Management of hematological complications of malignancy and chemotherapy: The role of hematopoietic growth factors

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ABSTRACT

Cancer related syndromes involving haematopoesis and the process of hemostasis are not exceptional. The hematopoietic disturbances related to cancer include erythrocytosis, cancer related anemia, and either thrombocytosis or thrombocytopenia. Pancytopenia with erythroblastosis in peripheral blood is usually the consequence of bone marrow invasion and might be a terminal phenomenon. Treatment is supportive and includes transfusions of packed red blood cells, eventually platelets when needed. It is sometimes associated with disseminated intravascular coagulation when appropriate measures are required. Nevertheless this syndrome is usually a sign of generalized malignancy, not any more candidates for cytotoxic treatment.

Erythrocytosis has been traditionally associated with erythropoietin producing tumors such as renal cell carcinoma, hepatocellular carcinoma and cerebellar hemangioblastoma. In the clinical practice this syndrome is extremely rare. Erythrocytosis secondary to tumors is usually not high enough to require treatment.

Thrombocytosis is quite common in cancer patients and is usually associated with advanced disease. Thrombosis and hemorrhage are rarely associated with cancer thrombocytosis and if not associated with hypercoagulability syndrome does not require treatment. Anemia in cancer patients most commonly affects the form of the normocytic and normochromic anemia of chronic disease. It is supposedly caused by a number of factors including iron metabolism and storage disturbance and deficient erythropoietin production. Recombinant erythropoietin has been advocated in low-grade cancer anemia but the issue remains controversial.

The most important hematological disturbances in cancer patients are migrating thrombophlebitis and disseminated intravascular coagulation. Migrating thrombophlebitis is most often seen in patients with adenocarcinoma, especially in mucin producing adenocarcinomas of the gastrointestinal tract. It can also occur in breast, ovarian, prostate, and especially pancreatic cancer. The treatment of this disorder includes treatment of the underlying malignancy as the most effective measure when possible. Treatment should also include heparin application but it is frequently ineffective; better results are obtained with low molecular weight heparins, enoxaparin sodium being possibly the most effective drug at the moment available.

Disseminated intravascular coagulation in cancer patients may occur in several prognostically different settings:

- As a terminal event in disseminated malignant disease; in this situation the specific treatment is usually ineffective and very often only symptomatic treatment is required.
- As a component of the tumor lysis syndrome; in this situation we are dealing with a chemotherapy responsive tumor and every effort of treatment with antithrombin III preparations, platelets transfusions and low molecular weight heparins is required.
- As a potentially transitory event during febrile neutropenia caused by gram-negative bacteria; this potentially fatal complication should be dealt with most seriously in order to save the patient. Treatment includes all measures as in the disseminated intravascular coagulation related to tumor lysis syndrome.

The synthesis of recombinant hematopoietic growth factors has opened a new era in treating cytopenic complications of both malignancy and chemotherapy. The thrombopoietins for treatment of cytotoxic drug induced thrombocytopenia are still in very early investigational clinical phases. Thrombocytopenia related to cancer or to cytotoxic chemotherapy is best treated by platelet transfusions. Treatment of cancer or chemotherapy related anemia by different recombinant erythropoietins has been and still remains a topic of controversy. Erythropoietins have been claimed to have beneficial effects in low-grade cancer and chemotherapy related anemia especially the anemia during chemotherapy with platinum derivatives. The beneficial effects claimed for erythropoietins include better chemotherapy efficacy, relief of the so-called fatigue syndrome and improvement of quality of life. Several trials have assessed the impact of erythropoietin administration in low-grade anemia patients receiving chemotherapy. The results were not equivocal. There are data suggesting that erythropoietin administration positively affects quality of life; these data apparently need more
detailed evaluation. It has been stated that although some of the results indicate that epo-
gous or allogenic stem cell transplantation or for mobilization of peripheral blood stem cells
immediately prior or simultaneously with chemotherapy there is a risk for severe thrombo-
radiotherapy to the chest due to increased rate of complications and death. If they are given
nemia and even less in the therapy of afebrile neutropenia. Their use is contraindicated during

The application of these factors is not indicated in the general therapy of febrile neutro-
penia only in the category of high-risk febrile neutropenia i.e. febrile neutropenia lasting
for more than 7 days, or associated with hypotension or sepsis, or associated with pneu-

Secondary prophylaxis is indicated in the following situations:
- Further infections in the next treatment cycle considered life threatening.
- Need for chemotherapy dose reduction below threshold of efficacy.
- Need for delay of next treatment cycles if considered detrimental for response achieve-
ment and/or compromising cure rate or disease free and overall survival.

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radiotherapy to the chest due to increased rate of complications and death. If they are given
immediately prior or simultaneously with chemotherapy there is a risk for severe thrombo-
cytopenia. They should not be applied in patients with chemotherapy induced bone marrow
aplasia and severe thrombocytopenia. The use of hematopoietic growth factors in autolo-
gous or allogenic stem cell transplantation or for mobilization of peripheral blood stem cells
is outside the scope of this presentation.

SUGGESTED LITERATURE
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