



## Correspondence

## Re: methotrexate infusion followed by uterine artery embolisation for the management of placental adhesive disorders: a case series



Sir—Babaei *et al.*<sup>1</sup> reported that intra-arterial methotrexate infusion followed by uterine artery embolization (UAE) was performed in 12 patients with abnormally invasive placenta as a placenta left *in situ* strategy: the uterus was preserved in seven patients (58%). Here, the terminology of placenta accreta spectrum (PAS) disorders will be used, based on the recent recommendation by the International Federation of Gynecology and Obstetrics (FIGO).<sup>2</sup> We have some concerns and clarifications.

Firstly, indications for this interventional radiological procedure were: (1) patients' desire for uterus preservation, or (2) very difficult caesarean hysterectomy; however, the number of patients accounted for (1) or (2) was not described. Our protocol for severe PAS is that caesarean hysterectomy should be performed<sup>3</sup> with temporary aortic balloon occlusion, and an *in situ* strategy should be employed under the following three conditions: (i) parametrial placenta invasion, (ii) placental invasion into the bladder trigone, or (iii) engorged aberrant vessels with marked communication with abdominal-wall vessels.<sup>4</sup> Condition (i) requires preparation of the parametrium and thus radical hysterectomy; condition (ii) requires bladder-trigone resection and uretero-vesical neo-anastomosis; and condition (iii) usually indicates inflow from the aorta proximal to aortic balloon occlusion and thus hysterectomy may cause uncontrollable bleeding. Caesarean hysterectomy for these conditions is beyond our surgical skills and may cause maternal death, meaning that there is no choice but to adopt an *in situ* strategy. Thus, whereas success means uterus preservation in scenario (1), it means saving mothers' lives in scenario (2). Let us assume an extreme scenario: difficult surgery was expected in all 12 patients, and all 12 patients actually survived; the success rate was 100%. The criteria of difficult hysterectomy can be modified according to the capability or policy of each institute. It would be useful to know the criteria for difficult surgery and how many of the 12 patients were considered difficult, accounting for scenario (2). Data interpretation is different between scenarios (1) and (2).

Secondly, it would be useful to know the intra-operative findings at delayed hysterectomy after UAE. The effectiveness of UAE in an *in situ* strategy is controversial.<sup>5</sup> We are

concerned that UAE may cause marked collateral circulation at the time of delayed hysterectomy. In standard hysterectomy, vessel ligation should be performed in a step-by-step manner in the order of round ligament vessels then utero-ovarian vessels, and subsequently, the uterine artery. Collateral circulation usually varies between patients, and thus, the route, features, and degree are unpredictable, which may prevent routine vessel ligations, resulting in very difficult surgery.

Thirdly, whether methotrexate had an additional effect on UAE is doubtful. Beta human chorionic gonadotropin ( $\beta$ hCG), produced by trophoblasts, may be a marker for evaluation of the effectiveness of methotrexate-induced trophoblast necrosis.<sup>6</sup> It would be useful to know what the serum  $\beta$ hCG levels were during the course of methotrexate administration. Although methotrexate targets rapidly dividing cells (first-trimester trophoblasts), it does not target those dividing more slowly (third-trimester trophoblasts).<sup>5,6</sup> Of the 167 patients with an *in situ* strategy, only one maternal death occurred, which was ascribed to methotrexate toxicity and subsequent septicemia.<sup>7</sup> Considering this, a recent statement discourages the use of methotrexate.<sup>5,6</sup>

We commend Babaei *et al.* for providing important data; however, it would be useful to obtain more data regarding the practical issues and the rationale to add methotrexate.

### Conflicts of interest

The authors declare no conflict of interest.

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