

## Letter to the Editor (case report)

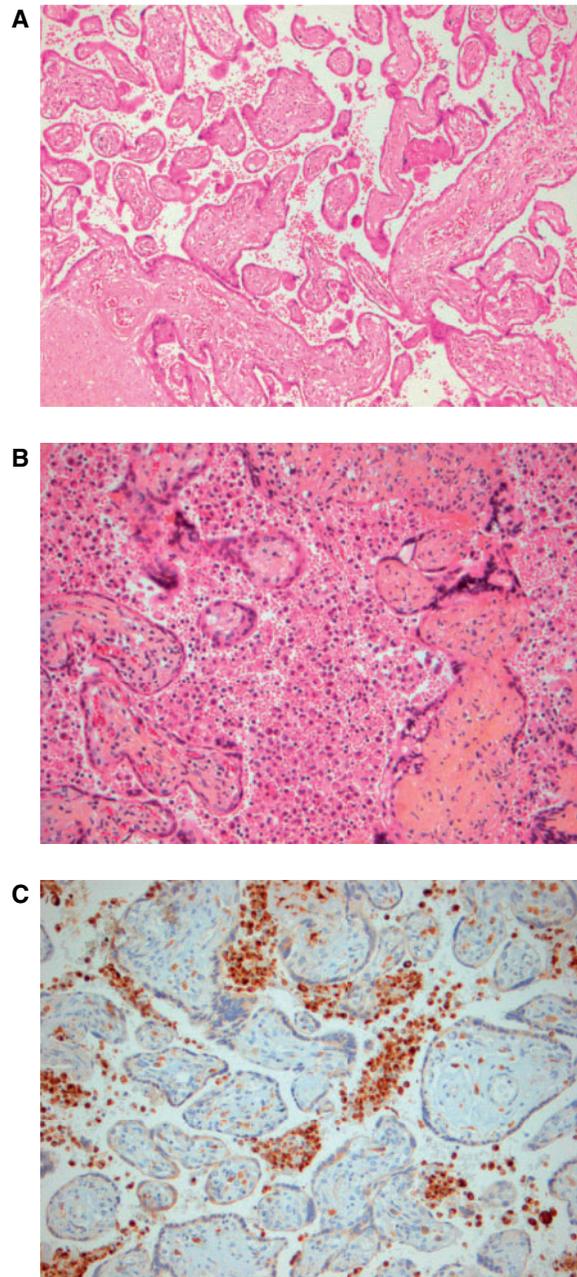
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**Fetal death in primary SS associated with chronic intervillitis**

SIR, Chronic intervillitis is a rare and poorly understood disease characterized by intervillous infiltrates of maternal origin. The intervillitis infiltrates from mononuclear cells (monocytes, histiocytes) correlate with placental insufficiency, and result in intrauterine growth restriction, intrauterine fetal death and spontaneous miscarriage [1]. Chronic intervillitis aetiology is not well established. Recent physiopathological studies have argued in favour of an immune response resulting from an abnormal maternal reaction to the placental tissue, which could preferentially implicate T-lymphocytes. Thus chronic intervillitis could be associated with autoimmune diseases, such as antiphospholipid syndrome (APS), but its association with other autoimmune disorders has not yet been determined [2]. We describe the case of a pregnant woman with underlying primary SS who presented intrauterine fetal death in relation with chronic intervillitis of the placenta.

A 38-year-old woman, *gravida 2 para 1*, with no significant past medical history had isolated intrauterine growth restriction during the previous pregnancy. In the 12th week of pregnancy she complained of having had a dry mouth, dry eyes and swelling of the salivary glands, as well as RP for the previous 2 months. There was no argument for any other associated autoimmune disease, in particular SLE or APS. She had positive ANAs (1/1280e), with anti-Ro/SSA and anti-La/SSB. Antibodies against dsDNA, Sm, anti-phospholipid, thyroglobulin and transglutaminase were all negative. The screening of thrombophilia (ATIII, protein C, S, homocysteinaemia, factor V and II mutations) was normal. The serum dosage of vitamin D (25OHD3) was 28 ng/ml. The diagnosis of primary SS was confirmed according to the American European Consensus Criteria. HCQ (400 mg/day) with aspirin (100 mg/day) was started at 16 weeks of pregnancy. Regular weekly fetal cardiac echocardiography did not detect any fetal cardiac abnormalities. An US examination at 26 weeks of pregnancy showed a normal biparietal diameter (50th percentile), head (50th percentile), abdominal circumferences (70th percentile) and the absence of oligohydramnios. At 30 weeks of pregnancy sudden fetal death occurred. A fetal autopsy did not reveal any abnormality. In particular, a fetal cardiac examination did not reveal cardiac fibrosis or inflammation. The placenta showed intense mononuclear cells and inflammatory cell infiltrates involving >75% of the intervillous space without villitis (Fig. 1). Immunological staining was positive with

**Fig. 1** Histopathological picture of the placenta. **(A)** Histopathological picture of normal intervillous space (HES,  $\times 20$ ). **(B)** Histopathological picture showing massive inflammatory infiltrates of intervillous space (HES,  $\times 20$ ) **(C)** Positive immunological staining with anti-CD68 antibodies.



anti-CD68 antibodies (Fig. 1). She was pregnant again 6 months later, and the pregnancy resulted in a live-born baby without any complications at the 38th week of gestation with HCQ (400 mg/day), aspirin (100 mg/day) and prednisone (10 mg/day), started just before the pregnancy.

Reports on pregnancy outcomes beyond neonatal lupus and congenital auriculoventricular (AV) block are rare in primary SS, in contrast to the situation in SLE. Beyond intrauterine AV block and neonatal lupus syndrome, it is usually anticipated that SS is not associated with unfavourable pregnancy outcome [3]. Even fetal cardiac echocardiography did not reveal abnormalities, and AV block can be sudden. AV block cannot be excluded in our case, as no intrauterine growth restriction was noted during pregnancy, but cardiac histological examination was normal. The use of steroids is not routinely recommended in pregnant patients with SS. The chronic intervillositis associated with primary SS has not yet been reported.

The risk of recurrence of chronic intervillositis seems to be high, but no treatment guidelines are currently available [1]. The use of steroids in association with aspirin could improve the obstetrical outcome, but is based mainly on a few case studies [4]. In a recent systematic review, the intervention with drug therapy was of no demonstrable benefit, but was not assessed in patients with underlying autoimmune disorder [1].

Although it is exceptional, our report raises the possible association of chronic intervillositis with primary SS and indicates the use of steroids with aspirin for our patient's next pregnancy. A study with a histological examination of the placenta is necessary to confirm the association of chronic intervillositis with SS and other autoimmune diseases.

#### Rheumatology key message

- In primary SS, obstetrical morbidity could be related to placental chronic intervillositis.

*Disclosure statement:* The authors have declared no conflicts of interest.

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#### References

- 1 Contro E, deSouza R, Bhide A. Chronic intervillositis of the placenta: a systematic review. *Placenta* 2010;31:1106–10.
- 2 Parant O, Capdet J, Kessler S *et al.* Chronic intervillositis of unknown etiology (CIUE): relation between placental lesions and perinatal outcome. *Eur J Obstetrics Gynecol Reprod Biol* 2009;143:9–13.
- 3 Hussein SZ, Jacobsson LT, Lindquist PG *et al.* Pregnancy and foetal outcome in women with primary Sjogren's syndrome compared with women in the general population: a nested case-control study. *Rheumatology* 2011;50:1612–7.
- 4 Boog G, Le Vaillant C, Alnoukari F *et al.* Combining corticosteroid and aspirin for the prevention of recurrent villitis or intervillositis of unknown etiology. *J Gynecol Obstet Biol Reprod* 2006;35:396–404.