**Pancytopenia – a common clinical problem**

Ed Zijlstra

E-mail: e.e.zijlstra@roctm.com

Box

**Case**

This patient was seen regularly at the internal medicine outpatient clinic of Queen Elizabeth central Hospital, Blantyre.

Female, 22 years, school teacher

Presenting complaint

* Feeling tired

History of presenting complaint

* Multiple visits to clinic and Accident and Emergency Department: recurrent anaemia
* Was given iron tabs, albendazole: no improvement
* Needed repeated bloodtransfusions

Physical examination

* Pale conjunctiva, otherwise normal

Investigations

* Hb 4.9 g/dL (N= 14-16 g/dL)
* MCV 88 fL (N=
* TWC 2.1 x 109/L (N=4-10 x 109/L)
* Platelets 78 x 109/L (N= 150-300 x 109/L)

Additional investigations

* Peripheral blood film: normal
* Bone marrow aspiration: aplastic anaemia
* HIV: negative

Management

* Blood transfusions every 6 weeks

She was referred to Johannesburg, South Africa.

Additional test were done:

* direct antiglobulin test +ve
* antinuclear factor: +ve, 1: 320, speckled pattern

Diagnosis: Evans syndrome -this consists of:

* idiopathic (autoimmune) thrombocytopenic purpura
* haemolytic anaemia
* associated with SLE

She was treated with prednisolone and azathioprine and had a good response; there more no more blood transfusions needed.

This case illustrates a common clinical problem that clinicians may encounter everywhere but that in areas with limited resources poses major difficulties. It is difficult to diagnose accurately and management often empirical and requires repeated blood transfusions.

**Pathogenesis and clinical presentation**

Pancytopenia means that all three cell lines in the blood (red cells, white cells and platelets) are reduced. Clinically this may result in anaemia, risk of infection and bleeding tendency. There is a long differential diagnosis; it is useful to distinguish between the main groups.(table)

Bone marrow aplasia may be the result of damage to the haematopoietic stem cells. Another term often used is aplastic anaemia which is actually a misnomer as it is not only about the red cells but white cells and platelets are also involved. Bone marrow aplasia may be caused by virus infections such as HIV itself or HIV-associated viruses. Drugs are another important cause; antibiotics such as chloramphenicol are widely used in LMICs and may lead to irreversible bone marrow destruction in 1:40,000 cases and there are many more examples of other drugs.

Alternatively, the bone marrow may not be damaged as such but the cell lines may be displaced by infiltration by a massive infection such as tuberculosis or malignancies such lymphomas. In this case the bone marrow may recover after treatment of the underlying condition.

The other causes, blood cell destruction and sequestration, are less common, but are more difficult to diagnose and may be not recognized easily in clinical practice. Sequestration of blood cells in a massively enlarged spleen may occur for example in the context of liver cirrhosis and portal hypertension, or in visceral leishmaniasis.

**Diagnosis**

In most settings, a full blood count should be possible leading to the diagnosis of pancytopenia as a syndrome. Reticulocyte count is helpful to assess production of red cells; it will be raised in increased peripheral destruction and low in reduced production.

A bone aspirate or biopsy is essential to differentiate between destruction of bone marrow (empty, few cells, replaced by fatty cells) and infiltration (malignant cells in lymphoma, positive Ziehl-Neelsen stain in tuberculosis.

Additional tests such as in the patient described are often not available and the cause of remains unclear.

The clinical assessment may provide clues to an underlying condition. Tuberculosis may be suspected in a patient presenting with cough, pleural effusion, ascites or lymphadenopathy; many patients will be HIV positive. Diffuse lymphadenopathy with hepato- and splenomegaly may point malignant lymphoma. Matted lymph nodes may point to malignancy. Vitamin B12 deficiency may be suspected in case of glossitis, subacute combined neuropathy; the red cells wil show macrocytosis.

**Management**

In case of bone marrow destruction, often recurrent severe anaemia with a clinical presentation of fatigue, shortness of breath, oedema or overt heart failure is common; repeated blood transfusions are needed that are not always safe and available.

In the case described, it was not possible to make a further diagnosis in Malawi because of lack of diagnostic capacity. Numerous repeated blood transfusions were given with all their associated risks of infection, fluid overload and transfusion reactions including dangerous delays in administration of blood because of lack of availability. Referral to South Africa in this case was possible; this may be done through a government- funded scheme or at the patient’s own initiative. The assessment in the South African hospital revealed a treatable underlying condition in this case that responded well to appropriate therapy and no further blood transfusions were needed.

|  |  |  |  |
| --- | --- | --- | --- |
| **Bone marrow aplasia** | **Bone marrow infiltration** | **Blood cell destruction** | **Sequestration** |
| Aplastic anaemia | Haematological malignancies   * leukemia * lymphoma * multiple myeloma * myelodysplastic syndromes | Disseminated intravascular coagulation | Hypersplenism   * liver cirrhosis * storage diseases * lymphoma * autoimmune disorders |
| Infections   * HIV * CMV * parvovirus B19 * viral hepatitis | Metastatic cancer | Thrombotic thrombocytopenic purpura |  |
| Nutritional   * vitamin B12 * folate deficiencies | Myelofibrosis |  |  |
| Immune destruction   * autoantibodies | Infectious diseases   * tuberculosis * fungal infections |  |  |
| Medication   * chloramphenicol |  |  |  |
|  |  |  |  |
|  |  |  |  |

Table. Causes of pancytopenia