SOHC
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Follicular T-Helper cell lymphoma of the Angioimmunoblastic type with associated Marginal zone lymphoma – a diagnostic and therapeutic challenge

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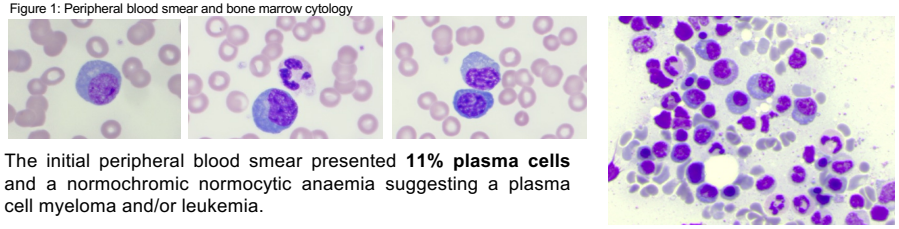
Objective:

We present a very rare case of a 78-year-old patient with progressive **generalized weakness** and **unintentional weight loss** within a period of three months, who was referred to our hospital with a suspected diagnosis of plasma cell leukemia. Further investigations revealed a **follicular T-helper cell lymphoma (FTHL) of the angioimmunoblastic type**, associated with an **EBV-positive marginal zone lymphoma**. This case highlights the challenging and misleading initial presentation mimicking plasma cell leukemia, as well as the complex diagnostic process and therapeutic difficulties.

Diagnostic findings:

Figure 1: Peripheral blood smear and bone marrow cytology



The initial peripheral blood smear presented **11% plasma cells** and a normochromic normocytic anaemia suggesting a plasma cell myeloma and/or leukemia.

However, flow cytometry of the peripheral blood demonstrated a **polyclonal plasma cell population** expressing physiological markers. Bone marrow cytology showed, in addition to plasma cells, lymphoplasmacytic and small lymphoid cells.

Figure 2 illustrates the immunphenotype of the polyclonal plasma cells (CD38++, CD138++) of the bone marrow (κ:λ ratio 3:1) with a physiological phenotype (green population). Yet there was an abnormal population with CD38++CD138dim expression (red population), with cytoplasmatic kappa light chain restriction, immunophenotypically neither fitting fully to plasma cell myeloma nor to mature B-cell lymphoma.

Figure 2

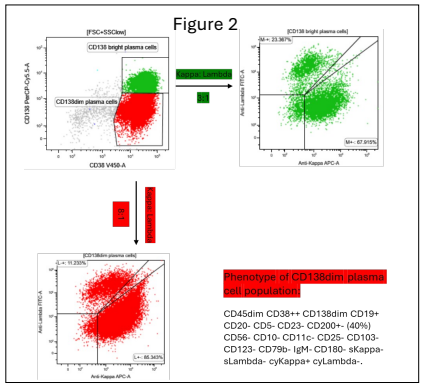


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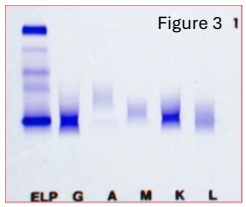
Figure 3



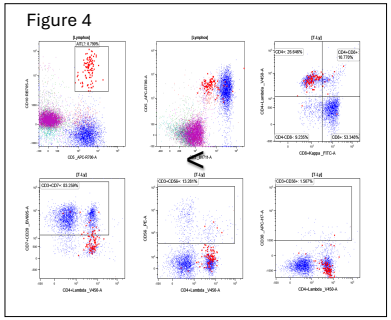
Interestingly, the hypergammaglobulinaemia in the peripheral blood (Figure 3), showed a **polyclonal nature,** thus as well not supporting the differential diagnosis of plasma cell myeloma nor lymphoplasmacytic lymphoma.

With ongoing uncertainty regarding the diagnosis, a PET CT-scan showing a diffuse FDG-avid lymphadenopathy and a subsequent **lymph node excision** were performed, initially showing the presence of a lymphoma with plasmocytoid differentiation, possibly a marginal zone lymphoma, in the histology.

After an interdisciplinary discussion and in consideration of the evidence of **EBV replication** in peripheral blood, the presence of EBV in the lymphoma cells was confirmed via in situ hybridization.
At this point, flow cytometry of the bone marrow demonstrated an abnormal CD3dim CD4+ CD10++ T-cell population with aberrant loss of CD7 expression (red population in figure 4), highly suggestive of a follicular T-Helper cell lymphoma (AITL type). This could be confirmed in the lymph node immunohistochemistry for **T-Helper cells (CD21) and follicular T-Helper cells (CXCL13, ICOS, PD1)** demonstrating a massive expansion of these cells out of the B zones, with a concomitant expansion of the network of dendritic cells.

The rare combination was also supported by the Next-Generation Sequencing findings, showing mutations in **TET2** and **RHOA** genes matching the FTHL (15%) and a **PAX-5** mutation, matching the MZL (70%).
An unusual therapy combination with **rituximab** (due to the evidence of EBV, despite negativity for CD20), **bendamustin** and **daratumumab** was initiated, according to the ECOG status and the diagnostic findings.
A follow-up CT scan showed a **significant regression of the lymphadenopathy** two weeks after treatment initiation and the patient showed a protracted **clinical improvement** with a cessation of the B symptoms within the first moth of treatment.

Figure 4



Conclusion:

This case highlights the **importance of integrative diagnostics** in **complex cases**, such as **EBV-associated MZL arising on the background of FTHL**, where **misleading initial findings** may **obscure the diagnosis**. Effective treatment can be achieved once the correct diagnosis is established and appropriate therapy selected.

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