

# MULTIPLE PRIMARY MALIGNANT NEOPLASMS IN THE MODERN THERAPEUTIC ERA - RECURRENT\REFRACTORY MULTIPLE MYELOMA AND SYNCHRONOUS SKIN SQUAMOUS CELL CARCINOMA: A CASE REPORT - COINCIDENCE OR BIDIRECTIONAL ASSOCIATION?



Kalysta Oliveira Resende Borges¹; Cairo Borges Junior ¹; Bianca Vitória Resente Almeida²; Giulia Manuella Resende Almeida²; Hiago Sousa Pinheiro¹; Fabio Augusto Meneses Sousa¹; Poliana Pezente¹; Carlos Augusto Moreira Silva¹; Marcos Fraga Fortes¹; Sândrea Ozane do Carmo Queiroz³.

<sup>1</sup>Oncológica Tapajós, Santarém-PA. <sup>2</sup>Centro Universitário IMEPAC, Araguari- MG. <sup>3</sup>Hospital Regional do Baixo Amazonas, Santarém-PA.

# Introdução

Cases of multiple primary malignant neoplasms (MPMNs) involving a solid tumor and a hematologic malignancy are rare. Multiple myeloma (MM) is the second most common hematologic malignancy, constituting 1-2% of malignancies worldwide and 2% of all cancer deaths. Austin A et al. (2016) published a retrospective cohort study of 205 myeloma patients, demonstrating a higher occurrence of skin cancer among MM patients compared with controls (26.8% vs. 16.1% in controls; p = 0.009), notably squamous cell carcinoma (SCC) (p = 0.016). Squamous cell carcinoma (SCC) of the skin is a malignant tumor (non-melanoma) that affects the cells of the skin epidermis. Immunosuppressed patients, prolonged sun exposure and sunburn; Clear Skin; Red hair, blue eyes and heredity are risk factors for an increased incidence of skin cancer. The diagnosis of skin SCC is made by physical examination, dermoscopy and histopathological analysis. Most squamous cell skin cancers are diagnosed and treated early, when they can still be removed or treated with local therapies.

### Casuística e Métodos

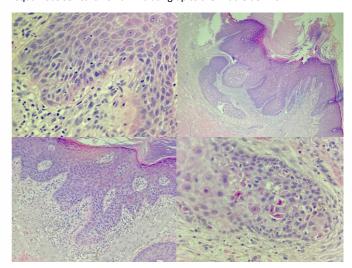
JRR, 62-year-old male, married, with level III of education, coming from and residing in the city of Santarém-Pará. The patient was admitted on August 2, 2016 to the urgent and emergency hospital environment in the city of origin, with extensive lytic bone disease, bedridden and confined to bed due to pain, with an increase in nitrogenous waste, anemic syndrome, hypercalcemia, in which was treated for the initial signs and symptoms and referred for follow-up by the Oncohematology specialty at a private clinic in the Western Amazon. As a personal history, in relation to habits, he denied smoking, alcoholism, use of illicit drugs and denied a history of endocrine and vascular diseases, heart diseases and surgeries. No history of exposure to ionizing radiation therapy. Patient was diagnosed with multiple myeloma R-ISS III on August 30, 2016 and treated with four cycles of the CyBorD chemotherapy protocol (cyclophosphamide, 300 mg/m² orally, bortezomib, 1.5 mg/m<sup>2</sup> SC and dexamethasone, 40 mg orally, on D1, D8, D15 and D22, every 28 days for 4 cycles) evolving with complete response, being submitted to autologous HSCT in April 2017. He continued in maintenance with thalidomide and monthly zoledronic acid until September 2019. Patient relapsed\ refractoriness in December 2019, where he started rescue treatment with Daratumumab, Carfilzomib, Lenalidomide and Dexamethasone (Dara-KRd) with maximum response, which is the current treatment. In November 2021, he presented an ulcerative-vegetative lesion, poorly delimited, measuring 1.0 x 0.8 cm in the wrist of the right upper limb, in which he was referred for evaluation by the oncological surgeon. He performed an excisional biopsy of the tissue lesion, obtaining a histopathological result for well-differentiated squamous cell carcinoma infiltrating up to the mid-dermis, without perineural or vascular invasions. Presenting neoplasm-free lateral and deep surgical margins (2 mm margin). The patient remains under dermatological surveillance, with no new suspicious lesions and on systemic antineoplastic therapy for multiple myeloma.

This is a descriptive study of the Case Study type, made possible through research in the medical records of a specific patient, registration of the diagnostic and therapeutic methods to which the patient was submitted and literature review, without causing pain or discomfort to the participant, without involving the collection of biological material and non-profit.

# Resultados

The report demonstrates a case of synchronous neoplasms in which the interrelationship between the occurrences is discussed. A male patient, 5th decade of life, MM diagnosed at an advanced stage, residing in the western Amazon, a region with a humid equatorial climate, with an average temperature of 27.9°C, with unequivocal sun exposure and presenting a primary hematologic malignancy with considerable immune dysfunction, having been submitted to myeloablative chemotherapy, relapse/refractory after HSCT with proven prolonged immunosuppression, both risk factors involved in the carcinogenesis of skin SCC, diagnosed 4 years after the first neoplasm in a relapse phase and during salvage chemotherapy. The early diagnosis of SCC of the skin allowed curative treatment, without interfering in the treatment of MM. Patient clinically well, being treated for MM, with no new evidence of PMS.

**Figure 01**: Histopathological lesion in MSD with well-differentiated squamous cell carcinoma infiltrating up to the middle dermis.



## Conclusão

The association between multiple myeloma and secondary solid neoplasms is not fully established. Analysis of population data revealed a bidirectional association between these two malignancies, notably in relation to immunological dysfunctions and therapeutic regimens. However, the scarcity of recommendations and guidelines limits the establishment of a direct correlation between multiple myeloma and skin SCC in the context of the report. In general, the risk of developing hematologic MPMNs should increase with longer duration of follow-up after the diagnosis of MM. Most studies did not explicitly decipher the relevant question of which factors favorably influence the occurrence of PMS, nor did they suggest mechanisms on how to avoid them. Based on the available evidence, the potential risk of MPMNs in MM is generally not expected to alter the current therapeutic decision-making process. Knowledge of the potential onset of PMS is imperative for early diagnosis and successful outcomes. Since the development of a second myeloma cancer remains substantially lower than the risk of death from multiple myeloma, active surveillance remains the best strategy in the early detection and screening of potential PMS and specific treatments.