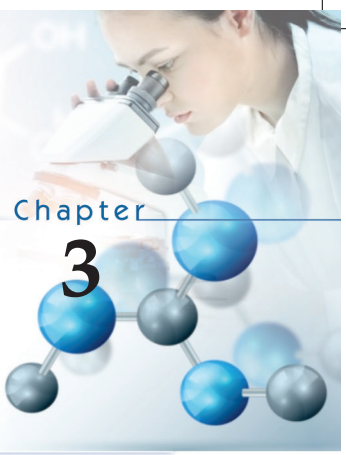


Chapter 3

Chemistry of Amino Acids and Proteins

ECE 3.1: MULTIPLE MYELOMA

A 45-year-old man presented with continuous aching in lower back and tiredness. He had been well until 3 months back when he noticed decrease in his weight with a loss of about 8 kg. He was a non-smoker but had been suffering from recurrent episodes of respiratory tract infections for the past 2 years. Presently, he feels short of breath even after slight exertion.

On examination, he showed pallor and had a number of tender spots on bones, particularly on the spine. Blood film showed normochromic, normocytic anaemia. Biochemical analyses revealed raised calcium levels with deranged renal function tests. Total serum proteins were high with low serum albumin levels. Bence Jones proteins came out positive in urine.

Radiological examination of skull showed punched out lesions.

1. What is the probable diagnosis?

Ans: The most probable diagnosis is multiple myeloma.

2. Explain the sign and symptoms on the basis of diagnosis.

Ans: Major sign and symptoms seen in this patient are anaemia, bony pains and recurrent infections. The underlying biochemical basis is:

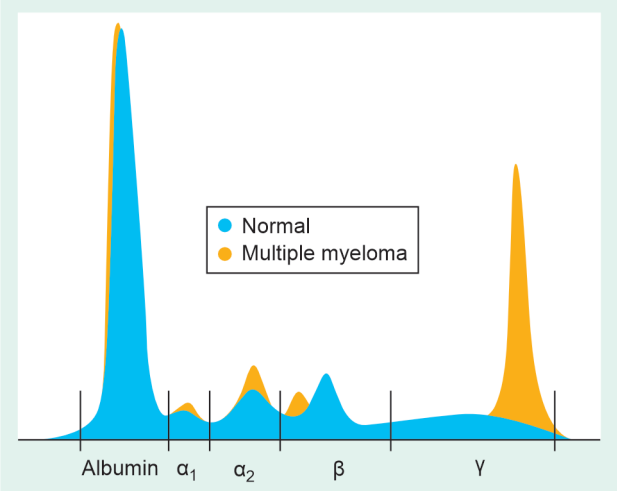
a. **Anaemia:** Erythropoietic bone marrow cells are replaced by malignant plasma cells resulting in anaemia, that leads to tiredness and shortness of breath.
b. **Bony pains:** Infiltration of malignant cells into bones results in localized pain, tenderness and increased risk of fractures.
c. **Susceptibility to infections:** Suppression of IgG synthesis, which are protective antibodies, by infiltrating cells results in increased susceptibility to infections.

3. Discuss other tests that can be done to confirm the diagnosis.

Ans: Various laboratory tests that can be done to confirm the diagnosis include:

a. Serum protein electrophoresis that shows a sharp M band
b. Immunofixation that confirms the type of immunoglobulins (e.g. IgG, Ig A, kappa or lambda light chains)
c. Bence Jones proteins: In some patients, dimers of immunoglobulin light chains (either kappa or lambda) are found in the urine. These chains show a characterstic differential heat solubility. Protein precipitation occurs between 40°C and 60°C while precipitates disappears between 85°C and 100°C. However, they reappear on cooling.

d. Serum free Ig light chains levels.



4. Why renal function tests were deranged in this condition?

Ans: The potential causes for derangement of renal functions are:

a. Obstruction of nephrons by proteins and hypercalcemia.
b. Bony metastasis.
c. Cytokines secreted from infiltrating malignant cells.

5. What are Bence Jones proteins? How are they detected?

Ans: Bence Jones protein is a monoclonal globulin protein or light chain immunoglobulin found in the urine. They are produced by neoplastic plasma cells. They can be kappa or lambda. These light chains can be immunoglobulin fragments or single homogeneous immunoglobulins. They are found in urine as a result of decreased kidney filtration capabilities due to kidney failure. They can be detected by Bradshaw urine test as they show a characterstic differential heat solubility.

6. Why is hypercalcemia seen in this patient?

Ans: Hypercalcemia is seen in this patient as the calcium is released from the bones due to increased bone resorption caused by osteoclast activation, especially due to hyperactivity of RANK/RANKL receptor.

7. Mention the treatment of this condition.

Ans: Treatment varies based on many factors, but may include one or more of the following interventions:

a. Chemotherapy
b. Corticosteroid medications,
c. Targeted therapy stem cell transplant
d. Biological therapy
e. Radiation therapy, and
f. Surgery

8. What are the prognostic indicators in this condition?

Ans: Various prognostic indicators of multiple myeloma are:

a. Serum β2 microglobulin levels with high level indicating poor prognosis
b. Hypercalcemia
c. Hypoalbuminemia
d. Anaemia
e. Renal impairment
f. Increased paraprotein levels
g. Urinary Bence Jones protein >12 g/24 hr