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ENDGAMES

CASE REPORT

Taught a lesson by taut skin

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A 45 year old man with a history of ulcerative colitis presented to his general practitioner because of Raynaud's phenomenon and itchy tight skin that had affected his hands and elbows bilaterally over the preceding few months. He was referred to a rheumatologist, who performed a series of immunological tests. The results included a positive antinuclear antibody staining pattern on immunoflourescence, with anti-RNA polymerase III antibodies identified on further testing. Tests for anti-centromere and anti-topoisomerase I (anti-Scl 70) antibodies were negative. The rheumatologist diagnosed a systemic connective tissue disorder.

When the skin symptoms worsened over the next few weeks the patient started to use over the counter ibuprofen to ease the pain associated with his tight skin. He subsequently presented to the emergency department with fatigue. His blood pressure was found to be 210/120 mm Hg. In addition to the skin abnormalities, bibasal fine inspiratory crepitations were detected on physical examination. Routine laboratory testing showed haemoglobin 75 g/L (reference range 130-180), creatinine 475 µmol/L (80 µmol/L one month previously (80-110), and lactate dehydrogenase 357 U/L (70-250). Electrocardiography showed T wave inversion in the lateral leads. He was excreting 1.15 g of protein in his urine per 24 hours and haematuria was detected on dipstick urinalysis.

Questions

1 What is the diagnosis?

2 What further test might help to confirm the diagnosis?

3 What factors predispose to this condition?

4 How is the condition treated?

5 What is the natural course of the condition?

Answers

What is the diagnosis?

Short answer

Scleroderma renal crisis, which results in a hypertensive emergency.[1]

Long answer

Our patient had diffuse cutaneous scleroderma. Figures 1 and 2 show taut shiny skin on his forearm and hands, with areas of hypopigmentation on the extensor surfaces. The skin was so tight that he developed contractures at the elbows (fig 1 shows the position of maximal extension). Resorption of the finger pulps results in spindle shaped fingers (sclerodactyly), which can be seen in fig 2. Severe acute kidney injury and hypertension in the setting of systemic sclerosis should prompt the doctor to consider the diagnosis of scleroderma renal crisis, which carries a high mortality.[1]

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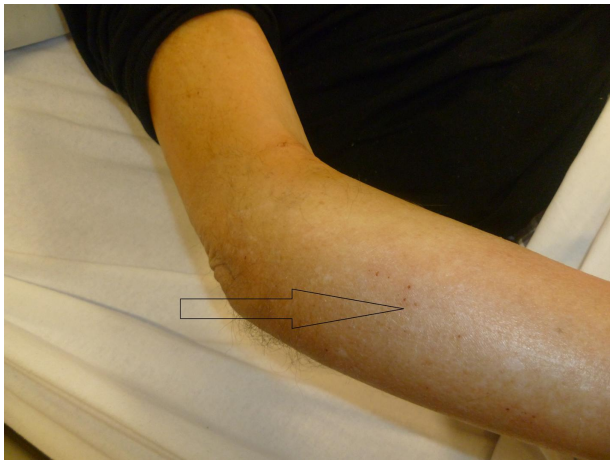

Fig 1 Patient's arm, showing taut shiny skin with areas of hypopigmentation (arrow)

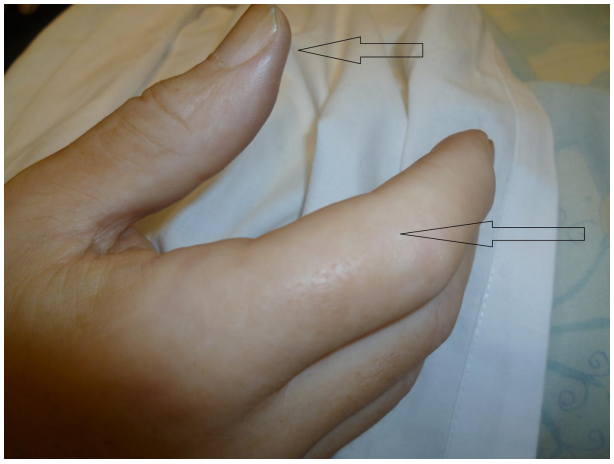

Fig 2 Loss of finger pulp (top arrow) and shiny taut fingers (bottom arrow)

2 What further test might help to confirm the diagnosis?

Short answer

Fundoscopy, which might show the presence of grade III or IV hypertensive retinopathy.

Long answer

Fundoscopy allows direct visualisation of the retinal tissue and vasculature. Figure 3 shows the patient's retinal photograph. The flame haemorrhages (ruptured, bleeding vessels) and cotton wool spots (retinal infarcts) confirm that an acute rise in blood pressure has overwhelmed the vascular autoregulatory processes. The lack of papillo-oedema shows that this is grade III hypertensive retinopathy.[2] This evidence of accelerated phase hypertension in the setting of systemic sclerosis is suggestive of scleroderma renal crisis.

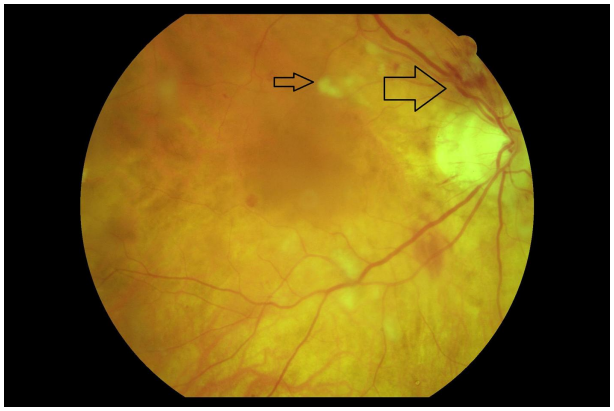

Fig 3 Fundoscopy, showing cotton wool spots (small arrow) and flame haemorrhages (large arrow)

Renal biopsy is not usually performed in classic cases because of the high risk of haemorrhage when mean arterial pressure is raised,[3] but in atypical cases it can sometimes help confirm the diagnosis. The characteristic pathological lesion is mucoid intimal thickening, with concentrically arranged myointimal cellular proliferation without inflammatory cells, otherwise known as onion skin lesions.[4] Fibroid necrosis may lead to narrowing and occlusion of the vessel lumen and ischaemia. Unlike the lesions seen in malignant hypertension in the absence of scleroderma renal crisis, the media of interlobular arteries is often thinned and surrounded by peri-adventitial and adventitial fibrosis.[4]

Other evidence of accelerated phase hypertension in our case included the ischaemic changes on electrocardiography (fig 4) and evidence of pulmonary congestion on examination, which are both manifestations of myocardial dysfunction. Acute heart failure commonly occurs in malignant hypertension because of raised systemic vascular resistance and decreased left ventricular compliance.[5] Similarly, the increase in serum creatinine indicates acute ischaemic injury to the kidney. Haematuria, proteinuria, and granular or cellular casts can also be seen, and—although pressure naturesis may occur initially—this can progress to oliguria or anuria.[4] The underlying damage to the microvasculature is indicated by evidence of microangiopathic haemolysis—schistocytes—on the blood film (fig 5), low haemoglobin values, and raised lactate dehydrogenase. Other signs of end organ dysfunction might include encephalopathy or stroke.

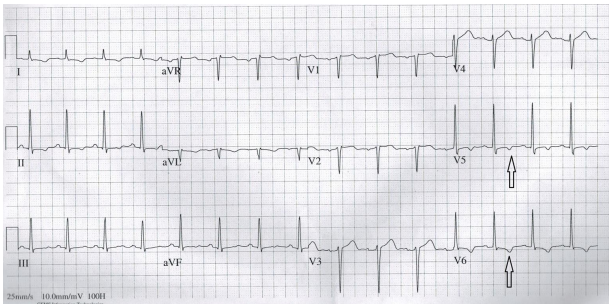

Fig 4 Electrocardiogram showing T wave inversion (arrows)

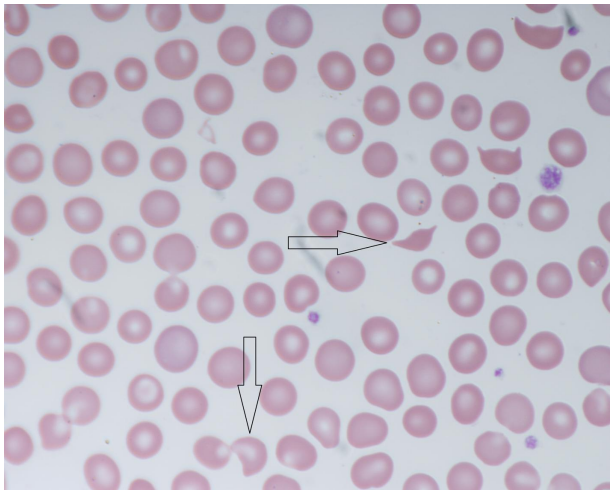

Fig 5 Blood film showing schistocytes (arrows)

In the clinical diagnosis of this condition it is important to note that about 10% of affected patients will be normotensive.[6] In this population an increase in blood pressure of 30/20 mm Hg above baseline is suspicious for a renal crisis.[4]

3 What factors predispose to this condition?

Short answer

Drugs, especially high dose corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs), are predisposing factors. The condition is also more common in certain subgroups of patients, such as those who are positive for anti-RNA polymerase III antibodies.

Long answer

Scleroderma renal crisis is a life threatening condition that presents as accelerated phase hypertension and usually develops within five years of initial diagnosis of scleroderma.[7] It is most common in patients with rapid skin progression, especially those who are positive for anti-RNA polymerase III antibodies. One case-control study reported the odds ratio for developing scleroderma renal crisis in the presence of anti-RNA polymerase III antibodies as 8.9 (95% confidence interval 2.6 to 29.6).[1] In most cases, plasma renin concentrations are greatly raised. It is unclear whether this is a primary phenomenon of the condition or secondary to renal ischaemia (particularly of the juxtaglomerular apparatus),[8] but a vicious circle ensues between renal ischaemia and vasoconstriction. Scleroderma renal crisis is classically precipitated by the use of high dose corticosteroids (generally above 15 mg per day),[9] NSAIDs,[10] and ciclosporin.[11] NSAIDs and calcineurin inhibitors probably cause intrarenal vasoconstriction, with the ischaemia that follows leading to the release of renin and angiotensin, whereas corticosteroids are known to raise renin concentrations.

Other factors thought to predispose to scleroderma renal crisis are new onset anaemia,[10] large joint contractures,[12] diffuse skin disease,[13] rapidly progressing skin disease,[14] high skin score,[12] cardiac involvement (for example, pericardial effusion),[12 15] presence of tendon friction rubs,[16] less than three years since diagnosis of scleroderma,[15 17] and a newly identified association with certain HLA haplotypes such as HLA-DRB1*and HLA-DRB1*1304.[18]

4 How is the condition treated?

Short answer

Angiotensin converting enzyme (ACE) inhibitors are the main form of treatment.

Long answer

Before the introduction of ACE inhibitors survival after scleroderma renal crisis was low, with most patients dying within three months.[19] One case series of 108 patients suggests that the one year survival increased from 18% to 76% after the introduction of these drugs.[20] A recent case-control study from Sweden reported the overall 10 year survival after scleroderma renal crisis was only 40%.[1] Classic reports used captopril, which was initially the only orally available ACE inhibitor. Because it is short acting, it can be introduced at low doses and uptitrated quickly, balancing the reduction in mean arterial pressure against the preservation of cerebral perfusion pressure.

Patients must be transferred to a high dependency or intensive care unit, with invasive monitoring of arterial pressures. Aim for a controlled reduction in blood pressure of about 10-15 mm Hg per 24 hours. Strict monitoring of extracellular fluid balance and cardiac monitoring are essential. In patients with scleroderma renal crisis and acute kidney injury, doctors must be vigilant about the need for renal replacement therapy. This is especially important because the acute kidney injury may render them unresponsive to intravenous diuretics and they may develop sudden life threatening pulmonary oedema as a result of left ventricular failure. No benefit has been shown for prostacyclin infusions, which were used routinely in the past.

5 What is the natural course of the condition?

Short answer

Prognosis is poor, with progression to end stage renal disease occurring in 20-50% of patients.

Long answer

Scleroderma renal crisis carries a poor prognosis—20-50% of patients will develop end stage renal disease and require dialysis. Those that do respond to treatment may need dialysis for many weeks, or sometimes months, as the renal tissue regenerates. In one of the largest published case series of 311 patients, only 6.8% no longer needed renal replacement at some point during follow-up,[21] although more recent data are more optimistic and suggest that 23-28% of patients could discontinue dialysis.[16 22] The factors associated with a poor prognostic have been well described.[16 23] They include serum creatinine greater than 265 µmol/L before the start of ACE inhibitors,[16] more than three days needed to control blood pressure, male sex, advancing age, and the presence of congestive cardiac failure. Patients who do recover independence from dialysis tend to have residual advanced chronic kidney disease.[20]

Patient outcome

This patient received aggressive early blood pressure control with captopril, but progressive decline in renal function necessitated institution of renal replacement. It is too early to know whether his renal function will recover enough for him to discontinue dialysis.

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Patient consent obtained.

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