Rare complications of diabetes

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Today's diabetes world is fast-moving and exciting; knowledge is accumulating at an astonishing rate. To help understand the present, however, it sometimes helps to examine the past.

In this installment of *Tattersall's Tales*, Robert Tattersall discusses a range of rare complications that can occur in people with diabetes, looking back at the history of their first recognition, their symptoms, prevalence and current clinical management.

I once asked a student why he hadn't included a particular condition in his differential diagnosis, to which he replied, "isn't it very rare?" "Yes", I said, "but you need to know about rare conditions so you will recognise them when they turn up." Some of the conditions I describe below, I only saw once or twice in 25 years but because I had read about them, I was able to make the diagnosis.

Antepartum pituitary infarction

Pituitary infarction in women is most common in the postpartum period and is usually a result of severe haemorrhage, a syndrome first described by the Liverpool pathologist Harold Sheehan (1900–1988) in 1937 (Sheehan, 1937). In 1971 Don Schalch and Zane Burday of Rochester, USA, reported three cases of antepartum pituitary infarction (Schalch and Burday, 1971). In each the woman, late in the third trimester, had a severe deep midline headache, which lasted up to 3 days and was almost immediately followed by a dramatic drop in insulin requirement (the Houssay phenomenon). After delivery, there was usually a failure of lactation followed by amenorrhoea and recurrent hypoglycaemia. The diagnosis of hypopituitarism was often delayed for several years, which regularly happened in the dozen or so cases reported in the past 40 years.

It has only ever been reported in women with diabetes and this may be because attention is drawn to it by the striking drop in insulin dose which prompts further investigation. In women without diabetes it is possible that the headache would be passed off as something else with her presenting years later with hypopituitarism and an empty sella.

Ocular nerve palsies

In 1929 James Collier (1870–1935), physician to the Royal Eye Hospital in London, reported that he had seen more than 30 cases of ocular palsy in the previous 20 years and apologised for "bringing forward a very old subject and for having said very little that is new"(Collier, 1930). His excuse was that there had been nothing on the subject in the English neurological literature. Most of his patients were over the age of 50 and did not recover, but he then recorded that:"One day I wanted a case for demonstration at St George's Hospital, and coming across one of right third and left sixth nerve paralysis with glycosuria at the Royal Eye Hospital, I sent the patient into St George's and dilated on the thrombosis of the nerve vessels and the hopeless outlook with regard to recovery. Afterwards my house physician demonstrated complete recovery of the nerves in the course of 3 weeks under a dietetic treatment alone. It is a remarkable fact that I have not since that time seen a single case which did not make a complete recovery."

Collier emphasised that the onset of paralysis was usually rapid and painless. He regarded unilateral paralysis of the 6th nerve as the commonest presentation followed by unilateral 3rd nerve palsy. Collier thought it likely that the pathology was haemorrhage into the nerve. He thought insulin speeded recovery but had admitted that many patients recovered spontaneously in the pre-insulin era. In 1967, Eduardo Zorilla and George Kozak reviewed 27 episodes of diabetic ophthalmoplegia in 24 patients at the New England Deaconess Hospital, Boston, between 1954 and 1966 (Zorilla and Kozak, 1967).

The sex incidence was equal and the age at onset varied from 25 to 77 years (average 61). The 3rd nerve was affected unilaterally in 15 patients and bilaterally in two. The other seven had 6th nerve palsies. The problem highlighted by the authors was that when the ophthalmoplegia was due to diabetes, a benign, self-limited course was to be expected. However, life-threatening conditions such as intracranial aneurysms, might need to be excluded by cerebral arteriography or pneumoencephalography, neither of which were trivial or safe investigations.

When I saw my first case of 3rd nerve palsy at King's, David Pyke told me that the distinguishing features of the diabetic variety were that the pupil was spared and that it was painless. His pithy advice was "tell him it will get better in a few weeks and send him home". He was right about the pupillary sparing which happens because the pupillary fibres are grouped on the outside of the nerve and are spared in diabetes but caught first by an aneurysm. He was also right to say that it gets better spontaneously; in one recent series 98% recovered completely within 3 to 6 months (Trigler et al, 2003). What he was wrong about was the lack of pain; most patients whether they have diabetes or not have pain, usually over the ipselateral eye. This often precedes the palsy by a day or two (Wickler et al, 2009) One puzzle is why the 4th nerve which has a longer course than the 3rd or 6th is so rarely affected by diabetes.

Pseudopapilloedema

This ill-defined condition, also known as diabetic papillitis, was first described in 1970 in three teenagers with long-standing diabetes who presented with haemorrhages and swelling of one or both optic discs which mimicked papilloedema (Lubow and Makley, 1971). The first had sudden visual loss but the other two, both 16-year-old girls, were picked up on routine examination;

they had bilateral changes and spontaneous resolution within 6 months. Most patients are young and have type 1 diabetes but cases have been described in type 2. The diagnosis is one of exclusion but the lack of visual symptoms and resolution of oedema differentiate it from ischaemic optic neuropathy (Heller and Tattersall, 1987).

Muscle infarction

This was first described in 1965 under the title "Tumoriform focal muscular degeneration in two diabetic patients" (Angervall and Stener, 1965). It usually occurs in diabetes of long duration with retinopathy and nephropathy. Since 1965 about 100 cases have been reported. Women (61%) are more commonly affected than men. The presentation is relatively stereotyped with acute painful unilateral swelling of the thigh muscles or less commonly the calf (Trujillo-Santos, 2003). There is no fever or signs suggestive of infection and the white count is usually normal. The ESR is raised in half the patients. Surprisingly creatinine kinase is usually normal. The condition is self-limiting and most patients recover within a month or two on bed rest and analgesia. Unfortunately it recurs in nearly half.

The diagnosis is potentially wide and many patients have had biopsies to rule out muscle tumours. However, the clinical picture and MRI appearance is usually diagnostic and biopsy should be avoided because it is often followed by clinical deterioration which delays recovery.

Mediastinal emphysema

In 1939 Louis Hamman (1887–1946) described a case of spontaneous mediastinal emphysema in a 16-year-old with diabetic coma (Hamman, 1939). It then seemed to be forgotten until 1968 when a single case in a 7-year-old boy was reported (McNichol et al, 1968). A year later Paul Beigelman et al reported four cases (Beigelman et al, 1969). The patients were between the ages of 15 and 29. One had experienced a previous episode that was treated surgically at another hospital, but all four recovered spontaneously. Up to 1989, 30 cases had been reported with an age range of 7 to 29 years. Patients are typically in their teens or twenties and men are affected more often than woman. A third had retrosternal chest pain and half also had subcutaneous emphysema. In every case the condition resolved spontaneously within 10 days (Watson and Barnett, 1989). It is also seen occasionally in vomiting from other causes. It is important to be aware of this condition because, alarming though it seems, it is benign and does not need invasive investigations.

Insulin oedema

In a case reported in 1928 by Aaron Leifer, a 41-year-old man with newly diagnosed diabetes was severely emaciated and "was ordered to bed and given black coffee, tea and orange juice several times during the first day. Saline enemas were given and hot water bags were applied to the feet and body." During the first 6 days when he received a total of 170 units of insulin his weight increased from 56.7 to 64 kg and he developed pitting oedema which was successfully treated with salt restriction (Leifer, 1928). Since then it has been recognised that insulin oedema can occur either in people starting insulin or in those whose glycaemic control is dramatically improved. In a series of 31 patients with generalised insulin oedema reported between 1928 and 2004, most were aged between 20 and 40 and most had type 1 diabetes (Kalambokis et al, 2004). Eighteen (58%) developed oedema after starting insulin of whom 13 (42%) had newly diagnosed diabetes. In 13 patients (42%), oedema occurred after insulin treatment was intensified. Oedema usually affects the legs and face but occasional patients have had pleural effusions or ascites. Swelling resolves spontaneously in about a half and the rest need diuretics. The mechanism is uncertain but the condition which insulin oedema most closely resembles is refeeding oedema or carbohydrate induced antinatriuresis, as seen in Japanese prisoners of war and other situations where starving people are re-fed (Schnitker et al, 1951).

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