Scurvy—a re-emerging disease with the rising cost of living and number of bariatric surgical procedures

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SUMMARY

This case presents a male in his early 50s with a bilateral painful petechial rash in the lower limbs, which occurred spontaneously without trauma. He also had macroscopic haematuria and macrocytic anaemia with mild neutropenia and lymphopenia. Vasculitis, autoimmune and haematological screens were negative. CT scan of his abdomen and lower limbs did not show any intra-abdominal bleeding or lower limb vasculitis. Skin biopsy was also unremarkable. His petechial rash continued to progress during admission. Further history revealed poor oral intake and cessation of his post-sleeve gastrectomy supplements due to financial constraints. A nutritional panel showed undetectable vitamin C levels, along with other nutritional deficiencies. He was diagnosed and treated for scurvy with ascorbic acid (vitamin C) 1000mg daily, and his painful rash and haematuria resolved. Scurvy is a re-emerging disease with the rising cost of living. It can present as early as a month after a vitamin C-deficient diet. Petechial skin lesions often occur especially in the lower extremities and may be mistaken for systemic vasculitis. The diagnosis is often made after an extensive diagnostic workup including imaging and biopsies, thus delaying treatment. Risk factors for scurvy include poor nutrition, gastric bypass surgery, dialysis, alcoholism, psychiatric history and eating disorders. This disease is easily reversible with supplementation, with a dramatic response seen within 24 hours. Failure to treat may lead to catastrophic haemorrhage, hence, early recognition and prompt treatment are vital.

BACKGROUND

Petechial rash often prompts further investigation into haematological, dermatological or vasculitis causes.[1] However, if the above investigations are negative and skin biopsy has not revealed a cause, there is a Renaissance-era diagnosis that is often overlooked but is easily investigated and treated.

CASE PRESENTATION

A man in his early 50s presented with an acute episode of extensive petechia and ecchymoses on both lower legs, discovered on waking from sleep. This was associated with lower limb pain. He denied any weakness, numbness or paraesthesia, but his mobility was limited due to pain. He also had a few episodes of intermittent painless macroscopic haematuria with a background of recent urinary tract infections (UTIs), postural dizziness and reduced appetite. He denied any neurological complaints, infective symptoms, any fever, recent trauma or travel. He did not have any chest pain, dyspnoea or abdominal pain. He had not recently commenced any new medication.

Medical history included iron deficiency anaemia requiring iron infusion, with no previous gastroscopy or colonoscopy to investigate an underlying cause. He had grand mal epilepsy well-controlled on carbamazepine and lamotrigine. He also had a sleeve gastrectomy procedure 8 years earlier. Other medical history included hepatic steatosis, hyperlipidaemia, asthma, mild bronchiectasis, hypertension, gastro-oesophageal reflux disease, migraine, vitamin D deficiency, iron deficiency and recurrent UTI. He was an ex-smoker with a 13-pack-year history. His medications included atorvastatin, carbamazepine, clonazepam, lamotrigine, fluoxetine, perindopril, amlodipine, pregabalin, propranolol, pantoprazole, a budesonide/formoterol inhaler and iron tablets. He was independent with activities of daily living. He lived alone at home, and was unemployed.

Examination

His vital signs were stable. He had a bilateral petechial rash on his lower limbs, extending from the lateral side of his abdomen to his ankles (figure 1& 2). There was non-pitting oedema on his lower limbs bilaterally. His calves were painful on palpation with no tenderness on passive movement. Pictures of his petechial rash are shown in figure 1.

There was no evidence of arthritis or synovitis. Lower limb pulses were present bilaterally with positive dorsalis pedis and posterior tibial signals on Doppler ultrasound. There was no scrotal involvement, nor any mucosal or genital ulcers. Examination of the cardiovascular, respiratory, abdominal and neurological systems was unremarkable.

Differential diagnosis at this stage was extensive. Life-threatening causes, such as active haemorrhage were ruled out in the first instance. Acute intraperitoneal bleeding was thought to be unlikely due to the lack of abdominal pain. He also denied any history of trauma to his abdomen or legs. An urgent CT abdomen done on arrival in the emergency department showed no evidence of active bleeding. Thus, the differentials were narrowed down to infection, vasculitis, autoimmune or haematological causes.

INVESTIGATIONS

His full blood count showed macrocytic anaemia with a haemoglobin of 77 g/L (ref: 135–180 g/L), mean cell volume of 114 fL (ref: 80–100 fL) and lymphopenia of 0.88×10^9/L (ref: 1.20–4.00$\times10^9$/L). His urea, electrolytes and creatinine were normal, with an estimated glomerular filtration rate

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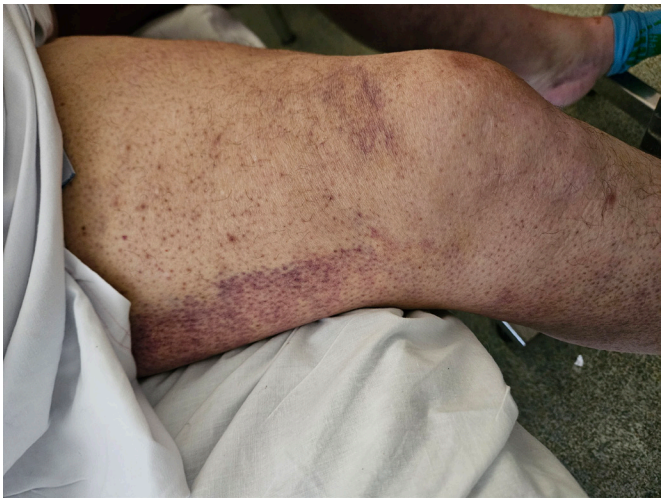

Figure 1 Lateral view of lower limb non-blanching petechial rash.

of >90 mL/min/1.73 m^2. His liver function tests were normal. His inflammatory markers showed a raised erythrocyte sedimentation rate (ESR) of 67 mm/h (ref: 1–15 mm/h) and C-reactive protein (CRP) of 80 mg/L (ref: <5.0 mg/L). Apart from a mildly elevated reticulocyte count of 9% (ref: 0.2–2.0%) and lactate dehydrogenase (LDH) of 376 U/L (ref: 120–250 U/L), which likely reflects a reactive response to chronic anaemia, the rest of his haemolysis screen (haptoglobin, Coombs test, coagulation studies and platelet count) were normal. His iron studies, thyroid function test, B12 and folate levels were also normal—ferritin of 177 μg/L (ref: 30–150 μg/L), iron of 12 μmol/L (ref: 9–30 μmol/L), transferrin of 29 μmol/L (ref: 23–43 μmol/L) and transferrin saturations of 21% (ref: 14–45%).

The blood film showed no morphological features of haemolysis but showed macrocytosis with hypersegmented neutrophils. Anti-nuclear antibodies, extractable nuclear antigen antibodies, anti-neutrophil cytoplasmic antibodies, complement C3 and C4, and cryoglobulin screen were all normal or not detected. Creatine kinase was 125 U/L (ref: 30–190 U/L). Coagulation factor assays showed no factor deficiencies. Serum-free light chain and serum electrophoresis were negative for a paraprotein.

ECG showed normal sinus rhythm, with normal axis and normal QRS complexes. Urinalysis showed 2+ blood and trace levels of protein, but no leucocytes or nitrites. There was no growth on urine microscopy, culture and sensitivity. Chest X-ray showed his lungs were clear with no evidence of pulmonary infiltrates.

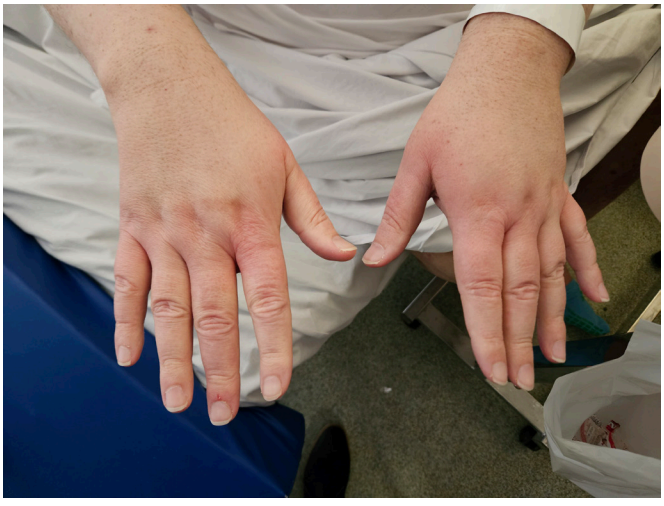

Figure 2 Progression of rash and oedema to his upper limbs.

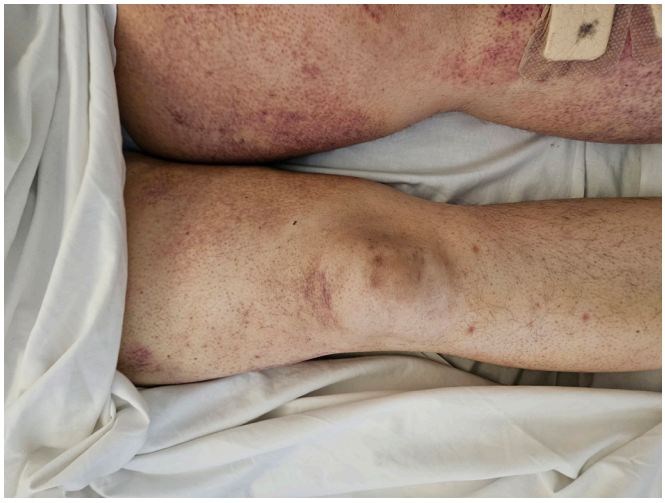

Figure 3 Anterior view of lower limb non-blanching petechial rash. Dressing in the left lower leg is overlying the punch biopsy site.

CT scan of the abdomen, pelvis and lower limbs with contrast showed no retroperitoneal haematoma nor evidence of intra-abdominal bleeding. There was evidence of prior sleeve gastrectomy. Thigh vessels were patent. There was generalised and marked subcutaneous soft tissue oedema in both thighs extending distally, worse on the left. There was mild to moderate asymmetric expansion of the muscles of the anterior compartment of the left thigh and posterior compartment of the right thigh. No rim-enhancing or drainable focal collection was identified.

A skin biopsy was also performed which revealed minor nonspecific inflammatory changes with no evidence of vasculitis or obstructive vasculopathy.

DIFFERENTIAL DIAGNOSIS

Over the next few days of his hospital admission, his petechiae and ecchymoses continued to progress. The rashes subsequently became more extensive with increased bruising, swelling and pain in both legs. His upper limbs had also started to develop new rash and oedema, as shown in (figure 3).

Haematology and immunology teams were consulted. The impression was that his neutropenia was longstanding for many years, and the reticulocytosis was reactive due to underlying anaemia. Bone marrow biopsy was not indicated at this stage due to insufficient evidence of underlying haematological process. An underlying vasculitis or autoimmune process was unlikely given the negative antibodies and normal skin biopsy result.

Further history revealed that the patient's living circumstances were poor. He had financial constraints and therefore neglected his diet. His meals mostly comprised processed food, lacking in vegetables or fruit. Sometimes he would skip meals, which occurred more frequently in recent weeks. He had also stopped taking the vitamin and mineral supplements prescribed following gastric bypass surgery as he was unable to afford them. An underlying nutritional deficiency was therefore suspected.

A nutritional panel revealed a very low vitamin D level of 16 nmol/L (ref: >50 nmol/L) and undetectable vitamin C of <1 mg/L (ref: 4.0–14.0 mg/L). He was therefore diagnosed with scurvy as the cause of his petechial rash, macrocytic anaemia and macroscopic haematuria.

TREATMENT

He was commenced on ascorbic acid (vitamin C) 1000mg daily, cholecalciferol 125μg daily, folic acid 5mg daily, and multivitamin 1 tablet daily. A dietitian review was organised, and a meal plan was created. He also started eating a lemon daily.

OUTCOME AND FOLLOW-UP

His rash subsequently subsided and his repeat vitamin C level also showed improvement. His haematuria also resolved with treatment of his scurvy, without the need for any invasive urological investigation. He was discharged home on regular vitamin supplements.

DISCUSSION

Scurvy is a disease caused by vitamin C (ascorbic acid) deficiency.[2] It was first reported in ancient Egyptian, Greek and Roman literature.[2] Then, during the Renaissance era, British and European sailors were dying from an unknown disease, which was later discovered to be scurvy.[2]

Scurvy manifests with petechiae, perifollicular haemorrhage, ecchymosis, gingivitis, oedema, anaemia, arthralgia and impaired wound healing.[3] Constitutional symptoms include weakness, malaise, joint swelling, arthralgia, anorexia, depression, neuropathy and vasomotor instability.[4] It can present after approximately 4 weeks in those who consume <10 mg/day of vitamin C.[5 6] The haemorrhagic skin lesions may be mistaken for systemic vasculitis.[7] It can also weaken collagen triple-helix structures and weaken capillaries. It can cause significant mucosal and gastrointestinal bleeding. The coagulation parameters are often normal, as in our case.[8]

Our patient did not have any clinical evidence of infection or inflammation to explain the elevation in his CRP and ESR. However, this is a common phenomenon described in various literature and can mislead clinicians into into suspecting an underlying inflammatory illness.[9] There are several reports of elevated acute phase reactants (CRP, ESR and serum amyloid A) that occur in patients with scurvy.[9] A murine study showed that vitamin C-deficient rats have increased in acute phase reactants despite no inflammatory stimuli.[10] However, the mechanism remains unknown.[10]

Our patient also had macrocytic anaemia with hypersegmented neutrophils. The detection of hypersegmented neutrophils is sensitive and specific for megaloblastic anaemia, commonly caused by Vitamin B12 or folate deficiency.[11] Vitamin C has a role in B12 and folate metabolism and has been shown to influence folate concentration, folate metabolism-associated gene expression and protects reduced folate from oxidation thus increasing bioavailability.[12] These effects may account for the finding of macrocytic anaemia in cases of scurvy. In a cross-sectional study, vitamin C supplement users had a 25% higher plasma folate concentration compared with the control group.[13] In another study, it was found that folate metabolism-associated gene expression was influenced by vitamin C intake.[14] Due to its rarity, scurvy-associated anaemia is not well recognised by clinicians and can result in extensive evaluation, increasing healthcare costs and patient morbidity.[12] Bone marrow biopsy is not that helpful in distinguishing vitamin C deficiency from vitamin B12 or folate deficiency.[12]

Musculoskeletal pain may be severe and may cause difficulty in weight-bearing, especially in the paediatric population.[15] Characteristic findings on MRI are sclerotic and lucent metaphyseal bands, with periosteal reaction and adjacent soft tissue oedema.[16]

Scurvy is still seen as a disease of the past, especially in developed countries.[17] However, sporadic cases of scurvy occur, especially in the elderly, patients with alcoholism and children with psychiatric or developmental problems.[17] There is often a delay in diagnosis after an extensive diagnostic workup including imaging and biopsies.[16]

Risk factors for scurvy include poor dietary habits, malnutrition, alcoholism, gastrointestinal disorders (such as inflammatory bowel disease), smoking, low socio-economic status, eating disorders and psychiatric illness, abdominal surgery (such as small bowel resection and bariatric surgery), obesity, dialysis and medications that affect absorption of vitamin C (such as corticosteroids and proton pump inhibitors).[8 18 19]

In Australia, the rising cost of food (up 5.9% in the last 12 months) is making it harder for families to afford meals.[20 21] The increasing cost of living means that people are more reliant on lower-cost foods, which tend to be poor in nutritional value.[20]

Patients who have undergone bariatric surgery are also at risk of developing micronutrient deficiency.[22] Although they are particularly susceptible to fat-soluble vitamin deficiencies (vitamins A, D, E and K), if combined with a poor diet, they can also be deficient in vitamin C.[22 23] There are multiple case reports of patients developing scurvy as a complication post-bariatric surgery, often presenting with spontaneous petechiae or ecchymoses of the skin.[22–24] Our patient had multiple risk factors, namely, poor dietary habits, obesity, previous bariatric surgery, use of proton pump inhibitors and low-income status. His history of iron, vitamin D and folate deficiencies were also clues to his underlying nutritional deficiency.

The diagnosis of scurvy is often made on a clinical basis but can be supported by reduced levels of vitamin C (ascorbic acid) in serum or buffy-coat leucocytes.[17] Symptoms typically occur when plasma concentration of vitamin C level are less than 0.2 mg/L (11 μmol/L).[25] However, recent intake of vitamin C may normalise plasma concentration when serum measurement is performed, despite tissue levels still being deficient.[26] Measurement of vitamin C levels in leucocytes is more accurate, but this test is not widely available.[26]

The treatment for scurvy is vitamin C supplementation. A wide range of replacement doses have been used successfully. In children, the recommendation is 100 mg of ascorbic acid three times daily for 1 week and then once daily for several weeks until they have fully recovered.[27] Adults are treated with 300–1000 mg daily for 1 month.[3] The response to vitamin C supplementation is often dramatic, as in our case.[17] It is reported that even one replacement dose of vitamin C can stop gastrointestinal bleeding, and capillary stability is established within 24

Learning points

- Scurvy is a re-emerging diagnosis in the current era of a rising cost of living and increasing number of bariatric surgeries. This is associated with poor nutritional intake, alcoholism, gastrointestinal disorders and surgical resection, psychiatric disorders, use of proton pump inhibitors, and dialysis.
- Scurvy manifests initially with a petechial rash, gingivitis, oedema and/or impaired wound healing. As it progresses, haemorrhagic complications may occur.
- Scurvy should be suspected in vasculitic presentations. A low serum vitamin C level is diagnostic.
- Scurvy is easily reversible with vitamin C supplementation.

hours.[8] It may take up to 2–3 weeks for other symptoms, such as skin lesions, to heal.[8] Clinicians should be aware of this fatal but easily curable condition that may still occur in this modern age.[17]

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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