CASE REPORT

An allergic reaction following intrauterine insemination

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Intrauterine insemination is a common procedure used for the treatment of different causes of infertility. Adverse reactions associated with this procedure are very rare and usually the procedure is well tolerated by the patient. We report a case of an allergic reaction after intrauterine insemination. The patient developed fever, difficulty breathing and wheezing in both lung fields. Although a low concentration of penicillin in the medium was used, it caused a significant allergic reaction. When intrauterine insemination was performed in subsequent cycles with an antibiotic-free medium, no allergic reaction occurred, and the procedure was well tolerated by the patient. A careful allergy history is essential in patients pursuing infertility treatment where antibiotics are utilized. Patients who are known to be allergic to penicillin should have semen prepared by an antibiotic-free medium.

Key words: allergic reactions/intrauterine insemination/penicillin

Introduction

Intrauterine insemination (IUI) has been used for the treatment of unexplained infertility, cervical and immunological factor infertility, and in cases of male subfertility (Cruz et al., 1986; Dodson et al., 1987). The pregnancy rates using IUI combined with ovulation induction are significantly higher than those using IUI in unstimulated cycles for these indications (Kemmern et al., 1987; Plosker et al., 1994). Sperm processing for IUI leads to a better recovery of the motile spermatozoa. While many clinical IUI programmes prepare their own media, others purchase media from commercial suppliers. To protect against infection, streptomycin sulphate and penicillin G can be added to the media. Some women are known to be allergic to these substances but, given the low concentration of these antibiotics delivered during the insemination, there has been only one reported case of an allergic reaction following IUI (Smith et al., 1992). We report another case of IUI followed by an allergic reaction when penicillin was used in semen processing.

Case report

A 26-year-old female with a 2-year history of primary male factor infertility was treated with IUI. She was known to be allergic to sulpha drugs. There was no history of hayfever. She had been in good general health with no significant medical or surgical problems in the past. After full and informed consent, the couple agreed to undergo ovulation induction with clomiphene citrate (Serophene; Serono Canada, Toronto, Canada) on days 3–7 of the menstrual cycle, followed by IUI using the husband’s spermatozoa. This was performed on the 2 days after the spontaneous luteinizing hormone (LH) surge. A commercial kit (Ovuquick; CADNA Diagnostic, Toronto, Canada) was used to detect the LH surge.

Husband’s ejaculates were collected by masturbation on two consecutive days and the two specimens were processed through a two-step Percoll gradient as discussed previously (Tanphaichitr et al., 1988). The pellet fractions were washed once in human tubal fluid (HTF; Irvine Scientific, Santa Ana, CA, USA) containing 10% of the patient’s heat-inactivated serum and then were resuspended in a final volume of 0.5 ml of the same medium for the insemination. The concentration of penicillin in HTF is known to be 100 units/ml, while the concentration of streptomycin sulphate is known to be 50 µg/ml. In the volume used for each IUI there were 45 units of penicillin G and 22.5 µg of streptomycin sulphate.

IUI was performed on days 14 and 15 of the menstrual cycle without difficulty. The patient reported mild midline low back pain and a temperature of 37.8°C on the day following each insemination. Pelvic examination on the day of the second IUI was normal. Cervical cultures were reported as negative. Two days following the last IUI, the patient’s symptoms disappeared and did not return. Her menses occurred on day 30 of her cycle. A pelvic examination was done on day 2 of the next cycle and this was normal. A second cycle of ovulation induction was commenced. IUI was again performed on days 14 and 15 of her cycle. Over the next two days, the patient reported more severe back pain, difficulty breathing and a fever of 38.8°C. She was seen and examined. There was evidence of wheezing in both lung fields together with fever. A pelvic examination was negative, with no evidence of ovarian enlargement. A complete blood count revealed an elevated white count (14.2×10^9/l) with neutrophilia of 10.7×10^9/l. She was given an antihistamine orally and improved over the next 2 days.

β-human chorionic gonadotrophin was positive and real-time transvaginal ultrasound at 8 weeks confirmed the presence of a single fetus with no evidence...
of ovarian enlargement. The pregnancy was complicated by abruptio placenta and intruterine fetal death at 35 weeks gestation.

After a few months, the patient decided to go through IUI again using the same regimen, but this time semen preparation was performed using an antibiotic-free medium. She had three cycles of clomiphene citrate and IUI without any adverse reactions. Following the third attempt, pregnancy was achieved. Her pregnancy was uneventful, and she was induced at 40 weeks gestation because of macrosomic fetus. She had a vaginal delivery complicated by shoulder dystocia and a deep vein thrombosis. Subsequent to these events she underwent skin testing for penicillin and was shown to be allergic to penicillin.

Discussion

Complications associated with intrauterine insemination are very rare. The prevalence of pelvic infection has been reported to be 1.83 per 1000 women undergoing IUI (Sacks and Simon, 1991). Anaphylactic reaction due to bovine serum albumin used for semen preparation has been reported (Sonenthal et al., 1991; Wuthrich et al., 1995). The IUI procedure involves processing of the semen sample before insemination takes place. Semen preparation is performed to wash out the seminal plasma containing prostaglandins, which may induce uterine contractions, while allowing insemination of a small volume of motile, normal sperm in high concentrations. The medium used for processing the semen sample contained a minimal amount of antibiotics to prevent infection.

Reactions to penicillin in the general population are frequent and the incidence ranges from 1–10% in patients treated with penicillin (Erfmeyer, 1981; Sher, 1983), making penicillin the most common cause of allergic drug reaction (Deswarte, 1984). Penicillin allergy is not dose-related and can range from mild skin reactions, such as maculopapular rash, to life-threatening anaphylaxis causing laryngeal oedema, bronchospasm or hypotension. This patient developed lower back pain and fever of 38.8°C and she had disseminated wheezes on auscultation. Hypersensitivity reactions to streptomycin administration may also occur. Skin reactions are reported in about 5% of patients and severe exfoliative dermatitis and anaphylaxis have occurred but appear to be dose-related (Reynolds, 1996). Allergies to sulphur have been reported to occur in 3.5% of the population and the most common adverse effects include gastrointestinal symptoms (nausea, vomiting, anorexia) and sensitivity skin reactions (rash, urticaria) but haematological reactions and fatal hypersensitivity reactions have occurred (McEvoy et al., 1997). This patient gave a history of allergy to sulphur but not to penicillin or streptomycin. In subsequent cycles when an antibiotic-free medium was used, no allergic reaction occurred, indicating that her allergy symptoms were related to penicillin used in medium.

Are the antibiotics used in media for assisted reproductive technologies necessary? In IUI, microbial contamination may arise from the seminal fluid. A positive semen culture may reflect commensal rather than a true infection. In in-vitro fertilization (IVF) and embryo transfer, the cause may be related to seminal fluid or the oocytes which are retrieved transvaginally (Cottell et al., 1996). Cottell et al. (1997) suggested that the most likely cause of bacteriospermia is related to contamination, and that semen processing in an antibiotic-rich medium can eradicate 95% of organisms. The question remains: does the contaminated semen affect the fertilization, cleavage, and pregnancy rates? Liversedge et al. (1996) reported that antibiotic therapy for asymptomatic male partners with positive semen cultures may be detrimental to the outcome of IVF. Antibiotics introduced through the ejaculate into the vagina may encourage the overgrowth of potentially antibiotic-resistant flora which may be introduced into the embryo culture system following transvaginal oocyte retrieval. Egbase et al. (1996) reported that microbial infection of the cervix decreased the pregnancy rate after embryo transfer. This infection may influence implantation rate. Magli et al. (1996) evaluated the importance of the use of antibiotics in culture media and concluded that antibiotics have an adverse effect on the growth rate of preimplantation embryos. They suggested that antibiotics may interfere with the timing of cleavage events, either by delaying or blocking development.

Using antibiotics in media for processing samples for IVF may be justified knowing that the oocytes will be inseminated and incubated at 37°C for 24 h, which gives the microbes the proper environment for growth. This may affect fertilization and cleavage rate, although the previous study (Magli et al., 1996) did not support this idea. Is the use of antibiotics similarly justified in IUI and IVF with intracytoplasmic sperm injection (ICSI)? A randomized controlled trial comparing antibiotic and antibiotic-free media for the preparation of spermatozoa for IUI, IVF and ICSI with ICSI is needed.

References


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