

Hematological abnormalities within primary Sjögren's syndrome

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Hematological abnormalities are rather common within primary Sjögren's syndrome (SS). This should be known by clinicians who take care of these patients as this knowledge could reduce the (unnecessary) remittances to the hematologist. In general the exact etiopathophysiological processes are unknown but the general conception is that the diseases are secondary to the systemic rheumatic SS disorder and in most cases they are thought to be due to an imbalance between various cytokines. The secondary hematological disorders can be seen in the erythrocytes, the leukocytes and/or the thrombocytes.

Iron-deficiency causing hypochromic microcytic anemia is somewhat over-represented in patients with primary SS and non-exocrine organ involvement. This is most common in patients with repeated attacks of purpura hypergammaglobulinemia Waldenström. The extravasation of erythrocytes can be so manifest that it results in iron-deficiency in the circulating blood. However, the total amount of iron in the whole body is increased due to the increased deposit of iron in the skin. Whether these patients should be advised to take iron tablets or not is a subject for discussion. Increased iron load will secondarily lead to further deposit of iron in the skin and this gives a dark discoloration that is a cosmetic problem especially to young female Caucasians.

The tiredness which is common in patients with iron deficiency anemia will not usually be reduced significantly with iron treatment, because the genuine SS-fatigue is so pronounced.

Normochromic normocytic anemia is observed in patients with primary SS and ongoing active non-exocrine organ involvement.

Pure red cell aplasia is a very rare disease. However, based upon case reports it seems to occur with an increased frequency in patients with primary SS (1, Manthorpe unpublished). We have, during the last six years, tried all conventional treatments in a young female patient (Manthorpe unpublished) but have had only little and transient success. However, a rise in reticulocyte counts combined with reduced need for blood transfusions were observed for some weeks following both treatment with anti-CD52 antibody and also at a later stage following stem cell rescue (autologous bone marrow transplantation) (Manthorpe unpublished).

Various abnormalities can be observed in the leukocyte counts. Most commonly found is leukopenia which is observed in 15-30% of patients with primary SS (1-3). The lower limit for the normal range might differ from $3-4.5 \times 10^9/\mu\text{l}$ between laboratories. Lymphopenia is quite often found (1-3), and granulocytopenia can be observed as well. A recent investigation among our own patients has shown that 20-25% of patients with primary SS have eosinopenia, i.e. $<50 \times 10^6/\mu\text{l}$, at the time of diagnosis (Kadir; manuscript). Persisting abnormal values for basophilocytes and monocytes have hitherto not been described. In a male patient with primary SS, we have observed isolated severe panleukopenia ($<1.0 \times 10^9/\mu\text{l}$) during 8 years and that without increased frequency of infections (Manthorpe unpublished).

When the various lymphocyte subpopulations are counted, it has been shown that 5-6% of patients with primary SS have CD4+ T-lymphocytopenia (4-6). The CD4+ T-lymphocytopenia is mainly observed in those SS patients who are anti-ENA (anti-SS-A, anti-SS-B) antibody and/or ANA positive (6) but not in those who are IgM-RF positive (6). Future studies may show if it is the patients with CD4+ T-lymphocytopenia who primarily develop malignant non-Hodgkin lymphoma.

Thrombocytosis is not usually observed even in patients with active involvement of non-exocrine organs. This is in contrast to patients with rheumatoid arthritis in whom thrombocytosis may be a good indicator for disease activity.

Thrombocytopenia is now and then observed but in most cases it is only a pseudothrombocytopenia (7,8). This is differentiated from a true thrombocytopenia by counting the thrombocytes both with solutio citratis glucosi fortis (ACD) and with K₂EDTA as anti-coagulantia. The use of K₂EDTA in such cases results in aggregation of thrombocytes. Pseudothrombocytopenia is thought to be due to agglutination caused by interaction of circulating immune complexes with platelet membrane Fc receptors (8). If not detected it might lead to a superfluous splenectomy. Pseudothrombocytopenia can be observed in other rheumatological diseases but is most commonly observed in patients with primary SS (8).

Autoimmune idiopathic thrombocytopenia (AITP) might also occur with increased frequency in patients with primary SS. However, it is our impression that only a few ITP patients are investigated for SS even though they might complain of dry eyes, dry mouth, arthralgia in small joints and/or fatigue.

We have recently observed the development of myelofibrosis in a male patient with primary SS of more than 15 years duration who simultaneously had chronic bilateral parotitis (9). Following treatment with IVIg the clinical situation stabilized and nearly normalized (hemoglobin >100 g/l and thrombocytes >100x10⁹/μl) during the following 3 years of observation (9). A similar positive IVIg response have been seen in a patient with early myelofibrosis secondary to systemic lupus erythematosus (10).

Multiple myeloma seems to occur seldom in patients with primary SS but was recently described in four Japanese patients (11). The frequency of malignant non-Hodgkin lymphoma is known to be much increased in patients with primary SS. Members of the European concerted action on SS has just finished a study on this subject among leading European SS-centres (12) and the topic is dealt with by others at this congress.

The various hematological abnormalities in patients with primary SS should be treated (almost) as in other patients. Most of the clinical situations described above do not require any specific treatment, but if so required it is advisable that rheumatologists discuss treatment options with experienced hematologists.

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