Weber-Christian panniculitis and auto-immune disease: a case report

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SYNOPSIS A case is described of Weber-Christian panniculitis accompanied by a gammaglobulin disturbance which preceded by five years the diagnosis of an autoimmune hepatitis and pancytopenia. Also associated was the onset of diabetes mellitus, found at necropsy to be related to pancreatic islet amyloid deposition. This case reinforces the view that Weber-Christian panniculitis may be an adipose response to a variety of immunological stimuli.

The Weber-Christian type of panniculitis is a recurrent febrile illness characterized by multiple symmetrical subcutaneous nodules or plaques which resolve, leaving characteristically depressed atrophic areas (Cairns, 1968). Histologically (Lever, 1967) there are three phases: (1) degeneration of fat cells accompanied by an inflammatory infiltrate composed of neutrophils, lymphocytes, and macrophages: abscess formation does not occur; (2) infiltration with macrophages, many laden with fat and some multinucleate: in some areas macrophages with foamy cytoplasm completely replace fat cells; (3) fibroblasts intermingled with lymphocytes and plasma cells replace foam cells: collagen is laid down, resulting in fibrosis.

Steinberg (1953) reviewed 43 cases with systemic symptoms and signs, and he concluded these to be malaise, fatigability, generalized aching, chills, night sweats, fever, nausea or vomiting, hepatomegaly, splenomegaly, normochromic normocytic anaemia, leucopenia or leucocytosis, and elevated or depressed platelet count. Milner and Mitchinson (1965) reviewed 11 published necropsy reports on patients with systemic involvement and reported a further case. In these cases there was involvement of subcutaneous and retroperitoneal, mesenteric or epicardial adipose tissue. They recommended the name systemic Weber-Christian disease where the typical lesions are present in subcutaneous and visceral adipose tissue, and Weber-Christian panniculitis where the lesions are confined to the subcutaneous adipose tissue. This terminology is adhered to herein.

Case Summary

A 7-year-old girl was first seen in October 1960 with tenderness, swelling, and redness of the skin behind both knees, over the right foot (fig 1), and over the cutaneous surface of the right tibia of a few days' duration. The mother remarked that her daughter had recently been feverish. One year previously she had suffered similar pain, tenderness, and redness behind the knees, but this had settled spontaneously; otherwise she had always been healthy. She had an older brother who was an insulin-dependent diabetic and had necrobiosis lipoidica diabetorum. Apart from the lesions mentioned, there was no abnormality on examination. Laboratory investigation revealed a white cell count of $8.5 \times 10^9/l$, an ESR of 20 mm in the first hour (Wintrobe), and a total plasma protein of 72.5 g/l (albumin 34 g/l, globulin 38.5 g/l) with an increased gammaglobulin component on electrophoresis. Thymol turbidity was 4 units (normal range 0.4 units) and cephalin flocculation 3+ (normal range 0.1+). LE cells were not seen in the blood. An oral and an intravenous glucose tolerance test were normal, serum cholesterol was 7.4 mmol/l. A biopsy (fig 2) taken from the lesion on the foot showed 'areas of fat necrosis, accumulation of leucocytes including neutrophil polymorphonuclear leucocytes, and macrophages with foamy cytoplasm. Histologically the appearances are those of a Weber-Christian disease' (Dr W. Guthrie). She was treated with oral prednisolone, initially 60 mg/day which was tailed off over the next five months. Four months after the onset of the previous lesions (February 1961), while on steroid, she suffered a similar lesion on the right wrist and left forearm. This settled and, apart from fat atrophy of the affected areas (fig 3), she remained

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Fig 1 Area of Weber-Christian panniculitis on dorsum of right foot: the lesion was red and painful, and felt hard.

Fig 2 Skin biopsy from dorsum of right foot. Adipose tissue is infiltrated with inflammatory cells and fat-laden macrophages (Haematoxylin and eosin $\times 335$).

well. Four years later (January 1965) she suffered a two-week feverish illness with cough and coryza. A week later an area of swelling, 7.5 cm in diameter, appeared on the lateral aspect of the left ankle, which on biopsy was histologically similar to the

earlier biopsy. There was no other clinical abnormality. Laboratory investigation showed a hypochromic anaemia (Hb 9.8 g/dl), general leucopenia (WBC $3.1 \times 10^9/l$), plasma protein 73 g/l (albumin 35 g/l, globulin 38 g/l), and plasma electrophoresis

Fig 3 Loss of subcutaneous adipose tissue at site of an old lesion on left forearm.

suggestive of increased beta and gammaglobulins. ESR was 23 mm in the first hour (Wintrobe). Antibodies to thyroid, stomach, and blood vessels were negative at this time (Dr J. S. Beck), and the Wassermann reaction was negative. She recovered from this attack without treatment.

She remained well for five years, but in April 1970 when aged 16 years she complained of thirst and polyuria. On examination splenomegaly (3 fingers) was noted but no other abnormality. Laboratory investigations revealed: glycosuria, an ESR of 90 mm in the first hour (Westergren), a serum glutamic oxaloacetic transferase of 86 SF units (normal range 0-33), a plasma bilirubin of 22 $\mu\text{mol/l}$, a haemoglobin of 7.4 g/dl (hypochromic microcytic film), a white cell count of $2.8 \times 10^9/\text{l}$ (no primitive cells seen), and a platelet count of $45 \times 10^9/\text{l}$. Australia antigen and antibody were negative. A sternal marrow examination showed erythroid hyperplasia with depleted iron stores. Red cell half-life was 18 days (slightly reduced) but there was no sign of splenic sequestration. She was diagnosed as having diabetes mellitus and hepatic cirrhosis.

She developed skin hypersensitivity to all forms of insulin except Actrapid (porcine base neutral pH). Her diabetes was eventually controlled with this agent.

In April 1971, one year after splenomegaly had been noted, the direct antiglobulin test was found to be positive, and antibody (subsequently shown to be IgG₁ C3d) was demonstrated on the red cell surface: IgM antibody, which agglutinated enzyme-treated erythrocytes (titre 1:128) and lysed the same

cells (titre 1:64), was found in the serum (Dr S. M. Worledge, Royal Postgraduate Medical School, London). At this time the patient suffered from severe crop of perineal warts, and two years later (February 1973) she developed herpes genitalis.

Right-sided abdominal pain became very troublesome and she was investigated by Professor Sherlock's Unit at the Royal Free Hospital, London (February 1973). The following results were obtained at this time: plasma IgG 29.7 g/l (5.0-16.0 g/l normal range), IgA 3.15 g/l (1.25-4.25 g/l normal range), and IgM 3.3 g/l (0.5-1.8 g/l normal range). The lipid profile was normal. The antimitochondrial antibody was weakly positive. The anti DNA antibody was 'slightly raised', but the antinuclear factor was negative. The gastric parietal cell antibody was positive. The Wassermann reaction was positive but the Treponema immobilization test was negative. Liver biopsy showed intact lobular architecture with expanded portal tracts infiltrated with a mixture of inflammatory cells, including many plasma cells combined with bile duct proliferation and disruption of the limiting plate. The parenchyma showed mild fatty change and nuclear vacuolation. There was no cholestasis nor siderosis. The liver disease was placed somewhere in the spectrum of autoimmune liver disease, between primary biliary cirrhosis and active chronic hepatitis (Professor S. Sherlock).

Subsequently she developed progressive liver cell failure and in April 1975 she died.

PATHOLOGICAL SUMMARY

The body was of a young icteric adult female

Fig 4 Section of liver showing increased fibrous tissue, distortion of lobular architecture, bile duct proliferation, and some fatty change of hepatocytes (H and E $\times 65$).

Fig 5 Section of pancreas stained with sulphated alcian blue/van Gieson. The islet (centre) contained a blue amorphous material (appearing black in this photomicrograph) which had the staining characteristics of amyloid ($\times 335$).

Except for some patchy atrophy over the calves there was no abnormality of fat distribution. The liver showed a macronodular cirrhosis, the spleen weighed 1570 g and measured 30 × 15 × 10 cm, and there were moderately severe oesophageal varices. The pancreas appeared macroscopically normal. Red marrow was present throughout the femoral shaft. Macroscopically no sign of inflammation of retroperitoneal, mesenteric or epicardial fat was noted. Grey pus (from which enterococci were cultured) was found underlying insulin injection sites on the thighs.

Histological examination of the liver showed a macronodular cirrhosis, with bile duct proliferation (fig 4). The limiting plates of hepatic lobules were well defined. The spleen was congested, but macrophage activity was not prominent. Pancreatic acinar tissue appeared normal, but the islets contained a hyalin material which showed dichroic birefringence with a Congo red stain and was blue with an alcian stain (fig 5): this was thought to be amyloid material. Adipose tissue from the periureteric area showed occasional small foci of invasion by plasma cells and fat-laden macrophages. Mesenteric and epicardial adipose tissue showed no abnormality. Other organs showed no significant histological abnormality.

Discussion

The aetiology of the adipose damage in Weber-Christian panniculitis and systemic Weber-Christian disease is unknown. An immune mechanism may initiate or perpetuate the adipose damage. It has been described in association with tuberculosis (Tilden *et al*, 1940; Beerman, 1953; Macdonald and Feiwel, 1968), glomerulonephritis (Spain and Foley, 1944), myositis (Kiernan and Burger, 1960), intrahepatic sclerosing cholangitis, vasculitis, and positive LE cells (Hellstrom and Perez-Stable, 1966), leucopenia (Friedman, 1945), leucopenia and leuc-agglutinins (Rosenstock, 1968), pancytopenia (Wyatt 1969), hypersplenism, megaloblastosis, and pancytopenia (Mitsutani *et al*, 1973), and following withdrawal of steroids given in treatment of rheumatic fever (Smith and Good, 1956). A histologically similar condition (lupus erythematosus profundus) has also been described in association with systemic lupus erythematosus (Macoul, 1967), and Tuffanelli (1971) has demonstrated IgG antivasculature antibody, IgM, and complement at the dermal epidermal junction in this condition. Experimentally Goddard (1947) produced lesions histologically similar to Weber-Christian panniculitis by the injection of sublethal doses of ovalbumen into previously sensitized guinea-pigs: he regarded this as an Arthus phenomenon. The clinical and histological features

of Weber-Christian panniculitis have also been produced by the repeated self-injection of milk (Ackerman *et al*, 1966). Weber-Christian panniculitis is also reported in association with insulin-dependent diabetes mellitus (Machacek, 1948) in four cases, of which two were also hyperthyroid (one with multiple hypersensitivities).

In the case reported here, histologically typical Weber-Christian panniculitis accompanied by a plasma globulin elevation (elevated IgG component) preceded by five years the diagnosis of an autoimmune hepatitis with autoimmune haemolytic anaemia, leucopenia, thrombocytopenia, and associated herpes genitalis. It similarly preceded the onset of diabetes mellitus, which was related to localized amyloid deposit in pancreatic islets. The presence of amyloid in pancreatic islets was found to occur in 50% of diabetics over 50 years of age (Ehrlich and Ratner, 1961) but is rare in juvenile diabetes (Bell, 1952). This islet cell abnormality may be related to immune complex disease resulting from insulin treatment (Rao *et al*, 1974) or it may be that an islet cell antibody (MacLaren *et al*, 1975) was present as well as the other antibodies noted.

Macdonald (1970) has described Weber-Christian panniculitis as a disorder of unknown aetiology, varying greatly in clinical presentation and outcome, and including cases which have been acute, chronic, fulminating, transient, febrile, and nonfebrile. In his original description, Weber (1925) suggested that the condition was allied to other forms of panniculitis sometimes found in erythema induratum and erythema nodosum. In the case discussed here, it is tempting to speculate that Weber-Christian panniculitis is not a nosological entity but rather an adipose component of a severe autoimmune disease.

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