

Figure 2. a. Histopathology showing a diffuse infiltrate in the dermis and hypodermis (H.E., 40X). **b.** Cellular infiltrate forming mantles on the dermis, which follow hair follicles and blood vessels. Note that the epidermis and the papillary dermis are preserved (H.E., 100X).

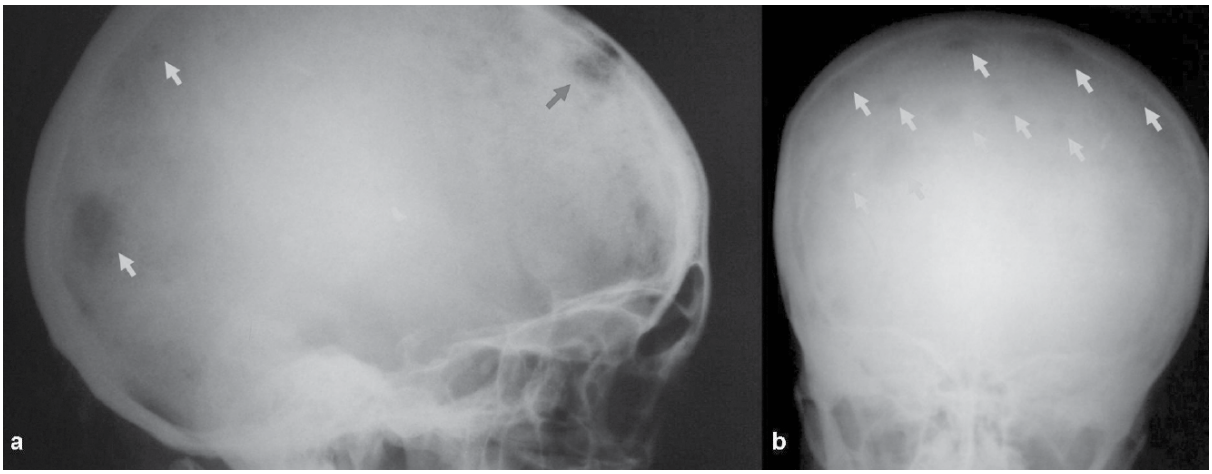

Figure 4. a. X-ray latero-lateral incidence of the skull, revealing radiolucent areas that represent the osteolytic lesions (yellow arrows). The red arrow shows the osteolytic lesion in the topography underlying the most significant skin nodule, suggesting the lesion origin. **b.** X-ray postero-anterior incidence of the skull, evidencing several osteolytic lesions (yellow arrows).

The diagnosis of this complication, regardless the subtype, tends to occur in late stages of the disease and show high tumor load, with an estimated tumor mass of 2 to 3 Kg.[8] According to Durie and Salmon classification system, stage III has a tumor load > 1.2 X 10^{12} m^2 and global survival median is 52.1 months.[2] However, the presence of cutaneous infiltration is correlated with a more aggressive clinical systemic course and suggests a poorer prognosis, in which the mean survival is 12 months, no matter the staging and the established therapy.[8]

Cytogenetic analysis studies showed higher prevalence of 13q, 11q and rb-1 deletion in aggressive clinical cases, including extra-medullary affection.[8,9,10]

We concluded that skin affection tends to occur in patients with multiple myeloma in late stages of the disease and shows a high tumor load, thereby leading to the association with a worse prognosis, with survival of few months. Our patient had a 5-month survival after developing the skin lesion, which reflects the aggressive nature of the disease.

| Statement of Ethics

The authors have no ethical conflicts to disclose.

| Conflicts of Interest

The authors have no conflicts of interest to declare.

Noriega, L.F. *et al.* Multiple myeloma with secondary cutaneous plasmacytomas: case report. **Clinical Oncology Letters**. 2016;2(1):19-22.

| References

1. Kyle R, Gertz O, Witzig T, Lust J, Lacy M, Disperenzi A, Fonseca R, Rajkumar S, Offord J, Larson D, Plevak M, Thernaeu T, Greipp P. Review of 1027 patients with newly diagnosed multiple myeloma. Mayo Clinic Proceedings. 2003;78:21–33.
2. Hungria VT, Crusoe EQ, Quero AA, Sampaio M, Maiolino A, Bernardo WM. Guidelines on the diagnosis and management of multiple myeloma treatment: Associação Brasileira de Hematologia e Hemoterapia e Terapia Celular Project guidelines: Associação Médica Brasileira - 2012. Rev Bras Hematol Hemoter. 2013;35(3):201-17.
3. Palumbo A, Anderson K. Multiple myeloma. N Engl J Med. 2011 Mar 17;364(11):1046-60.
4. Agarwal A, Mahadevan D. Novel targeted therapies and combinations for the treatment of multiple myeloma. Cardiovasc Hematol Disord Drug Targets. 2013 Mar 1;13(1):2-15.
5. Bird JM, Owen RG, D'Sa S, Snowden JA, Pratt G, Ashcroft J, Yong K, Cook G, Feyler S, Davies F, Morgan G, Cavenagh J, Low E, Behrens J; Haemato-oncology Task Force of British Committee for Standards in Haematology (BCSH) and UK Myeloma Forum. Guidelines for the diagnosis and management of multiple myeloma 2011. Br J Haematol. 2011 Jul;154(1):32-75.
6. BULEFARB SM. Cutaneous manifestations of multiple myeloma. AMA Arch Derm. 1955 Dec;72(6):506-22.
7. Pereira N, Brinca A, Tellechea O, Gonçalo M. Plasmocitoma cutâneo metastático em doente com mieloma múltiplo. Revista SPDV. 2012;70(3):387-90.
8. Requena L, Kutzner H, Palmedo G, Calonje E, Requena C, Pérez G, Pastor MA, Sangueza OP. Cutaneous involvement in multiple myeloma: a clinicopathologic, immunohistochemical, and cytogenetic study of 8 cases. Arch Dermatol. 2003 Apr;139(4):475-86.
9. Tricot G, Barlogie B, Jagannath S, Bracy D, Mattox S, Vesole DH, Naucke S, Sawyer JR. Poor prognosis in multiple myeloma is associated only with partial or complete deletions of chromosome 13 or abnormalities involving 11q and not with other karyotype abnormalities. Blood. 1995 Dec 1;86(11):4250-6.
10. Königsberg R, Zojer N, Ackermann J, Krömer E, Kittler H, Fritz E, Kaufmann H, Nösslinger T, Riedl L, Gisslinger H, Jäger U, Simonitsch I, Heinz R, Ludwig H, Huber H, Drach J. Predictive role of interphase cytogenetics for survival of patients with multiple myeloma. J Clin Oncol. 2000 Feb;18(4):804-12.