Unusual presentation of more common disease/injury

Iron deficiency in a male with multiple myeloma

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Summary

A 58-year-old man with long standing unexplained iron deficiency anaemia presented with severe hypercalcaemia and was subsequently diagnosed with multiple myeloma. Anaemia in multiple myeloma is usually normochromic and normocytic.¹ To our knowledge, there are no reported cases in the English literature of true iron deficiency associated with multiple myeloma. Our case highlights the importance of pursuing the aetiology of iron deficiency, especially in a middle aged male. It also reinforces the fact that severe hypercalcaemia usually has a malignant aetiology.

BACKGROUND

Iron deficiency and multiple myeloma are two commonly encountered medical conditions in primary care. There is no case report in the English literature of iron deficiency anaemia as the predominant anaemia in multiple myeloma. The purpose of writing this case report was to describe an uncommon coexistence of these two disorders and try to explore the association between the two.

CASE PRESENTATION

A 58-year-old Caucasian man presented to the emergency department with a 2-week history of confusion, dizziness and balance problems. He also complained of worsening back and leg pain aggravated by walking. This pain was less responsive to the methadone which he was taking for chronic back pain which a year previously had been clinically diagnosed as degenerative disk disease and supported

Table 1 Basic laboratory results

	6 Months previously	At presentation	Normal range
Complete blood count			
White blood cells	10.6	11.3	4.8–10.8 th/mm ³
Haemoglobin	14.0	15.5	14.0–18.0 g/dl
Haematocrit	43	46.5	42–52%
Platelets	314	179	130–400 th/mm ³
Iron indices			
Mean corpuscular volume	75.2	85.4	80–94 fl
Mean concentration of haemoglobin	23.9	28.7	27–31 pg
Ferritin	12.4	232	28–365 ng/ml
Total iron binding capacity	416	409	250–450 µg/dl
Serum iron	33	16.0	35–150 µg/dl
Per cent iron saturation	7.9	30	20–50%
Complete metabolic profile			
Sodium	137	134	136–145 mmol/l
Potassium	4.8	3.8	3.5–5.1 mmol/l
Bicarbonate	101	96	22–29 mmol/l
Chloride	27	26	98–107 mmol/l
Blood urea nitrogen	15	93	8.4–25.7 mg/dl
Creatinine	0.8	5.3	0.7–1.3 mg/dl
Alkaline phosphatase	105	115	40–150 U/l
ALT (SGPT)	48	31	0–55 U/l
AST (SGOT)	62	31	5–34 U/l
Total protein	7.2	8.4	6.4–8.3 g/dl
Albumin	3.6	3.7	3.5–5.0 g/dl
Bilirubin	0.2	0.5	0.2–1.2 mg/dl
Calcium	10.3	17.7	8.9–10.8 mg/dl
Glucose	64	179	70–99 mg/dl
Magnesium		1.2	1.6–2.5 mg/dl
Phosphorus		5.8	2.3–4.7 mg/dl

ALT, alanine aminotransferase; AST, aspartate aminotransferase; SGOT, serum glutamic oxaloacetic transaminase; SGPT, serum glutamic pyruvic transaminase.

Figure 1 Skull x-ray showing multiple punched out lesions.

Figure 2 Bone marrow biopsy smear with reticulin stain (special stain for iron) showing decreased iron stores.

by an MRI. He had been followed in the continuity clinic for more than 2 years for iron deficiency with microcytic anaemia which were diagnosed based on his low iron stores, low mean corpuscular volume (MCV) and low haemoglobin. His laboratory values 6 months earlier were as follows: haemoglobin 10 (14.0–18.0 g/dl), haematocrit 30 (42–52%), MCV 64 (80–94 fl), mean concentration of haemoglobin 19 (27–31 pg/ml), ferritin 4.2 (28.0–365.0 ng/dl),

total iron binding capacity (TIBC) 409 (250–450 µg/dl), per cent iron saturation 3.9 (20–50) and albumin 3.6 (3.5–5.0 g/dl) (table 1). The aetiology of his iron deficiency remained unclear despite extensive investigation. Occult bleeding from the gastrointestinal tract is considered to be the most common cause of iron deficiency anaemia in patients without an obvious source of blood loss.² This was ruled out by upper and lower gastrointestinal endoscopy and small

bowel follow-through. Haemoglobinopathies resulting in haemolysis and subsequently iron deficiency anaemia were ruled out by peripheral blood smear (PBS) and haemoglobin electrophoresis. CT of the chest, abdomen and pelvis were performed to rule out obvious malignancy as a cause for iron deficiency.

The patient was non-adherent with his scheduled appointments and management. He was prescribed oral iron supplements and was being considered for intravenous iron because of non-compliance and poor response and was to have a bone marrow biopsy if he did not respond to intravenous iron. Other significant past medical history included hypertension and chronic obstructive pulmonary disease. Physical examination revealed tachycardia, mild tenderness in the epigastrium, lower ribs in the paraspinal region and bilateral sacroiliac joint and a slight antalgic gait on the left side which had not changed from baseline. His initial laboratory results were significant for mild leukocytosis with a white blood cell count of 11.3 (4.8–10.8 th/mm^3), hyperglycaemia with blood glucose of 179 (70–99 mg/dl), acute renal failure with creatinine of 5.3 (0.7–1.3 mg/dl), hypercalcaemia with calcium of 17.7 (8.9–10.8 mg/dl) (6 months previously his calcium was 8.5), phosphorus of 5.8 (2.3–4.7 mg/dl), intact parathyroid hormone of 8 (10–60 pg/ml), immunoglobulin G (IgG) monoclonal spike on serum protein electrophoresis and β_2 microglobulin of 6.10 (0.6–2.4 mg/l) (table 1).

A skeletal survey showed multiple punched out lesions consistent with multiple myeloma. Bone marrow biopsy showed plasmacytosis of 85%, suppressed trilineage haematopoiesis and decreased marrow stainable iron (figures 1, 2 and 3).

TREATMENT

The patient was managed with intravenous fluids, steroids and zoledronic acid. His creatinine had normalised a week later at outpatient follow-up.

OUTCOME AND FOLLOW-UP

The patient is currently being followed by our haematologist/oncologist for multiple myeloma and is being treated with lenalidomide and dexamethasone. His iron indices changed dramatically when he was diagnosed with multiple myeloma (haematocrit 37.5, MCV 85.4, ferritin 232 and per cent iron saturation 30) (figures 4 and 5).

DISCUSSION

Iron deficiency anaemia is commonly caused by blood loss from the gastrointestinal tract. Other uncommon causes include idiopathic pulmonary haemosiderosis, paroxysmal nocturnal haemoglobinuria or insufficient iron supply. Overall, 7%–47% of cases are idiopathic even after extensive investigation.³ The two most important disorders to be differentiated from iron deficiency are the anaemia of chronic inflammation (both the serum iron and TIBC will be low, with a normal or increased level of serum ferritin) and thalassaemia (presence of target cells and tear-drop shaped red cells on PBS, normal to increased serum ferritin levels and a normal to increased red blood cell count).

The annual incidence of multiple myeloma in the USA is approximately 4–5 per 100 000. The most common presenting symptoms are bone pain (58%) and fatigue (32%). Lytic lesions are found in about 67% of patients. Hypercalcaemia is present in 28% of patients at the time

Figure 3 Bone marrow biopsy smear showing a typical plasma cell with eccentric nucleus and 'cogwheel' appearance of nucleoli.

Figure 4 Trend of iron indices over 2 years.

Figure 5 Trend of ferritin level over 2 years.

of diagnosis and sometimes requires emergent treatment. Anaemia is the most common haematological complication in patients with malignant diseases and is found in 60–90% of cases with multiple myeloma. However, the anaemia is usually normocytic and normochromic. The mechanism in most patients is inadequate production of red blood cells due to either erythropoietin deficiency from accompanying renal failure, pronounced marrow replacement by myeloma cells or cytokine-mediated marrow suppression.^{1 4 5 6} Upregulation of hepcidin (a hepatic hormone) in response to inflammatory stimuli has been suggested as a mechanism of anaemia in multiple myeloma. Upregulation of hepcidin causes trapping of iron in the reticuloendothelial system resulting in decreased availability of iron leading to anaemia. Some preliminary reports also suggest a role of tumour suppressor gene p53 in the pathogenesis of anaemia accompanying cancer.^{7 8 9}

In a Mayo Clinic review of more than 1000 patients with multiple myeloma, 1% of patients had an MCV lower than 80 fl; three of 10 tested patients had a low serum iron value.¹

Non-secretory multiple myeloma is a rare variant of multiple myeloma where there is no gammopathy. Some case reports give a history of iron deficiency in this particular type of multiple myeloma,¹⁰ but, to our knowledge, there are no theories suggesting the mechanism of iron deficiency. Also, our patient clearly did not have non-secretory multiple myeloma since he had IgG monoclonal spike on serum protein electrophoresis. It is possible that there is inadequate utilisation of iron in multiple myeloma, although our patient's decreased iron stores do not support this hypothesis.

Is there any relationship between our patient's iron deficiency and multiple myeloma? The answer to this question remains unclear. We think that this occurrence of iron deficiency in multiple myeloma had to be coincidental unless the myeloma protein was targeting some iron storage protein.

Since iron deficiency is a commonly encountered condition in primary care, our case highlights the importance of being persistent in pursuit of the aetiology and close monitoring.

Learning points

- ▶ Iron deficiency in a young male warrants pursuit of the aetiology and close monitoring.
- ▶ Malignant aetiology should be ruled out for severe hypercalcaemia.
- ▶ Multiple myeloma may be a cause of iron deficiency, although the mechanisms have yet to be discovered, and should be ruled out in a patient with unexplained iron deficiency.

Competing interests None.

Patient consent Obtained.

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