Earliest Ultrasound Finding of Implantation?

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Purpose: Our purpose was to verify our earlier observation of an altered endometrial echo character during the periimplantation period, signifying the earliest detection of implantation by ultrasound.

Methods: The transvaginal ultrasound study used a 7.5-MHz probe on day 6 following preembryo transfer.

Results: Of 31 embryo transfers studied, 8 (25.8%) were positive for this sign on day 6, whereas 9 patients later showed a gestational sac, giving an accuracy of this sign of 88.8% (8 of 9).

Conclusions: The normal secretory-phase endometrium shows a typical, evenly distributed hyperechogenicity described earlier by Hackeloer (1). In some cases of proliferative phases, too, this echo pattern has been reported by others (2, 3), and observed by us in stimulated and unstimulated cycles, and has been named type A endometrium by Gonen et al. (4) Both these varieties are seen to have an even, unbroken outline at the anterior and posterior myometrial-endometrial interphase. We report what we believe to be the earliest ultrasound picture of implantation, resembling this variety of endometrial echo but having an irregular outline (Fig. 2).

KEY WORDS: endometrium; implantation; transvaginal ultrasound; trophoblastic proliferation.

INTRODUCTION

Following embryo transfer after traditional IVF or micromanipulation, the clinician and the recipient couple are both eager to confirm the viability of the pregnancy by studying the implantation, gestational sac, yolk sac, and primitive cardiac activity of the embryo. In our experience, the appearance of a gestational sac by transvaginal ultrasound has been detected between day 18 and day 27 after embryo transfer, which is

similar to an earlier report (5). With this experience, we programmed our U.S. study 18 days after embryo transfer in all IVF/ICSI preembryo recipient women.

During these ultrasound studies done after embryo transfer we noticed that, in some cases, an irregularity in the outline of the heterogeneously hyperechoic secretory endometrium occurred at one pole (Fig. 2) The echoes of these posttransfer endometria resembled myometrial infiltration by malignant endometrial lesions reported in some cases (6, 7) and could possibly correspond to trophoblastic proliferation. On follow-up scan of these patients, done after 14 to 18 days, a gestational sac having a transverse diameter between 2 and 4 mm appeared within this irregular, hyperechoic zone. Subsequently the first posttransfer ultrasound was started earlier than before, and day 6 posttransfer was the earliest day when this irregularity could be seen in one case.

MATERIALS AND METHODS

Keeping this finding in mind, we started a prospective series including 31 embryo transfers following traditional and micromanipulated IVF cycles between January 1995 and December 1995. Only those patients in whom more than two good-quality embryos had been transferred were included in the study. In these patients we performed a quick transvaginal gray scale ultrasound on day 6 following transfer. The exposure time was kept at 30 to 60 sec. Peripheral blood β hCG was measured on the day of a scan showing this sign, i.e., day 6 posttransfer. Urine was tested for pregnancy 12 to 15 days later. The machine used for the study was a Philips SDR 1550 XP with a 7.5 transvaginal probe.

RESULTS

Of a total number of 31 transfers, 8 patients (25.8%) were seen to show endometrial outline irregularity.

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Fig. 1. Normal secretory-phase endometrium. Arrows delineate the smooth endometrial/myometrial interface.

The peripheral β hCG level measured on the day of the scan varied between 2.2 and 46.5 mIU/ml. The patient in whom β hCG was seen to be 46.5 mIU/ml was later seen to carry a triplet pregnancy. On retrospection, it was realized that the said sign had been more extensive, involving the anterior and posterior endometrial/myometrial interphase, in this patient. The gestational sac, studied later, confirmed viable implan-

tation in all of these patients and in another in whom we had failed to detect this sign on day 6.

So in this series of 31 patients, 9 implantations occurred. One case ended in early abortion. The sign being discussed was seen in eight patients of the nine implantations confirmed by visualizing a gestational sac.

Hence in this initial study the diagnostic accuracy of the ultrasound sign was 88.8%.

Fig. 2. Implantation endometrium. Arrows delineate loss of outline regularity of invading trophoblast.

Table 1. Data Analysis of Transfer Cycles Showing the Positive Implantation Sign on Day 6 Posttransfer.

Total No. of embryo transfer cycles	No. in which ultrasound implantation sign was recorded	Mean serum β hCG on day 6 in these 31 patients (range) (mIU/ml)	No. of cases showing gestation days posttransfer	Multiple implantation	Early abortion
31	8 (25.8%)	16 (2.2–46.5)	9 (29.3%)	1 (set of triplets)	1

DISCUSSION

Since the first successful IVF pregnancy in 1978, great improvements have been made in controlled ovarian hyperstimulation, oocyte retrieval, and embryo culture protocols to enhance success in IVF cycles. The most uncertain part of the IVF cycle is implantation, which has been reported to occur later (8) than that of in vivo fertilization, and until it is confirmed, a state of apprehension and expectation prevails. Early signs of implantation in the form of ultrasound visualization of endometrial features, proposed to be related to vascular changes associated with decidua formation, have been reported (9). Such features, however, are not confirmatory for implantation alone since a similar echo is seen in several other situations, *viz.*, an endometrial polyp with degenerative changes or cystic endometrial hyperplasia.

Enhanced endometrial blood flow has been recorded as early as day 27 of the normal menstrual cycle, with

a corresponding serum β hCG level of 156 mIU/ml (10). In contrast, this sign reported to be related to implantation, showing irregularity of the endometrial outline giving a visual impression of “burrowing,” reported here has been seen to be diagnostic at a mean serum β hCG level of 16 mIU/ml (Table I).

The endometrial pattern of each individual IVF cycle is studied not only during folliculometry but also at retrieval. The implantation burrowing sign gives a stark contrast in the echo pattern compared to that of the proliferative phase seen earlier in the patient and can be focused with adequate experience. It has been reported (11) that “the texture of endometrium in stimulated cycles is different than in spontaneous cycles,” and some images can be confused with gestational sacs (5) in such circumstances. But our “trophoblast burrowing sign” has never been recorded in the absence of implantation, even though in some cases the endometrium might have been quite thick and hyperechoic, the outline remained rather regular.

Fig. 3. Multilayered triple-line (B-type) endometrium.

Fig. 4. Vascular supply of late proliferative multilayered (B-type) endometrium.

It appears significant that five of these eight patients had shown a "multilayered triple-line" (2) endometrium (Fig. 3) and vascular flow within Zones 3 and 4 (12) (Fig. 4) during follicular monitoring in the proliferative phase. We are undertaking a larger series to confirm the findings discussed.

CONCLUSIONS

In conclusion, we like to state that the "trophoblast burrowing sign" can be detected with significant accuracy as early as day 6 after embryo transfer by high-frequency transvaginal ultrasound. If implantation failure can be detected early, expensive luteal support and rest can be withdrawn. Reduction of cost is especially relevant for the economically backward patients seen frequently by us. Though we are encouraged by this interesting finding, we feel that the sample is too small for any statistical significance. A larger workup could provide further illumination.

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