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CASE REPORT

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Superfetation occurring in connection with gamete intrafallopian transfer: a case report

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Abstract This observation reports a case of superfetation which occurred in connection with gamete intrafallopian transfer (GIFT). The macroscopic and histological examination of a spontaneous abortion from a 33-year-old woman (15th week of pregnancy) revealed the existence of two embryos with a monochorionic diamniotic placenta (developmental age approximately 41 days) and two fetuses and a fetal remnant with a trichorionic and triamniotic placenta (developmental age approximately 98 days). The large developmental age difference of embryos and fetuses cannot be explained by retardation, because the embryos showed adequate development with the development of their placenta. Moreover, the usual causes of intrauterine growth retardation could be excluded as could retention of the embryos since the tissues showed no autolytic changes. Consequently the large developmental age difference is explained by assuming that the embryos developed from successive ovulations. A second nidation of blastocysts had occurred after the GIFT concurrently with the clinically reported hyperstimulation syndrome.

Key words Superfetation · Gamete intrafallopian transfer · Hyperstimulation syndrome

Introduction

Superfetation, a very rare event in humans is defined by the development of further embryos during pregnancy. Since 1932 only very few cases of natural [4, 7] or drug induced [1] superfetation have been reported. Here we describe for the first time a case of superfetation which occurred in connection with gamete intrafallopian transfer (GIFT).

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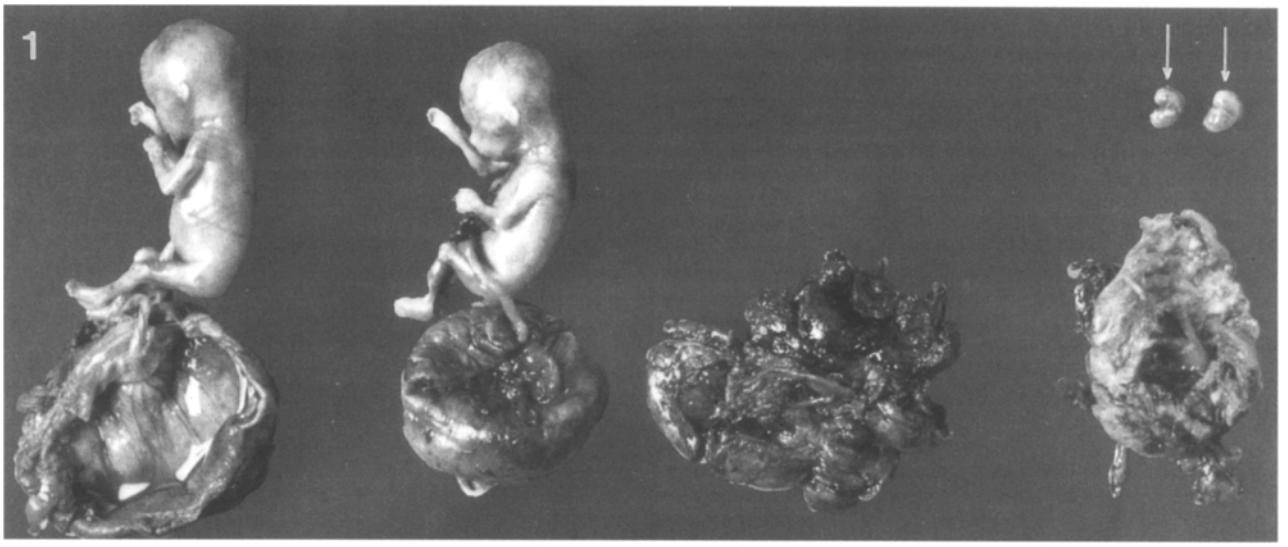
Case report

A 33-year-old patient who entered the GIFT programme with a history of infertility of more than 3 years, presented the typical clinical findings of the polycystic ovary syndrome: polycystic ovaries with oligomenorrhoea, elevated leuteinising hormone (13U/l), hyperandrogenaemia, and adiposity with insulin resistance. The patency of the fallopian tubes was shown by laparoscopy (1991) but infertility treatment with clomiphene and human menopausal gonadotrophins (hMG) over a period of more than 2 years failed to induce a pregnancy. The results of the husband's semen analysis were normal according to WHO criteria. The patient received the standard hMG treatment starting with two ampoules of Pergonal on days 3, 4 and 5 of the cycle followed by daily application of one ampoule until day 9. Intranasal buserelin (900 µg/day) was administred in a flare-up protocol starting on day 1 of the cycle [8]. Ultrasound examination on day 8 (30 September 1992) revealed one leading follicle of 15 mm diameter in the right ovary, two follicles 13 mm in diameter in the left ovary and multiple small follicles (0.8 mm). The œstradiol 17-beta (E_2)-value was 638 pg/ml. One ampoule of hMG per day was administered until 3 October 1992. At Op.m. two ampoules of Predalon [10000 U human chonionic gonadotrophin (hCG) were given to induce ovulation and 36 h later on 5 October 1992) the laparoscopic GIFT was performed. Three mature oocytes and 300000 motile spermatozoa were transferred to the left fallopian tube. A total of 11 follicles were punctured and 9 oocytes were recovered. After the pregnancy had been confirmed on 22 October 1992 (hCG in serum: 6138 U/L; progesterone 40 ng/ml), ultrasound examination carried out 1 week later showed an intrauterine twin pregnancy with amniotic sacs measuring 10 mm and 9 mm in diameter with yolk sacs of 5 mm and 3 mm diameter, respectively. On 10 November 1992 further transvaginal ultrasound examination confirmed a triplet pregnancy and in addition a hyperstimulation syndrome (GIII) was diagnosed. Under conservative treatment the ovarian hyperstimulation syndrome decreased while the further development of the triplet pregnancy was normal. When on 29 December 1992 the patient was hospitalised with heavy vaginal bleeding the ultrasound examination showed two intact fetuses with positive cardiac activity. Spontaneous incomplete abortion occurred on that day (week 15 of pregnancy).



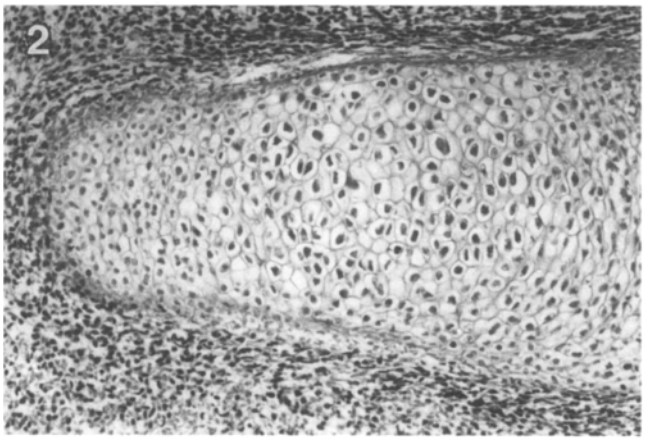


Fig. 1 Macroscopic autopsy findings consisting of two fetuses and a fetal remnant (not shown) with a trichorionic triamniotic placenta, a single placenta and a pair of embryos with a monochorionic diamniotic placenta (*arrows*)

Fig. 2 Detail of the pair of embryos

Fig. 3 Embryonic cartilagenous blastema of the embryonic limb bud, ×250

Pathological findings

At autopsy a pair of embryos with a monochorionic diamniotic placenta, and a further pair of fetuses, a fetal remnant (not shown) with a trichorionic triamniotic placenta, were seen (Fig. 1).

The crown-rump length (CR) of the embryos measured 16 mm and the heads were approximately as large as the trunk (Fig. 2). The hand plates were paddle shaped, whereas the leg buds had a lancet like appearance. At the caudal end of the trunk there was a tail bud and in the pigmented eyes the lens anlagen were clearly visible. In the histological section of the hand plate the typically radial oriented precartilage blastemas of the fingers [2] could be seen showing no signs of ossification (Fig. 3). The epidermis consisted of a single layer of cells and the adnexae of the cutis were completely missing. Both embryos fulfilled morphological and histological criteria of embryos for Carnegie stage 17 [6] having a developmental age of approximately 41 days. The placenta consisted of a few blunt villi which were covered by two layers of trophoblastic epithelium comprised of an outer layer of syncytiotrophoblast and an inner layer of trophoblast, the syncytiotrophoblast exhibiting a delicate brush border. The villous stroma appeared myxoid and nearly avascular as only a minimal number of small vessels with large immature endothelial cells were visible. Small fibrin deposits could be found in the intervillous space. The placenta exhibited no signs of inflammation, especially no signs of villitis could be seen.

The CR of the fetuses, which showed a normal gross anatomy without malformations, measured 85 mm and 90 mm (Fig. 1). Based on the CR length percentiles the age of the two fetuses was estimated to be about 98 days. The fetal remnant of the third placenta measured approximately the same CR length and had been damaged during transport and was therefore not documented photographically. The histological evaluation of the fetal remnant, when compared to the other two fetuses, showed the same histological maturity and some autolytic alterations.

The villi of the placentas were covered by two layers of trophoblastic epithelium, an outer layer of syncytiotrophoblast and an inner layer of trophoblast. No cell boundaries were visible between the nuclei of the syncytiotrophoblast, which formed a layer of uniform thickness around the periphery of the villus. The villous stroma was formed by loose primitive mesenchymal tissue in which Hofbauer cells were diffusely distributed. The vascularization of the stroma consisted of small, centrally located vessels lined by large immature endothelial cells. Fibrin deposit were found within the villous stroma and in the intervillous space. Genetic analysis to confirm the same maternal origin of all fetuses and embryos was not carried out because the number of the placentas, fetus and embryos was registered soon after abortion; mix-up of identities is excluded.

Discussion

This morphological examination revealed the existence of two embryos, two fetuses and a fetal remnant which were delivered by spontaneous abortion at the 15th week of pregnancy. The different developmental stages of the embryos and fetuses cannot be explained by retardation, because the embryos showed adequate development compared with the development of their placenta. Moreover, the usual causes of intrauterine growth retardation (vascular or chronic renal disease, severe anaemia, smoking, addiction to drugs and infection of the placenta) can be excluded, as can retention of the embryos since the embryonic tissues showed no autolytic alterations. Therefore the large developmental age difference of about 50 days is only explained plausibly by assuming that the embryos developed from successive ovulations. This implies that, in this case, a second nidation of a blastocyst had occurred after the GIFT, with subsequent development of further embryos for at least 50 days.

Ultrasound examination documented a triplet pregnancy with the fetuses only; the two embryos (at that time blastocysts) could not be demonstrated due to the presence of multiple ovarian follicles (hyperstimulation syndrome).

It has been proven in primates [3] that the ovary is not overtly refractory to gonadotrophin stimulation during pregnancy and that ovulation can be induced experimentally. These findings may theoretically be applied to humans, hence the reports of rare oocytes which have been obtained from pregnant women [4, 5]. It therefore seems plausible that despite ongoing pregnancy the high plasma concentrations of gonadotrophins and the luteal supplementation with hCG have allowed another ovulation followed by fertilisation and implantation of the oocyte.

Interestingly another author [4] reported a case of natural superfetation with nearly identical age of embryos and fetuses and similar age differences to those described here. It therefore appears that such an extreme condition may only be stable for several weeks and that the great difference in developmental stages is incompatible with further development, resulting in an endocrine dysregulation causing the death of one of the fetuses or embryos.

These findings demonstrate the possibility of superfetation occurring after GIFT and therefore show that the human ovary may not be overtly refractory to gonadotrophin stimulation during pregnancy induced by this method.

The findings stress the importance of periodic and precise ultrasound examination during early stages of GIFT-induced pregnancies to diagnose and threat the hyperstimulation syndrome and prevent further ovulations.

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