Acute to chronic blood loss and nonregenerative anemias

Scăderea acută până la cronică a sângelui și anemiile non-regenerative

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Non-regenerative anemias / ineffective or reduced erythropoiesis

These non- or poorly regenerative anemias are usually normocytic-normochromic. Exceptions include microcytic-hypochromic anemia due to iron deficiency, anemia associated with hepatic shunt as well as very rarely anemia of chronic disease and macrocytic anemias with FeLV infection and folate deficiency in cats and some forms of myelodysplastic anemias. Clinically the following classifications are being made which may also reflect a continuum.

- **Refractory anemias** are non-regenerative, usually mild to moderate, with normal to increased leukocyte and platelet counts, suggesting a failure of erythropoiesis due to an extra-marrow disorder such as anemia of chronic/inflammatory disease, chronic renal disease, cancer and endocrine disorders.
- **Aplastic anemias** are characterized by pancytopenia (anemia, leukopenia and thrombocytopenia) and aplastic or hypoplastic bone marrow suggesting an intra-marrow disorder caused by irradiation, chemicals, infection or lympho- and myeloproliferative disorders.
- **Myelodysplastic syndromes** are a group of related bone marrow disorders characterized by cytopenias and normal or hypercellular bone marrow with a relative excess of blast cells that may rarely progress to overt leukemia.

- **Nutritional deficiency anemias**
  - Iron deficiency (usually still regenerative)
    - chronic blood loss
    - chronic malabsorption
  - Vitamin deficiencies
    - Cobalamin (vitamin B_{12}) deficiency (receptor defect)
    - Dietary folate deficiency
    - Gastrointestinal malabsorption with folate or/and cobalamin deficiency

- **Chemical-induced aplastic anemias**
    - Idiosyncratic drug and other reactions
    - Chemotherapeutic and immunosuppressive agents
    - Irradiation
    - Exogenous and endogenous estrogens (only in dogs)

- **Anemia associated with infection**
    - Ehrlichiosis
    - FeLV and FIV – infection
    - Parvovirosis (more leukopenia)
    - Other infectious diseases

- **Anemia of chronic disease**

- Anemia of inflammatory disease
- Associated with many organ disorders

- **Anemia associated with bone marrow infiltration**
  - Osteopetrosis (congenital, hereditary pyruvate kinase deficiency only in dogs)
  - Myelofibrosis/osteosclerosis (secondary)
  - Lympho-/myeloproliferative diseases (leukemias, multiple myeloma)
  - Rarely metastatic neoplasia

- **Anemias associated with organ disorders**
  - Renal disease (erythropoietin deficiency)
  - Liver disease
  - Endocrine diseases (hypothyroidism, hypoadrenocorticism)

Other laboratory tests

Routine laboratory tests are required in the diagnostic approach of non-regenerative anemia patient, including a chemistry screen and urinalysis, in order to define other organ disorders. Infectious disease screens for tick and flea transmitted and other infections depending on the geographic area may be very important. Other specific tests may help in further defining the cause of the anemia. Serum iron concentrations are low in iron deficiency anemias due to blood loss (which generally remain somewhat regenerative), can also be slightly low with renal insufficiency (gastrointestinal ulcers), but are normal along with adequate bone marrow iron stores in many other diseases with non-regenerative anemia. Serum iron levels may be low in anemia of chronic disease, but bone marrow iron stores should be adequate. Bone marrow from cats generally contains low iron accumulation. Other nutritional elements such as vitamin B_{12} and folate may need to be determined as they may result in cytopenias.

Therapeutic principals for non-regenerative anemias

Animals with non-regenerative anemia due to reduced or ineffective erythropoiesis have a guarded prognosis, but can benefit from specific and symptomatic therapy. Ideally, the cause of the anemia is corrected by treating the underlying disease or removing the triggering agent, such as an infectious organism or drug. Blood transfusion can provide immediate support for the critically ill patient. Except for animals with true iron or erythropoietin deficiency, no effective bone marrow stimulants are currently clinically available Except human recombinant erythropoietin).

As non-regenerative anemias are often relatively mild and develop slowly, animals usually tolerate the anemia well. However, it may progress to severe anemia, because of a complete lack of a bone marrow response or because another type of anemia is complicating the picture (blood loss and hemolysis). Severely anemic animals will benefit from blood type (and crossmatch) compatible transfusions, ideally in the form of stored packed red blood cells or fresh whole blood. Transfused erythrocytes will generally exhibit a normal survival, but because of the lack of regeneration, these animals may require repeated transfusions. During subsequent transfusions the red cell survival may be shortened because of the development of alloantibodies, thus it is imperative to assess compatibility by typing and crossmatching. The transfusion rate should be slow (< 10 ml/kg/hour), because these patients are generally volume expanded and are at risk of developing pulmonary edema and heart failure.

With the exception of anemic animals with chronic renal failure, the serum erythropoietin concentration is exponentially increased; in fact the highest serum erythropoietin concentrations are observed in animals with red cell aplasia and therefore additional erythropoietin administration would not be helpful. Recombinant human erythropoietin (Darbepoietin) weekly has been used in anemic animals with chronic renal failure. The dose is reduced and the interval extended as soon as the hematocrit reaches 25 to 30%. In addition iron is being supplemented orally and any hypertension is corrected. Erythropoietin supplementation improves the overall well-being of these patients, but does not correct the renal failure. Furthermore, animals may develop neutralizing antibodies against human erythropoietin. Recombinant human erythropoietin has also been used with some success in patients with anemia of chronic disease due to cancer in the hope that additional erythropoietin could override the inhibitory effects of the cancer on the bone marrow.

Other hematopoietic growth factors have also been tried in combination with erythropoietin for various forms of anemia, but currently there is insufficient data on their efficacy and safety. For decades androgens have been proposed for the stimulation of the bone marrow, but there is no good experimental or clinical evidence of its efficacy. Because idiopathic aplastic anemias are assumed to be due to immune mediated processes against precursor cells, a trial with immunosuppressive agents is often initiated, including prednisone, cyclosporine, and intravenous human immunoglobulin, but none have been documented to be effective beyond anecdotal reports.

In case of iron deficiencies long-term supplementation of iron in the form of iron sulfate/gluconate or intramuscular iron dextran can be highly effective. It is important that ferrous rather than ferric iron is administered and that parenteral routes are only used in case of malabsorption. Initially a red cell transfusion will also add quickly bioavailable iron for erythropoiesis. However, most other anemic patients do not experience iron deficiency, and thus the general use of iron supplementation is not recommended and can even be harmful to some animals. Furthermore, animals with vitamin deficiencies may benefit from parenteral supplementation of folate or cobalamin; this has proven highly effective in dogs with hereditary cobalamin malabsorption.

In conclusion, the diagnostic approach to anemias in small animals has been assisted greatly by new tools and tests. Their appropriate use will permit a more precise and rapid diagnosis and thereby effective therapy.

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