Hemepath Case 33: 65-Year-Old Female

HISTORY

A 65-year-old female visits her family physician. She is concerned as her fingers turn purple and become painful when she goes out for her morning jog. This is especially severe during the winter months. She also notices that she tires easily, and can no longer run as far as she used to. Her urine is sometimes tea-colored after one of these episodes.

Physical examination reveals a pale-looking female in no apparent distress. She is slightly tachycardic. Her hands and earlobes are cold to the touch, and her spleen is slightly enlarged.

CBC

Hgb (g/L)	Low
MCV	N
Reticulocyte Count	High
WBC	N
Plt	N

OTHER LABORATORY FINDINGS

LDH	High
Bilirubin	High

DESCRIPTION OF SLIDE

Peripheral Blood Smear

The peripheral blood smear shows florid RBC agglutination (see rectangles). It is difficult to evaluate erythrocyte morphology on this slide, although some spherocytes (see circles) and schistocytes (see arrows) seem to be present. A myeloid left shift is also evident.

Platelets are morphologically unremarkable. No abnormal circulating cells are seen.

*** To see the slide annotations in Imagescope, click on VIEW, then ANNOTATIONS, and then on the "eye" icon adjacent to the word "Layers". In the “Layer Attributes” box, a brief description of the annotations is provided. You may also click on individual layer region (e.g. region 1) in the “Layer Regions” box to locate each annotation – this is especially helpful in identifying annotations when the slide is not zoomed in. ***

MORPHOLOGICAL DIAGNOSIS

Cold agglutinin disease

DISCUSSION

Cold agglutinin disease (CAD) occurs when the body produces cold-reactive autoantibodies (usually IgM) against the I antigen on RBC membrane. In the visceral circulation where the temperature is 37°C, these antibodies do not bind to the erythrocyte membrane. However, in the cooler circulation of the hands and feet, the antibodies become attached to RBCs and activate the complement pathway, leading to intravascular hemolysis. RBCs may also be destroyed within the spleen (extravascular hemolysis) owing to destruction of complement-labelled RBCs by the reticuloendothelial system. CAD is different from warm autoimmune hemolytic anemia in that IgMs induce hemagglutination at a cooler temperature (<30°C).

There are two types of CAD: primary and secondary. Primary CAD is idiopathic. In secondary CAD, autoantibodies are produced following an infection (e.g. EBV, CMV, malaria, *mycoplasma pneumoniae*) or a B-cell malignancy (e.g. myeloma, lymphoma, Waldenström's macroglobulinemia). When exposed to the cold, patients with CAD frequently complain of acrocyanosis (purple, painful fingers and toes) due to obstruction of small blood vessels by aggregated RBCs. They also present with anemic symptoms (e.g. pallor, fatigue).

Aggregation of RBCs in the peripheral smear is not only seen in CAD, but may also be observed in other conditions – for example, following transfusion of an incorrect blood type. Cold agglutinins may be diagnosed when RBC agglutination is present on a room temperature (e.g. 20°C) smear but is not present on a blood smear prepared after 37°C incubation.