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Original article

Two miscarriages, consecutive or non-consecutive, does it change something?

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ABSTRACT

Objectives. – To assess the rate of anomalies in the etiological evaluation of patients presenting recurrent early miscarriages (RM) according to miscarriage chronology (number of miscarriages, history of live birth and succession of RM).
Methods. – Retrospective single centre study including RM, defined as at least 2 miscarriages at less than 14 weeks of gestation (WG) between the 1st January 2012 and the 31st December 2015. Clinical data and etiological evaluation include blood glucose levels, screening for antiphospholipid syndrome (APS), endocrine assessment, vitamin levels, pelvic imaging, karyotyping of both partners, chronic endometritis and thrombophilia screening.
Results. – Two hundred and eighty-eight patients were included over this period, 118 (41%) patients had no history of live birth. Two hundred and twenty-three (77%) patients had consecutive RM and 65 (22%) patients had non-consecutive RM. For consecutive RM, 62,8% had thrombophilic disorders versus 69,8% for non-consecutive RM ($P > 0{,}05$); 44,7% had endocrine disorders or vitamin deficiencies versus 39,7%; 34,6% of patients with consecutive RM had uterine anomalies versus 45,5% respectively. No difference was found depending on the recurrence of RM or the history of live birth ($P > 0.05$) apart from the age of the patient. Fifty-nine (17.4%) patients had uterine anomalies. There are 24 chronic endometritis on 31 biospsies performed. Seventy-eight (27%) patients were offered treatment. Ninety-four (90%) patients showed good therapy compliance. Eighty-one (78%) patients became pregnant.
Conclusion. – An etiological evaluation provides, for over half of the cases, an etiology or the identification of risk factors responsible for RM, as well as in some cases offering an adapted, efficient, therapeutic approach. This evaluation should be offered regardless of the obstetric history of the patient.

Introduction

An early miscarriage is the spontaneous loss of a pregnancy before 14 weeks of gestation (WG) [1]. Early miscarriages concern over 15% of pregnancies [2]. Recurrent early miscarriages (RM) affect 1 to 2% of women of child-bearing age [2]. The Royal College of Obstetricians and Gynaecologists (RCOG) defined RM as the loss of three or more consecutive pregnancies before 24 WG [3]. The French National College of Obstetricians and Gynaecologists (CNGOF) defined RM as the loss of three or more consecutive pregnancies before 14 weeks of amenorrhea [4]. For over 50% of patients with RM a cause is identified, thus justifying an etiological approach [4–8]. The diagnostic approach for this etiological evaluation includes thorough questioning, a clinical examination and paraclinical tests [7]. The difficulty in caring for these RM has incited several authors to draw up guidelines concerning investigation and treatments [8]. New guidelines in clinical practice for RM were drawn up in 2014 by the CNGOF [9]. First-line paraclinical testing for RM is now clearly defined (Fig. 1).

There have been several French studies on the etiology of RM but none of them addressed the profitability of the evaluation suggested by the CNGOF in 2014 [7,10–12]. Few articles concerned therapy compliance and the length of time between adapted care of RM and pregnancy [5,13–15].

Our objective was to assess the efficiency of an etiological evaluation for cases of RM according to obstetric history and to

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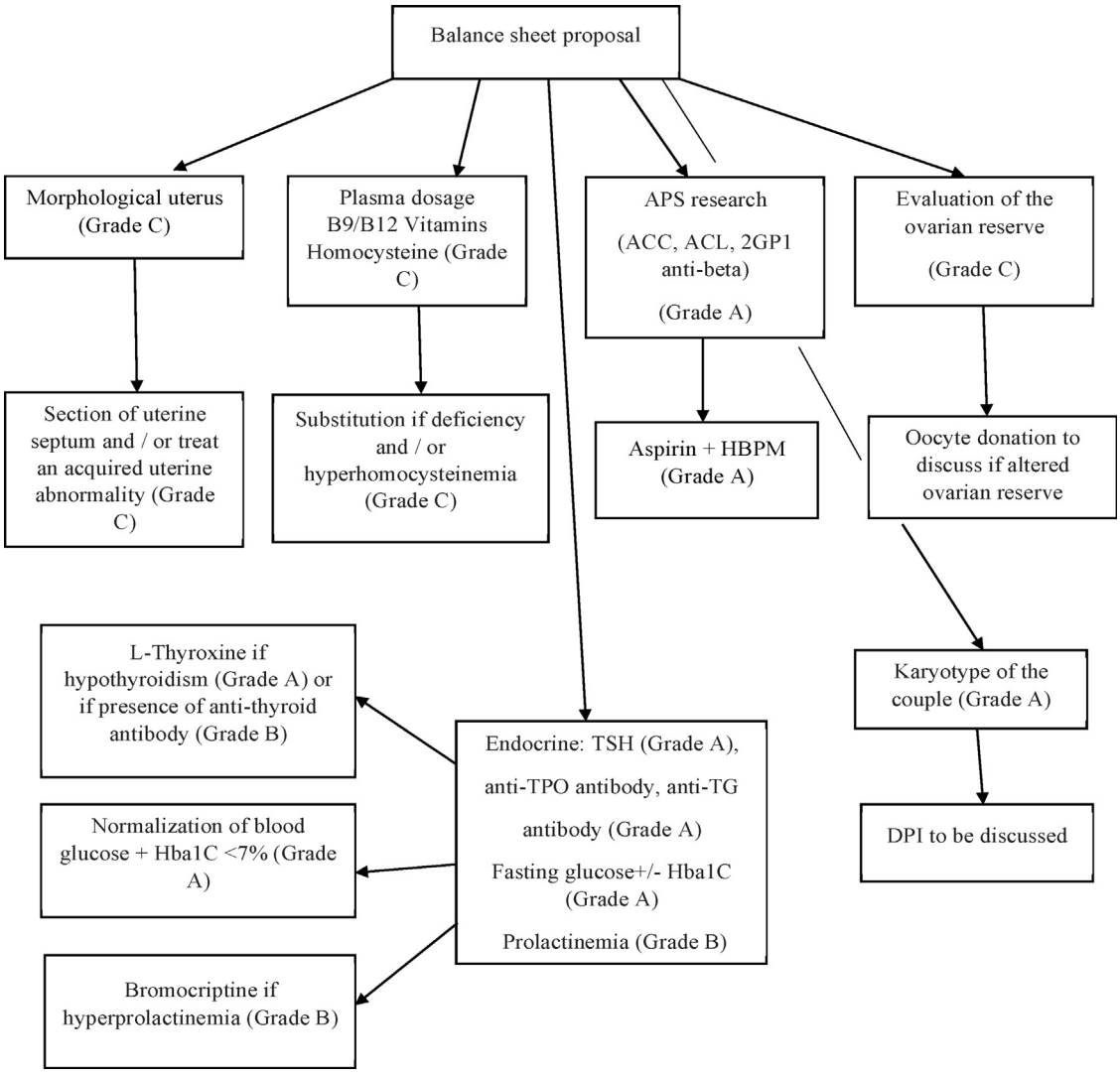

Fig. 1. Algorithm of early recurrent miscarriage (3 or more consecutive miscarriages before 14 WG in a couple) evaluation and associated management. ACC: anticoagulant circulating; ACL: anticardiolipid antibodies; DPI: préimplantation diagnosis; HBPM: heparin of low molecular weight; SAPL: antiphospholipid syndrome; TG: thyroglobuline; TPO: thyropéroxydase; TSH: thyréostimuline. CNGOF French national college of obstetricians and gynecologists 2014.

whether the RM were consecutive or not. The main objective was to assess the rate of anomalies in the etiological evaluation. Secondary objectives were to assess this rate according to obstetric history: history of live birth and/or the succession of RM.

Material and methods

This is a quantitative, retrospective, study of a cohort of patients who had at least 2 miscarriages, consecutive or not, before 14 WG, addressed at regional multidisciplinary consultation meetings (MCM) "thrombophilia, internal medicine and pregnancy" at the Gynépole Assistance publique–Hôpitaux de Marseille (AP–HM: public hospitals of Marseille) in the Obstetrics and gynecology ward, France between the 1st January 2012 and the 31st December 2015. Inclusion criteria were: RM > 2 miscarriages, consecutive or not, before 14 WG. Exclusion criteria were: < 2 miscarriages, history of pre-eclampsia, retroplacental haematoma, intra-uterine growth retardation, foetal death in utero or of late miscarriage. All of the patients fulfilling criteria were included in the study. According to the conclusions of the MCM, patients could be offered treatment, a consultation with a specialist in internal medicine, endocrinology, dietetics or addictology. Data was collected in two steps.

For the first step, a review of the clinical files discussed at a MCM was made between 2012 and 2015. Data collected included: age, Body mass index (BMI), personal history, the practitioner who prescribed the evaluation, data from the etiological evaluation, the RCP's conclusion, the venous thromboembolism (VTE) score drawn up according to: several risk factors (age > 35, gravidity, parity > 4, BMI > 30, smoking > 10 a day, personal medical history, first degree family history of VTE), personal history of thrombophilia and personal history of VTE. A strategy was offered to reduce the risk of thromboembolism: for a score of 0 no treatment was prescribed, a score between 1 and 2: prescription to wear support stockings, a score between 3 and 5: prescription to wear support stockings and to take low molecular weight heparin for 6 weeks post-partum, a score of over 6: prescription to wear support stockings and to take low molecular weight heparin throughout pregnancy and for 6 weeks post-partum.

In compliance with the CNGOF guidelines [9], the etiological evaluation included: fasting blood glucose (3.6–6 mmol/L), antiphospholipid syndrome screening: APS (lupus anticoagulants (present or absent), anticardiolipin antibodies (IgG < 22 U, GPL; IgM < 10U, MPL), anti-beta 2 glycoprotein 1 antibodies (IgG < 8 U/mL; IgM < 8 U/mL), thyroid stimulating hormone (TSH: 0.2–5 mUI/L) with the presence of antithyroid (antithyroperoxidase [< 34 UI/mL]

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