Chronic neutrophilic leukemia, a rare and challenging diagnosis when associated to myeloma.

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Introduction: Chronic neutrophilic leukemia (CNL) is a rare BCR-ABL1 negative myeloproliferative neoplasm with often aggressive evolution without stem cell transplantation (SCT). The association with plasma cell dyscrasia has been reported, but relationship remains unclear.

Case report: A 68-year-old female patient with monoclonal gammopathy with lambda expression and no clinical symptoms develops isolated neutrophilia over $50x10^9$/L. PET scanner is normal. BCR-ABL, JAK2, FIP1L1, PDGFRα and β, FGFR1, CSF3R are negative, FISH shows duplication 1q, and NGS reveals no clonal mutation. Bone marrow biopsy reveals 10,5% of clonal plasma cells corresponding to myeloma but also hypercellularity > 90% with expanded neutrophilic granulopoiesis. The latter, associated with persisting neutrophilia leads to CNL diagnosis according to WHO 2016. Hydroxyurea is started and SCT is considered, but not done because of slow evolution and stabilization with hydroxyurea. After 14 months of follow-up, PET scanner shows bones evolution and VRd (bortezomib, lenalidomide and dexamethasone) is started with partial response at three cycles and white blood count cells normalization.

Discussion: Considering the rarity of CNL, a particularly high number of CNL cases is associated with plasma cell dyscrasia, mostly preceding myeloma but few cases had been described simultaneously. Distinguishing CNL from a leukemoid reaction may be challenging. It is now accepted that neutrophilic expansion represents an associated myeloproliferative disease rather than usual reactive and infiltrative leukemoid response to the plasma cell population.
It is currently not clear whether CNL and plasma disorder are clonally related or whether neutrophilia occurs secondarily. Both clonal and non-clonal neutrophilia with plasma dyscrasia have been reported. This identification is not routinely performed in our academic centers and therefore, definitive diagnosis of CNL and adequate treatment requires carefulness. Experience shows that prognostically, myeloma associated CNL may be related to longer life expectancy.

Conclusion:
Future, particularly clonality research, should help to better understand the uncertain status of myeloid clonality in myeloma and the relationship between plasma cell dyscrasia and CNL as the adequate treatment strategy.