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Auto-erythrocyte sensitisation syndrome – an unusual cause of bruising

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ABSTRACT Autoerythrocyte sensitisation syndrome or Diamond-Gardner syndrome is a rare disorder characterised by painful and spontaneous purpura occurring in women with mental health problems. It should be considered in the differential diagnosis of spontaneous, painful bruising, especially in patients with mental health problems. Awareness of this condition may prevent unnecessary investigations and allow early referral to psychiatry or psychology. We present the case of a 45-year-old woman who was referred to our haematology clinic with a history of recurrent episodes of spontaneous painful bruising. She had already attended rheumatologists and dermatologists and was proving to be a diagnostic dilemma. Extensive investigations, including full blood count, coagulation screen, factor VIII complex and connective tissue screen, were normal. An autoerythrocyte sensitisation test resulted in the appearance of a bruise preceded by tingling and a stinging sensation similar to her usual symptoms. Although not mentioned in the referral letter and not elicited at the initial consultation, on further questioning a history of psychiatric morbidity was obtained. Having established the likely diagnosis, the patient was agreeable to referral for psychiatric support.

KEYWORDS Autoerythrocyte sensitisation syndrome, Gardner-Diamond syndrome, painful purpura, psychogenic purpura, spontaneous purpura

DECLARATION OF INTERESTS No conflict of interests declared.

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CASE REPORT

A 45-year-old woman was referred to the haematology clinic for investigation of a ten-year history of intermittent spontaneous bruising associated with arthralgia. She had previously been investigated by rheumatologists and dermatologists with no cause identified. The clinical pattern was of recurrent episodes of bruising over a short period of time with prolonged periods (more than six months), which were symptom-free. The bruising predominantly affected her fingers, although more recently she had had two episodes of severe bruising on the dorsum of her foot.

Each episode was described as a sudden pain lasting between 10 seconds to 15 minutes, followed by swelling and a 'bursting feeling' in the affected region. As the swelling subsided, bruising appeared with complete resolution over the following week.

The patient had no personal history of bleeding, in particular no menorrhagia, and had had two uncomplicated vaginal deliveries. The family history was unavailable (she was adopted as a child). There was no history of trauma, hobbies or occupational activities predisposing to her ecchymoses. Her only past medical history was of coeliac disease, diagnosed three years previously. She was not taking aspirin or non-steroidal anti-inflammatory drugs. Although there was no bruising at her clinic visit, she brought photographs, taken by her husband, of previous episodes (Figure 1). Her full blood count, coagulation profile (PT, APTT and TCT), factor VIII complex (factor VIII, von Willebrand antigen and vWF RICOF) and thrombo-philia screen, including lupus anticoagulant and anti-cardiolipin antibodies, were normal. The auto-antibody screen, including anti-nuclear antibody (ANA), was negative. A thyroid function test was normal.

A psychiatric history was obtained at the patient's second clinic visit following specific questioning. She admitted to a long history of recurrent depression, anxiety and psychogenic dyspareunia. She had received intermittent treatment over the years but was not on any regular medication at the time of the initial consultation.

With the unusual pattern of bruising, the associated pain, the normal laboratory results and the psychiatric history, a diagnosis of autoerythrocyte sensitisation syndrome (AES) was suspected and an AES test performed (Figure 2). There are several reported methods of performing the test with no standardisation. We used the method described by Vun and colleagues in 2004,[1] with minor modifications. A peripheral blood sample from the patient was collected in a sterile tube containing citrate solution as an anticoagulant. The sample was centrifuged to isolate the erythrocytes, which were rinsed twice with normal saline. The erythrocytes were then mixed with normal saline to achieve a 75% haematocrit.

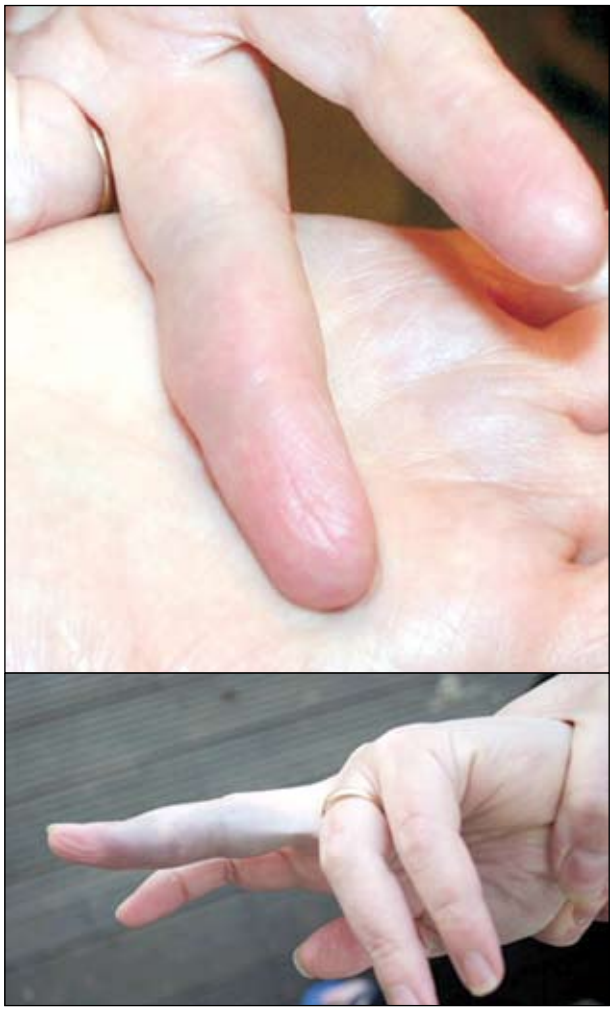

FIGURE 1 A 45-year old woman was referred to the haematology clinic with a history of recurrent episodes of spontaneous painful bruising and, as subsequently emerged, a psychiatric history. The full blood count, coagulation screen, factor VIII complex and connective tissue screen were normal. A diagnosis of autoerythrocyte sensitisation syndrome was made.

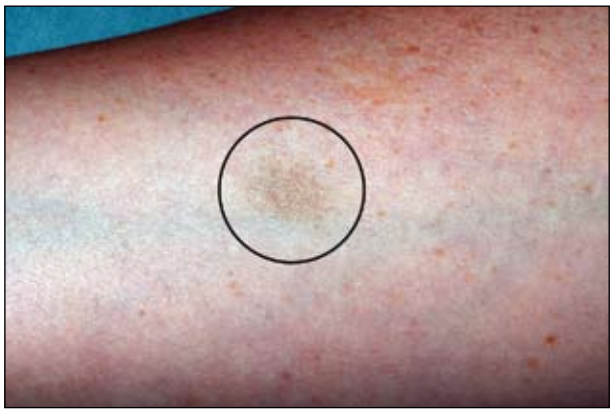

FIGURE 2 The AES test described by Vun and colleagues[1] in 2004 was carried out, with minor modifications, on the patient's forearm. Following the injection of the autologous red cells, the patient noticed a tingling sensation similar to her earlier reports at the site, and within 24 hours of the initial test developed a bruise.

Using a 26-gauge needle, 0.1 ml of the solution was injected intradermally into the patient's right forearm. The patient's left forearm served as a control into which was injected 0.1 ml of normal saline. The patient was blinded to the constituents of the injections. There was no immediate reaction in either arm. Over the next few hours she reported a tingling sensation at the red cell injection site and noticed a faint bruise. The bruise was 15 mm in diameter at the 24-hour review. There was no change to the size of the bruise or the symptoms for the next 24–48 hours. The bruise started fading thereafter. Meanwhile on the control forearm there was no reaction or bruising at the needle puncture site.

DISCUSSION

Autoerythrocyte sensitisation syndrome or Diamond-Gardner syndrome is a rare disorder that was first described in 1955 in four women manifesting abnormal responses to bruising, characterised by the development of an area of painful ecchymosis at the site of trauma, followed by progressive erythema and oedema.[2–5] Gardner and Diamond proposed that this represented a syndrome in which patients were sensitive to their own red cell stroma and suggested the condition's currently accepted name.[2]

Autoerythrocyte sensitisation syndrome is typically seen in adult females, although paediatric and male patients have also been described.[2,6,7] The largest series of 71 AES patients was reported by Ratnoff in 1989.[8] The authors termed the syndrome 'psychogenic purpura' in view of the association with psychiatric problems in the majority of patients described. A wide range of psychological disturbances, including depression, anxiety, difficulties in handling aggression and hostility, emotional lability, hypochondriasis, abnormal guilt, sexual maladjustments, masochism, hysterical and borderline personality disorders and obsessive compulsive disorders, have been reported in association with AES.[2,8–11] In children, Munchausen's syndrome by proxy is an important differential diagnosis to consider.

The skin lesions vary in size from 1–2 cm in diameter to the involvement of an entire limb. The lesions typically occur on extremities and rarely on the less accessible locations such as the back. In particular, lesions on the fingers have been reported.[12] Lesions are preceded by paraesthesia or pain.[10] The onset of AES may occasionally be preceded by surgical procedures or by other forms of trauma. Other associated complaints in patients with AES include headache, syncope, blurred vision, epistaxis, gastro-intestinal bleeding and pain in the abdomen, chest, muscles and joints.

The autoerythrocyte sensitisation test is used to support the diagnosis of AES.[2] Positive reactions have been reported with whole blood, washed red cells and

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occasionally with haemoglobin using haematocrit concentrations of 20–70%. Positive responses have also been documented for a large variety of other agents, including phosphatidyl serine, serum, platelet suspension, saline, histamine, serotonin, trypsin, DNA and copper.[1,8] The pathogenesis of AES is not well understood. It has been suggested that a positive skin test may indicate unidentified antigenic components of the erythrocyte membrane.[10,13]

An association with psychiatric problems is seen in the majority of AES patients, but a number of haematological and immunological abnormalities have also been described mostly as case reports. These include thrombocytosis, morphological abnormalities in RBC and functional platelet defects. A case of psychogenic purpura with abnormally increased tPA-dependent cutaneous fibrinolytic activity has also been published.[14]

A large number of treatments have been tried for AES with limited success. These include antihistamines, albumin infusions, corticosteroids, chemotherapy, antidepressants, hormones, vitamin C and splenectomy.[1] The prognosis of AES is good with no deaths reported from this syndrome or its complications.[8,10] In some individuals, the syndrome may remit for months or years and return at a time of severe emotional stress.[8]

Although in our patient there was only a mild reaction to the AES test, there was no other detectable haematological disorder and, furthermore, initiation of antidepressants had previously led to improvements in her symptoms. In summary, AES is a rarely reported condition of uncertain pathogenesis, found typically in adult females with psychological disturbances. A characteristic feature of the syndrome is a positive skin test following an intradermal injection of autologous red blood cells. It is important to recognise this syndrome to facilitate prompt referral to psychology/psychiatry services and avoid unnecessary, prolonged investigations.

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