Clinical cases: serum protein electrophoresis

Biochemistry

## Case number 1: Mr B, 72 years old, hospitalised in the Gastroenterology Department for abdominal pain, diarrhoea and vomiting.

Serum protein electrophoresis was performed (see Graph 1): this showed raised levels of β1-globulins and decreased levels of β2-globulins..

a/ Raised level of β1-globulins

Which test to perform first?

❶ Immunotyping
❷ Transferrin
❸ Ferritin
❹ Complement fractions C3 and C4
❺ Free light chains

graph 1

Answer: ❸. It is worth mentioning any iron deficiency (migrates in the β1 region on electrophoresis and is raised in iron deficiencies) and ferritin levels should be quantified: the result was = 13 ng/mL in our patient (reference values: 30 – 300). The comment added to the electrophoresis was as follows: "Increase in the β1-globulin fraction that is probably linked to the iron deficiency (through the increase in transferrin); quantification of ferritin assay added by the pathologist". If the ferritin level had been normal or increased, we would have performed immunotyping of the proteins to check that no monoclonal immunoglobulins (Ig mc) or free light chains (FLC) were present.
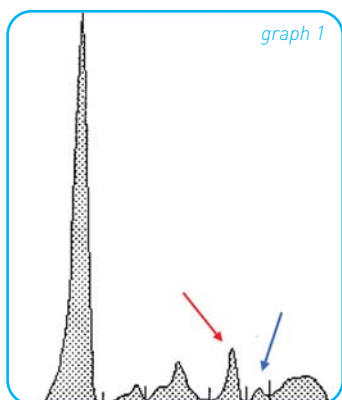
b/ Decrease in β2-globulins

Which test to perform first?

❶ Immunotyping
❷ Transferrin
❸ IgA
❹ Complement fractions C3 and C4
❺ Haptoglobin

Answer: ❹. Indeed, C3, IgA and IgM migrate in the β2 region. The results are C3 = 0.57 g/L (reference value: 0.9 - 1.8) and C4 = undetectable (0.1 - 0.4).

The comment added to the electrophoresis was as follows: "Decrease in the β2-globulin fraction: assaying of complement fractions C3 and C4 added by the pathologist. Hypocomplementemia should be interpreted in light of the clinical data".

Moreover, CH50 assaying was performed: CH50 < 10 kU/L (reference value: 37-66).

Under a hypothesis of systemic disease, screening for hypocomplementemia was also performed along with immunological and autoimmune profiles, despite the lack of clinical symptoms associated with this disease. The cryoglobulin screen was positive (type III, mixed polyclonal). The aetiological profile of this asymptomatic cryoglobulin revealed undetected hepatitis C (HCV serology testing was positive and confirmed by PCR), an indirect diagnosis was reached as a result of investigating an electrophoretic anomaly.

By looking over the patient's medical history, these anomalies (a decrease in β2-globulins and a decrease in complement C3) were revealed during several admissions to hospital.

Caution: the most frequent cause of a decrease in C3 is ageing of the serum sample, therefore, this should be checked first (this cause was not the cause for our patient, as the sample was collected shortly prior to testing).

Case number 2: Mr Z. 49 years old, admitted to the Rheumatology Department for recurrent chronic lumbar cruralgia.

Serum protein electrophoresis is performed systematically within the set of tests performed on admission (see Graph 2); the pattern showed no anomaly except for a decrease in α2-globulins..

Quelle analyse proposer ?

❶ Orosomucoid
❷ α2-macroglobulin
❸ IgA

④ Complement fractions C3 and C4
⑤ Haptoglobin

Answer: ⑤. Indeed, α2-macroglobulin and haptoglobin migrate in the α2 region; it is logical to start with haptoglobin quantification. Haptoglobin is <0.1 g/L (reference value: 0.3 – 2.0) in our patient, which is indicative of intra-vascular haemolysis.

graph 2
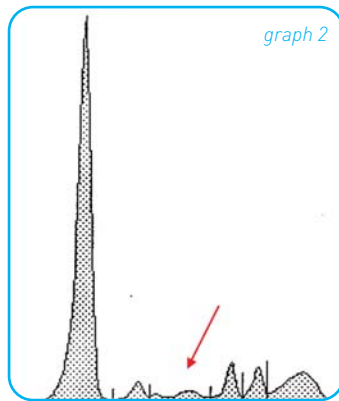
The comment added to the electrophoresis was as follows: "Decrease in α2-globulin related to the decrease in haptoglobin (assay added by the pathologist). Traits of intravascular haemolysis? This should be interpreted in light of the clinical data and the clinical picture".

To strengthen our hypothesis, we analysed the biological profile results of patient Mr Z: Hb = 13.2 g/dL (reference value: 13 –18) and LDH = 401 U/L (reference value: 210-420). The appearance of the plasma was not haemolysed and all of the results (haemostasis and biochemistry) were completely normal. It was therefore, a random and fortuitous discovery of intravascular haemolysis traits with a negative aetiological profile. To be periodically checked.
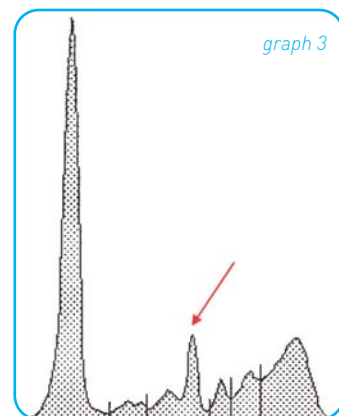
Case number 3: Mr S. 31 years old, admitted to hospital in the Infectious Diseases Department for the monitoring of disseminated tuberculosis.

Serum protein electrophoresis was performed and revealed raised levels of α2-globulins (see Graph 3).

Which test to suggest?
① Orosomucoid
② α2-macroglobulin
③ Immunotyping
④ C-reactive protein
⑤ Haptoglobin

graph 3

Answer: ③. Immunotyping was added by the pathologist: it showed a polyclonal distribution of seemingly normal looking immunoglobulins. Investigation of the electronic clinical file enabled us to see that the patient had had a chest, abdominal and pelvis scan with injection just a few hours before the blood sample was collected. The anomaly seen on the pattern therefore corresponds to α2-globulin interference caused by the migrating contrasting product.

Case number 4: Mrs V, 77 years old, admitted to hospital in the Internal Medicine department for ionic problems while being treated with diuretics.

Serum protein electrophoresis is performed systematically within the series of tests performed on admission (see Graph 4); the pattern showed a dissociation of α1- and α2-globulins: normal levels of α1 and increased levels of α2 with a suspicious appearance.

Which test to suggest?
① Nothing at all, it is surely interference after having had a scan with injection
② α2-macroglobulin
③ Immunotyping
④ C-reactive protein
⑤ Haptoglobin

graph 4

Answer: ③. 3. Immunotyping was added by the pathologist and concluded as follows: "evidence of a monoclonal IgA κ (peak estimated at 9 g/L on serum protein electrophoresis). This result should be interpreted in light of the clinical data".
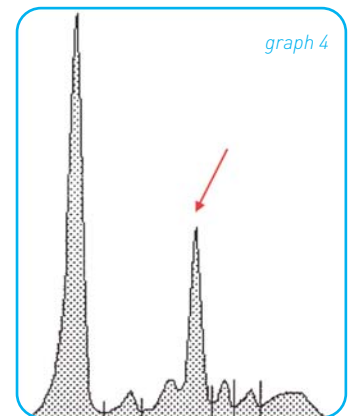
Complementary analyses were performed:
β2-microglobulin = 2.6 mg/L (0.8 –2.2)
FLC κ = 378 mg/L (3.3 –9.4)
FLC λ = 7.9 mg/L (5.7 –26.3)
κ/λ ratio = 47.9 (0.26 – 1.65)

The bone marrow count revealed a medullary infiltration of 20-30% of seemingly pathological plasma cells; the diagnosis of multiple myeloma was made.

Comment: this patient showed no hypercalcemia, no kidney failure and had no clinical symptoms suggestive of disease. This was a random and fortuitous discovery, which was revealed from the electrophoresis analysis and the additional investigations by the pathologist. The initial observation from the doctor was "context is likely to be post-inflammatory hyper α2-globulinemia".

Conclusion

Serum protein electrophoresis is a commonly used systematic test that is worthy of particular attention from the pathologist due to the high resolution of capillary electrophoresis (widely used today) that enables indirect detection of a significant variety of pathological situations if we just look carefully.

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