Livedo reticularis and pregnancy morbidity in patients negative for antiphospholipid antibodies

S Sangle, D P D'Cruz, G R V Hughes

**Background:** Livedo may be an independent risk factor for pregnancy morbidity, additional to the known risks associated with the presence of antiphospholipid antibodies (aPL).

**Objective:** To determine the prevalence of pregnancy related morbidity in patients with widespread livedo reticularis who are persistently negative for aPL.

**Patients and methods:** 52 patients with widespread livedo reticularis were studied: 31 fulfilled ACR criteria for SLE, 21 had a lupus-like illness; all were negative for aPL. All patients had livedo (racemosa or reticularis type) on their extremities, trunk, and/or buttocks.

**Result:** 33 (63%) patients had pregnancy related morbidity. 22 patients had up to 9 miscarriages, 15 patients had >3 miscarriages, 2 had 2 miscarriages, 4 had a fetal death (>10 weeks), 17 had pre-eclampsia, and 4 patients had premature delivery. 19 patients had no pregnancy related morbidity. Overall morbidity was similar in the patients with lupus and lupus-like disease.

**Conclusion:** Pregnancy related morbidity in lupus is known to be associated with the presence of aPL. This study suggests that pregnancy loss may also be independently associated with widespread livedo reticularis in patients who are aPL negative. A larger study is needed.

Livedo reticularis was included in the original clinical description of the antiphospholipid syndrome (APS, Hughes syndrome). It has since become recognised as a major feature of the disease. Indeed, it has been suggested that livedo constitutes an independent, additive, thrombotic risk factor in some patients with Hughes syndrome, including possibly, some patients with “seronegative APS”. The pathology of livedo has been well characterised. Clearly, the physical sign is a marker for vascular disease, both inflammatory vasculitis and thrombotic vascular disease such as Hughes syndrome.

Livedo reticularis is a common physiological finding, which is seen on the extremities and varies with cold weather and erect posture. However, widespread and persistent livedo reticularis is often associated with pathological features, including stroke, thrombosis, hypertension, and cardiac valvular abnormalities. Similarly, livedo is a common manifestation of APS, together with thrombosis, miscarriages, and thrombocytopenia.

Two pathological types of livedo are described. Ehrmann described livedo racemosa with irregular, ill-circumscribed and broken segments. The other type is livedo reticularis spread over more than one site (extremities, buttocks, and trunk). Both are generally known as livedo reticularis. Racemosa livedo is generally considered pathological and was associated with Sneddon’s syndrome. The livedo seen in patients with APS is regular and well circumscribed (livedo reticularis). We suggest that both types of livedo are pathological. For this reason in our cohort we have included patients with both types of livedo. The emphasis was on the extent rather than the type of livedo.

**RESULTS**

Thirty three of 52 (63%) patients had pregnancy related morbidity. Twenty two patients had up to nine miscarriages, all occurring at <10 weeks of gestation. Fifteen of these patients had more than three miscarriages, two had two miscarriages, four had a fetal death (>10 weeks of gestation). Seventeen patients had pre-eclampsia and four patients had premature delivery. Nineteen patients did not have any pregnancy related morbidity. Seventeen patients were smokers (five or more cigarettes/day for more than 3 years) and five were ex-smokers. Fifteen of the smokers or/ex-smokers had pregnancy related morbidity. All the ex-smokers were smokers during their childbearing years. Although seven of the 52 patients were hypertensive, only two had toxaemia of pregnancy. Five patients had lupus nephritis and were in total remission.

**DISCUSSION**

Of all pregnancies in the general population, 10–15% result in miscarriage and most occur in the first trimester (pre-embryonic or early embryonic). In lupus with APS the reported incidence of pregnancy morbidity is up to 42%, whereas in lupus patients negative for aPL, the incidence is no higher than in non-lupus patients. Thus it is unlikely that the high rate of pregnancy related morbidity in our cohort is due to SLE. Furthermore, six patients were hypertensive, but only two hypertensive patients had pre-eclampsia, which argues against hypertension as a cause of pre-eclampsia.

In summary, our preliminary study suggests that increased pregnancy loss might also be independently associated with APS, antiphospholipid syndrome; SLE, systemic lupus erythematosus.
widespread livedo reticularis in patients who are aPL negative. It appears that there is a separate group of patients negative for aPL who share many features of APS. We believe that this preliminary observation warrants a larger study of the significance of livedo reticularis in the assessment of patients with pregnancy loss and to determine whether there are as yet undiscovered autoantibody markers for “seronegative APS”.

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