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Tales of total proteins and globulins
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When the cells are removed from the blood, the remaining plasma is composed of water, nutrients, metabolites, hormones, electrolytes and proteins. The plasma proteins serve a number of functions, which include maintaining oncotic pressure, transporting nutrients, metabolites and hormones throughout the body, defending against infection and maintaining the integrity of circulation through clotting.

Many diseases alter the amounts of plasma proteins produced, and, hence, their concentrations in the blood. In the lab we are able to measure levels of various plasma proteins that aid us in making clinical diagnosis and decisions for example - C-Reactive Protein.

The amount of total protein in the body is the sum of albumin and globulins
Total Protein (TP) = Albumin (alb) + globulin (glb)

Reference ranges

Total Protein: 60-80 g/L

Albumin: 35-50 g/L

Globulin: 15-30 g/L

Albumin constitutes approximately 60% of plasma proteins and is produced by the liver. The rest of the plasma proteins are called globulins and are produced by different organs such as liver, endothelial cells, B-lymphocytes, etc

Globulins can be divided into 3 groups alpha, beta and gamma according to the speed they run on electrophoresis (size and negative charge). Immunoglobulins constitute 50% of gamma-globulins, and are produced by mature B lymphocytes also called plasma cells.

Both hypo and hyper gammaglobulinaemia signify disease states and it is important to identify them in time.

Globulin and therefore TP increase significantly in plasma cell disorders such as MGUS or Myeloma. An incidental raised high globulin is useful in suspecting myeloma.

In Leicester, traditionally only albumin and not globulins were measured. Therefore, when LFT and/or bone profiles were requested a TP value was not provided. Recently, at the request of Myeloma Team, the laboratory has agreed to include measuring globulins in the LFT and Bone profiles and give a result of total protein in their reports. This measure will thus help in the identification of possible myeloma cases and managing existing cases better without the need to undertake frequent repeat myeloma screens (immune-electrophoresis).

Interpretation

Raised TP and or total globulin

85% of myeloma patients have an intact paraprotein and hence their TP and globulin will be high at presentation (Case 1)

Please note that TP and globulin proportional to fall in paraprotein as patients respond to treatment for myeloma and rise again proportionately with a relapse.

Low Gamma globulin

Hypo-gamma-globulinaemia occurs in non-secretory and pauci -secretory myeloma, X linked hypo-gamma-globulinaemia, CLL, patients on immunosuppressive medications, post bone marrow transplantation, etc.

10-15% of myeloma patients does not have an intact paraprotein and may have only light chain excess, they often have hypo-gammaglb (Case 2)

Case Studies

Case 1:

78 years female admitted with chest pain and was evaluated in casualty

Blood results

Hb	67 g/L	(115-165)
MCV	90 fL	(80-99)
Ferritin	8 µg/L	(10-420)
Creatinine	59 µmol/L	(60-120)
Corrected Calcium	2.6 mmol/L	(2.2-2.6)
Total Protein	109 g/L	(60-80)
Albumin	26 g/L	(35-50)
Globulin Calculated	83 g/L	(18-30)
IgG	1.9 g/L	(6-16)
IgA	85.6 g/L	(0.2-4.0)
IgM	0.11 g/L	(0.5-2)

Interpretation

Please note that Hb and ferritin were both decreased and hence a diagnosis of iron deficiency anaemia would have been made. Therefore, without a TP, the diagnosis of myeloma could have been missed or delayed. Normally, a myeloma screen would only have been requested if there were clinical suspicion or features such as lytic lesions on X-Ray which were absent in this case.

As can be seen from above, TP and globulin were very high and hence a sample was sent for serum protein electrophoresis (myeloma screen) and patient was found to have a large paraprotein of 85.6 g/L and a diagnosis of myeloma was made. Also note profound suppression of IgG and IgM.

Case 2:

52 years old female with symptoms low backache for years, developed a clavicular mass and had some breast lumps. A CT thorax showed a 7 cm large destructive lesion in clavicle, other lytic lesions and suspected cord compression at T2, a provisional diagnosis of metastatic breast cancer was made. She was given steroids and radiotherapy for T2 mass. The clavicular biopsy shows plasmacytoma and diagnosis revised and patient referred to myeloma team.

A closer look at biochemistry could have pointed towards myeloma prior to the biopsy.

Blood results

Hb	147 g/L	(115-165)
MCV	99 fL	(80-99)
Ferritin	417 µg/L	(10-420)
Creatinine	56 µmol/L	(60-120)
Corrected Calcium	2.48 mmol/L	(2.2-2.6)

Total Protein	56 g/L	(60-80)
Albumin	41 g/L	(35-50)
Globulins	15 g/L	(18-30)
IgG	3.6 g/L	(6-16)
IgA	0.61 g/L	(0.8-4.0)
IgM	0.20	(0.5-2)

Interpretation

Note panhypogammaglobulinaemia and hence Immune/Protein electrophoresis (myeloma screen) should have been undertaken..

If you have any problem in interpretation please use advise and guidance for any of our specialties.

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