Lower limb oedema in diabetes

Rowan Hillson

Quincey (1719) advocated Pulvis Hydragosus for dropsy (oedema): ‘Take Cream of Tartar… Mechocan, Jalap… Dwarf-Elder seeds… Gamboge… Nutmegs… Mix into a Powder. This is an admirable good Medicine… It wonderfully brings down the swellings in Dropsies and Cachectick Constitutions.’

Later that century William Withering said: ‘In the year 1775, my opinion was asked concerning a family receipt for the cure of the dropsy. I was told that it had long been kept a secret by an old woman in Shropshire who had sometimes made cures after the more regular practitioners had failed… it was not very difficult… to perceive, that the active herb could be no other than the Foxglove.’

It did indeed cure the dropsy although usually while demonstrating the plant’s considerable toxicity.

Fluid accumulates in tissues when more fluid leaves capillaries than is cleared by the lymphatic system. Causes include: raised capillary pressure, for example in heart failure, fluid overload, or venous obstruction (such as thrombosis); reduced plasma osmotic pressure, for example with low plasma albumin; and increased capillary permeability, for example in infection or inflammation. Malformed or damaged lymphatics prevent adequate fluid drainage.

‘Hi I have very swollen feet, and lower legs are now Rock hard, I am not sure this is diabetes related help please????? Xxx.’

People with diabetes can get oedema virtually anywhere – legs, abdomen, lungs, maculae and may have multiple reasons for oedema. This article discusses lower limb oedema – of course if that is present, fluid retention may be present elsewhere. Some causes are discussed.

Lower limb oedema is usually obvious, often pitting on gentle pressure but non-pitting when chronic. Adipose tissue does not pit – but obese people may develop oedema. Symptoms of oedema include heaviness, aching or tenderness, skin discoloration, stiff joints, or weight gain. Fluid oozes from the tiniest skin damage, risking ulceration and infection in people with diabetes, especially those with neuropathy. Such leg ulcers are extremely difficult to heal.

Elderly or immobile people often have gravitational oedema – consider other causes.

Injury and inflammation

‘I have recently had my big toe amputated, and while in hospital my leg was quite swollen, but it went down and has been fine for weeks. However, over the last few (very hot) days, both feet, ankles and legs have swollen considerably… Is this just the heat… or could it be something more sinister? I am so scared that I may have further complications, don’t think I can take anything more right now.’

Trauma – whether accidental or surgical – is often associated with oedema. Inflammation, most commonly due to infection, for example diabetic foot disease or cellulitis, usually causes oedema and redness. Don’t forget Charcot foot in neuropathic patients.

Cardiac failure

People with diabetes are at high risk of heart failure. The National Diabetes Audit (NDA) showed a standardised ratio for cardiac failure of 466 among those with type 1 diabetes and 274 with type 2 (vs 100 among the general population). Among the people with diabetes in the NDA, 30.4% of non-emergency hospital admissions, and 32.5% of emergency admissions, were due to cardiac failure. People with diabetes whose problems included heart failure accounted for 29.3% of bed days for non-emergency hospital admissions and 32.6% of bed days for emergency admissions.

Among 9248 outpatients with chronic heart failure followed for a year, 36.5% had diabetes. After correcting for multiple potential confounders, those with diabetes were more likely to die from any cause (9.4% vs 7.2%; adjusted hazard ratio [HR] 1.28 [95% CI 1.07–1.54]), from cardiovascular disease (4.8% vs 3.8%; 1.28 [0.99–1.66]), and require admission for heart failure (13.8% vs 9.3%; HR 1.37 [1.17–1.60]), compared with patients without diabetes.

In patients with severe chronic lung disease, oedema may be due to right heart failure from pulmonary hypertension – cor pulmonale.

Low plasma albumin

The National Diabetes Audit found evidence of kidney disease in 71.9%; 0.3% had end stage kidney disease or were on renal replacement therapy. Some will have nephrotic syndrome – severe urinary protein leakage of ≥3.5g/24 hours with a serum albumin of <25g/L – with oedema, foamy urine, and fatigue.

Severe liver disease also causes fluid retention from low plasma albumin. A Scottish study found a prevalence of non-alcoholic fatty liver disease (NAFLD) of 42.6% among people with type 2 diabetes aged 61–76 years after excluding other causes. Most patients with NAFLD do not suffer severe liver damage but an American multivariate analysis showed that NAFLD increased overall mortality (HR 2.2 [95% CI 1.1–4.2]); 19% of those deaths were due to complications of liver disease.

Malnutrition, for example associated with tropical or fibro-calcific pancreatic diabetes, may cause oedema.

Endocrine

Hypothyroidism may cause myxoedema or mucus swelling (Greek Myxo) from mucopolysaccharides. In a Brazilian study, 6.4% of people with type 2 diabetes had hypothyroidism. A Spanish study found that the relative risk of new hypothyroidism in patients with type 2 diabetes was 2.81 (1.77–4.48) vs controls. Reported frequency is likely to vary due to varying laboratory and diagnostic methods. Thyrotoxic patients with cardiac failure may have oedema. Cushing’s syndrome causes oedema. Swollen ankles are common in pregnancy, but remember that pre-eclampsia is more prevalent in women with diabetes than in those without.
Venous causes
Varicose veins may cause oedema. So can deep vein thrombosis which may be the primary event – or develop in immobile patients with chronic oedema. Most studies indicate that people with diabetes are more likely to develop venous thromboembolism.\textsuperscript{15} NB: Does your oedematous patient need thrombophrophylaxis?

Medication
Insulin oedema
‘I was told 9 days ago that I am type 1 so as you can imagine this is all a bit new since coming out of hospital my legs and ankles are very swollen… I am on Lantis and Nova rapid at the moment if you have any ideas please let me know your thoughts.’\textsuperscript{14}

In 1928, Leifer described a 41-year-old man who developed pitting oedema of his legs a week after starting insulin for newly-diagnosed diabetes.\textsuperscript{15} Since then there have been case reports in adults and children.\textsuperscript{16} Most diabetologists see the condition occasionally. Insulin oedema seems more likely when insulin achieves rapid glucose lowering in someone with severe or prolonged hyperglycaemia. The oedema usually gradually resolves spontaneously. Other causes should be excluded.

Thiazolidinediones
In a two-year study, there was more likelihood of oedema when pioglitazone was added to metformin (7.6% vs 3.5% on gliclazide plus metformin), and when pioglitazone was added to sulphonylurea (10.7% vs 2.8% with metformin plus sulphonylurea).\textsuperscript{17} Pioglitazone may worsen heart failure. It has been suggested that thiazolidinediones increase fluid reabsorption in the renal collecting duct and also increase vascular permeability in adipose tissue.\textsuperscript{18} Much of the work has been done in mice.

Other medication
Other drugs can cause oedema – for example calcium channel blockers, non-steroidal anti-inflammatory, corticosteroids, and oestrogens.

Lymphoedema
Obesity and recurrent infection predispose to lymphoedema so this may be more frequent among people with diabetes than in others. Lymphoedema increases the risk of ulceration and infection. Treatment is challenging and may include compression bandaging which should be performed only by staff fully trained in this technique. Compression is dangerous in patients with severe arterial disease or neuropathy.\textsuperscript{19}

Challenges
Oedema can cause pain, distress, depression, limited mobility, and expense – for example among shoes. Subsequent ulceration and infection can be limb- or life-threatening. Swelling makes ankle-brachial pressure measurements and sensory testing unreliable. Avoid tests of pin-prick sensation in oedematous tissue and be careful with monofilaments. Do not inject insulin into oedematous areas as absorption is unpredictable.

Treatment of oedema depends on the cause(s) which is occasionally obscure. Sadly, too little attention may be paid to diagnosis in today’s time-pressured consultations.

Don’t miss heart failure – it is common among people with diabetes and responsible for a third of their hospital admissions. Remember that some heart failure patients will not have lower limb oedema.

Leg elevation can considerably reduce swelling so is a key part of treatment for most patients with oedema. Take great care to avoid pressure ulcers on heels or legs when using foot stools or in bed. Ulcers ooze infected fluid risking bacterial colonisation of furniture or pressure-relieving pads despite careful cleaning. People with chronic oedema may have sat with legs down for years. Patient perseverance is needed to help them get their feet up comfortably.

Patient education is vital – ‘Sit down, legs up!’ and ‘Always protect your legs’.

Summary
• Lower limb oedema is common in people with diabetes.
• Oedema is distressing and potentially dangerous.
• Seek the cause(s) to tailor treatment.
• Educate and support your patient.
• Protect swollen limbs carefully.
• Elevate swollen limbs safely.

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References