Simultaneous Medullary Infiltration by Merkel Carcinoma and Myeloblastic Leukaemia: A Case Report

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Abstract

Merkel cell carcinoma is a very aggressive primary skin tumour with a high risk of local recurrences and lymphatic and distant metastases. It has been associated with a high incidence of other skin tumours and hematologic malignancies.

We report a case of an 82-year-old male with recent skin diagnosis of Merkel cell carcinoma who presented bone marrow metastases concomitantly with the diagnosis of minimally differentiated acute myeloblastic
leukaemia. The cellular morphology of both pathologies was very similar, but flow cytometry made it possible to differentiate the two cell populations, playing a decisive role in diagnosis.

There are few reports of Merkel cell carcinoma coexisting with myeloid leukaemia, as in our case. Merkel cell carcinoma is more frequently associated with lymphoid line disorders.

**Keywords**

Merkel cell carcinoma, acute myeloid leukaemia, flow cytometry.

**Introduction**

Merkel Cell Carcinoma (MCC) is a rare cutaneous tumour of neuroendocrine origin with an aggressive course \(^1,2\). It mainly affects males, people over 50 years old, and it has a higher incidence among Caucasians and people who have a history of extensive sun exposure or weakened immune systems \(^3\). MCC cell origin is still unclear although it has been described that MCC cells express neuroendocrine markers \(^2\). It also remains unclear the exact causes of this disease. It has been suggested that a combination of factors, such as exposure to ultraviolet radiation, immunosuppression, and certain viral infections are involved in its pathogenesis\(^3\).

One of the most challenging aspects of Merkel cell carcinoma is its aggressive nature. This is because it has a tendency to progress rapidly and metastasize \(^3\). The tumour usually appears as a painless, firm, and rapidly growing nodule on sun-exposed areas such as the face, neck, and extremities. It can vary in colour from pink to red or purple and may resemble other benign skin conditions, making early diagnosis critical for better outcomes \(^2\).

Furthermore, among patients with MCC, more than 55% have an associated neoplasm, either previously or simultaneously. The most frequent associated neoplasm are skin tumours such as squamous cell carcinoma, basal cell carcinoma or melanoma, followed by chronic lymphatic leukaemia, lymphomas and various solid tumours \(^4,5\).

Thus, the diagnosis of Merkel cell carcinoma requires a multidisciplinary approach, which includes clinical examination, biopsy, imaging studies, and specialised laboratory tests.

Herein we describe a rare case of MCC concomitant with myeloblastic leukaemia where flow cytometry was crucial for the diagnosis.

**Case Report**

An 82-year-old male who underwent surgery 73 days prior for a retroauricular MCC, was admitted for surgical margin enlargement. His dermatological history included actinic keratosis, squamous-cell carcinoma, and basal cell carcinoma. He also reported pancytopenia for 6 months. Furthermore, the patient had a skin lesion of 4.5 cm under scar tissue, whose histological study showed positivity for CK20, synaptophysin, chromogranin, CD56, CAM5.2, and p53, confirming a local progression of MCC.

The haemogram showed haemoglobin 82 g/L, platelets 47\(\times 10^9\)/L, and leukocytes 0.92\(\times 10^9\)/L with 81% neutrophils. The peripheral blood smear revealed 3% blast cells.

The medullary aspirate was hypocellular and was 49% medium-to-large sized blastic cells, with rounded nuclei and punctate chromatin and without a nucleolus, which tended to cluster, showing nuclear moulding (Figure 1A and 1B). Myeloperoxidase and esterase were negative, while PAS was partially granular positive.

Flow cytometry (FC) detected infiltration by 23% blasts that were CD45\(^+\)dim CD34\(^+\)CD38\(^+\) HLA-DR\(^+\)CD117\(^+\) CD13\(^+\)CD33\(^+\)/- TdT\(^+\)CD99\(^+\)dim, compatible with acute myeloid leukaemia (AML) with minimal differentiation. In addition, 15% of cells with CD45\(^-\) CD56\(^+\) CD117\(^+\)CD24\(^+\) immunophenotypic profile were detected, which could correspond to MCC (Figure 1C and 1D).

Not enough metaphases were obtained to study the karyotype. The study of BCR-ABL, PML-RAR\(_2\), RUNX1-RUNX1T1, CBFB-MYH11, and the FLT3-ITD and NPM1 mutations was negative. NGS detected mutations in RUNX1, IDH1, TP53, SRSF2, and RB1.
In the bone marrow biopsy, a marked increase in CD34+ blasts were observed, compatible with acute leukaemia, and a small focus of cells positive for CAM5.2, CK20, and synaptophysin confirmed the infiltration by MCC (Figure 1E and 1F).

Given the diagnosis of MCC and RUNX1-mutated AML, the patient underwent palliative treatment and died 50 days later.

**Discussion/Conclusion**

MCC is an extremely rare and aggressive type of skin cancer. Although the exact causes of MCC are still unknown, it has been suggested that a combination of environmental factors may contribute to its development. Morphologically, MCC is composed of small cells of scattered or nodular distribution. Thus, during diagnosis, it is important to distinguish it from some types of lymphomas and leukaemias, with which it can be confused due to the blast-like appearance of the tumour cells and their possible scattered distribution. In this regard, it is useful to demonstrate positivity for CK20 and neuroendocrine markers such as CD56 and chromogranin. Although histology is the gold standard for the diagnosis of MCC, FC may be useful, showing the CD56+ CD45- profile and, occasionally, CD117+ and/or TdT+, as in our case.

MCC is more frequently associated with lymphoid line disorders. However, in our patient MCC was associated with AML. Both diseases developed concurrently, with the synchronous appearance of pancytopenia and a cutaneous tumour 6 months before, and also with the simultaneous infiltration of the bone marrow. Patients with AML and with TP53 and RUNX1 mutated belong to the adverse risk category according to the revised 2017 European Leukaemia Net recommendations. The diagnosis was difficult due to the similarity in the cellular morphology of the two diseases, and the scarce infiltration that the MCC presented in the biopsy. The role of FC for the diagnosis was decisive because it allowed us to distinguish between both cell populations.

In summary, MCC is an aggressive tumour that frequently metastasizes to the bone marrow and it is often associated with other neoplasm, specially skin tumours and lymphoid line disorders. We present a rare case of MCC and AML that developed simultaneously. Due to the similarity between the two cell populations and the limited medullary infiltration, FC was essential to establish the diagnosis.

**References**


**Fig. 1 a and b)** Bone marrow aspirate (May-Grünewald-Giemsa stain) shows (a) isolated blasts and (b) cluster of tumour cells. **c-d)** Dot-plots showing the immunophenotype by flow cytometry in the bone marrow sample. AML blast cells are represented in blue; MCC cells in red; lymphocytes in pink, monocytes in orange, neutrophils in green, eosinophils in yellow, mast cells in dark green, and the erythroid series in dark blue. **c)** Dot-plots showing the side scatter (SSC) of the total cellularity of the bone marrow sample against different markers. **d)** Dot-plots of the two types of blast cells. AML blast cells are CD45+dim CD34+ CD117+HLA-DR+ CD13+CD56- TdT+ CD105-CD36- and negative for B- and T-associated cytoplasmic lymphoid markers. MMC cells are CD45-CD34-CD117- HLADR- CD13-CD56+ TdT- CD105-CD36+. **e)** CK20 and (f) synaptophysin immunostains in MCC.