CLINICAL VIGNETTE

Benign Erythroblastemia

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The patient is a 58-year-old female with longstanding history of multiple sclerosis (MS) with abnormal CBC. Preoperative labs prior to back surgery, noted peripheral nucleated red blood cells on her complete blood count (CBC). Her CBC was otherwise unremarkable with no cytopenias and normal mean corpuscular volume. She reported that she was diagnosed with MS over twenty years ago and had been on a few therapies in the past, but for the last several years, she had very stable disease on natalizumab. Other problems included chronic back pain with multiple prior surgeries and another planned due to worsening pain. ROS included fatigue which she associated to inactivity due to pain and deconditioning. There no weight loss, fevers, chills, hematuria, abdominal pain, chest pain, shortness of breath or other concerning symptoms

Nucleated red blood cells represent immature red blood cell precursors that are noted in the peripheral blood.[1] Usually in healthy adults they are not noted in the circulation as maturation progresses from myeloid progenitor cells to proerythroblast to erythroblast and eventually the expulsion of the nucleus produces a reticulocyte that continues to mature into an erythrocyte that then moves into the peripheral blood.[1] Presence of nucleated red blood cells in the peripheral blood, indicates a disruption in erythropoiesis.[1] This can be seen in hemolysis whereby the marrow tries to compensate for the significant anemia by releasing less mature erythroid precursors.[1] Bone marrow injury often leads to nucleated red blood cells in the periphery as well.[1] Common causes include chronic and acute leukemias, myelodysplastic syndrome, and injury related to chemotherapy.[1] Given the significant correlation with hematologic disease, evaluation is usually warranted when blood tests note nucleated red blood cells.[1] Interestingly, presence and degree of nucleated red blood cells has been associated with poor prognosis in critically ill patients.[1]

Multiple studies have indicated that natalizumab can lead to an erythroblastemia.[2,3] The drug is a monoclonal antibody that reduces relapses in MS.[2,3] It is a recombinant antibody that targets subunits on integrins expressed on leukocytes.[2,3] It inhibits the binding of leukocytes to activated endothelial cells and consequently prevents extravasation and the permeation of immune cells across the blood-brain barrier.[2,3] Initial reports suggested erythroblastemia was a rare phenomenon, but further studies have indicated it is not an uncommon side effect.[2] One study examined blood samples on various MS treatments including natalizumab as well as healthy blood donors in the area.[2] They found the levels of nucleated red blood cells were much higher with natalizumab compared to other medications and healthy controls, specifically nucleated red blood cells were seen in >90% of this group compared to 0-7% in all other groups.[2] There did not seem to be a correlation with number of natalizumab cycles and degree of erythroblastemia.[2] While some other blood count abnormalities were seen such as anemia, these were also noted in other treatment groups.[2] No tear drop cells, schistocytes, dysplasia, or inclusion bodies were seen, to indicate secondary causes for the findings.[2] Another longitudinal study, examined all blood count changes for patients on only natalizumab for their MS treatment.[3] They found no differences in erythrocyte, hemoglobin/hematocrit, platelet or neutrophil counts when comparing values from prior to treatment and 18 months after treatment.[3] In contrast, white blood cell, lymphocyte, and eosinophil values significantly rose after the first infusion but remained stable for the duration of treatment.[3] No nucleated red blood cells were noted in pre-treatment samples, but were noted in 16% of patients after one infusion but the proportion of samples with erythroblastemia did not significantly change as treatment continued.[3] A small proportion of patients showed neutrophil precursors, but the degree of this finding did not change with time.[3] Some of the increased white blood cell findings were hypothesized to be related to the lack of movement of cells into the CNS, leading to concentration in the peripheral blood.[3]

Erythroblastemia was not related to hypoxic stress since there was minimal anemia seen, which was consistent across the other treatment groups.[2] It is felt that the drug has a consequent effect on the bone marrow milieu as well as stem cell development leading to CD34+ cells more quickly exiting the marrow and entering the peripheral blood than would otherwise happen outside of drug influence.[2] The molecules involved at the central nervous system barrier may also impact erythropoiesis.[2] These changes do not present long-term issues, and given the absence of short-term issues, these prior reports suggest aggressive testing should not be performed if the patient was asymptomatic and had no other signs of possible hematologic pathology.[2,3]

While usually the presence of peripheral nucleated red blood cells may warrant more extensive evaluation to rule out bone marrow or other hematologic pathology, in this case, she was clearly asymptomatic and had no other CBC or laboratory features to suggest undiagnosed disease. A review of her medication list identified a medication with a previously described risk of this abnormality. The literature suggested no further

evaluation was needed and to date, no risks have developed. She resumed care with her neurologist and primary care physician.

REFERENCES

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