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Successful pregnancy in patient with Kartagener's syndrome and infertility: case report and published work review

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Summary

Background: Kartagener's syndrome (KS), a subgroup of primary ciliary dyskinesia (PCD), is a rare genetic disorder that causes infertility and ectopic pregnancy presumably due to defective ciliary function in fallopian tube. *Case:* The authors report a 31-year-old female, who was diagnosed with KS, with primary infertility for six years. In vitro fertilization and embryo transfer (IVF-ET) was performed and the patient conceived successfully. *Conclusions:* For women with primary infertility associated with chronic respiratory symptoms, PCD should be highly suspected. Superovulation and intrauterine insemination would not increase the chance of pregnancy in women with PCD. IVF-ET is considered the optimum treatment of choice in infertile women with PCD.

Key words: Kartagener's syndrome (KS); Infertility; Case report; Pregnancy.

Introduction

Primary ciliary dyskinesia (PCD) is a rare autosomal recessive disorder that causes abnormal structure and/or function of motile cilia lining the respiratory tract, fallopian tube, as well as the flagella of sperm cells. Kartagener's syndrome (KS), a subgroup of PCD, is defined by the classic triad of chronic sinusitis, bronchiectasis, and situs inversus. Male patients are typically infertile as a result of totally immotile spermatozoa. Female fertility is more variable, as both fertile [1, 2] and infertile [3-6] patients have been reported.

Women with PCD are at risk of infertility and ectopic pregnancy presumably due to defective ciliary function in the fallopian tube [5, 7]. In this case report, the authors describe a female patient who presented for infertility secondary to KS and successfully conceived via in vitro fertilization and embryo transfer (IVF-ET).

Case Report

The patient in the present case was a 31-year-old female with a six-year history of primary infertility. She presented to the fertility unit at the present center on May 2012. Her medical history was significant due to the classic triad of KS (i.e., situs inversus, bronchiectasis, and chronic sinusitis) since childhood. Her partner was 32-years-old with normal secondary sex characteristics, reproductive system examination results, and laboratory workups, including hormonal evaluations and semen analyses. She had normal menstrual cycle without other symptoms or surgery history. Laparoscopy and hysterosalpingography were normal. She underwent two cycles of super ovulation and intrauterine insemination but still failed to conceive. In July 2013, she had her first IVF-ET trial but did not undergo ET due to ovary hyperstimulation. The second IVF-ET trial was successful two months later with frozen ET. Her pregnancy was complicated with recurrent episodes of productive cough which aggregated at 37 weeks of gestation. At 38+6 weeks of gestation, a cesarean section was performed because of poorly controlled respiratory problems and patient's requirement. A healthy male baby was delivered with uneventful prenatal course. After delivery, the authors advised the patient to undergo nasal mucosa biopsy but she refused.

Discussion

PCD is characterized by recurrent sinusitis, otitis media, and chronic respiratory problems, including bronchiectasis and difficulty clearing sputum. Approximately 50% of patients will fall within a subset of PCD known as KS. In addition to bronchiectasis and chronic sinusitis, these patients will also present with situs inversus, indicating the cilia of the patient was affected during embryonic development. The incidence of PCD is estimated at 1/16,000 births, based on prevalence of situs inversus and bronchiectasis [8]. However, only a few PCD patients carry a well-established diagnosis, which reflects the limited ability to diagnose this disorder [9, 10].

The present authors searched all published literature and references from relevant articles. Only six cases in four relevant articles were found [3-6]. Table 1 provides a summary of the clinical and obstetrical features of seven cases of female PCD associated with infertility that underwent IVF-ET for pregnancy. Although the gestational results were not reported in all of the cases the authors reviewed, the clinical presentations and gestational courses were de-

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Table 1. — *Summary of reported cases of primary ciliary dyskinesia and infertility.*

Case No.	First author	Age	year	Diagnoses	Nasal mucosa TEM result	Infertility duration (years)	Partner condition	Laparoscopy and hysterosalpingography and surgery history	Intrauterine insemination (times)	IVF-ET attempts (times)	Gestational course	Mode of delivery	Pregnancy results
1	Tseng-Kai Lin	32	1998	KS	positive	8	Normal	Mild degree of right peritubal and periovarian adhesion which underwent adhesiolysis	No	3	transient dyspnea	C-section, at 35 weeks	Two healthy newborns(twins)
2	S.A. Halbert	23	1997	KS	positive	3	Normal	Normal; Ovum recover accomplished by mini-laparotomy	No	1, failed	-	-	-
3	Laurie Mclean	28	2000	PCD	positive	5	Normal	Normal and no surgery history	Several times, all failed	1	Ongoing when reported	Ongoing when reported	Ongoing when reported
4	Laurie Mclean	33	2000	PCD	positive	4	Normal	Minimal endometriosis	No	1	Ended with ectopic pregnancy	-	-
5	Antoine Abu-Musa	27	2008	KS	-	5	Normal	Normal and no surgery history	4, all failed	1	Uneventful	Vaginally, at 38 weeks	Healthy female newborn
6	Antoine Abu-Musa	30	2008	KS	positive	7	Normal	Normal and no surgery history	Several times, all failed	1	Recurrent episodes of dyspnea and cough and preeclampsia	C-section, at 35 weeks	1,700-gram preterm fetus with a stableprenatal course
7	Our case	31		KS	-	6	Normal	Normal and no surgery history	2, all failed	2	Recurrent episodes of cough and difficulty in clearing sputum	C-section, at 38 weeks	Healthy male newborn

scribed in six cases. Before IVF-ET was used, four cases (cases 3, 5, 6, and 7) underwent several cycles of super ovulation and intrauterine insemination to no avail. All of the patients underwent IVF-ET for pregnancy; six cases were able to conceive, and case 2 failed in the single IVF attempt. Case 3 was still pregnant at the time of the report. Case 4 ended with ectopic pregnancy and underwent a right salpingectomy. Cases 1, 5, 6, and 7 were able to deliver the babies with only case 5 delivering vaginally; cesarean sections were performed in the three other cases because of various reported gestational complications including transient dyspnea, difficulty in clearing sputum, and preeclampsia. In the present case, cesarean section was performed due to poorly controlled respiratory problems and patient's requirement at 38+6 weeks of gestation. Babies delivered in cases 1, 5, and 7 were all healthy and case 1 delivered

twins. In case 6, the preterm baby had a stable prenatal course.

Men with KS have immotile spermatozoa and are, therefore, almost infertile. However, reports of fertility in women with KS have been variable [5, 7, 11]. The importance of cilia for the normal function of the fallopian tube is well established. The ultrastructure of the cilium consists of nine pairs of microtubular doublets surrounding two tubules that are enclosed in a central sheath. Both inner and outer dynein arms (DAs) contain ATPase activity that provides the energy for the doublets to slide over one another. This mechanochemical coupling is believed to be the source of the ciliary beat. The ultrastructure of the cilia in KS patients has been shown to consist of abnormalities of the DAs. Initially, the structural abnormalities of the cilia rendered the cell totally immotile. However, subsequent work has determined that cilia with ultrastructural abnormalities may be dyskinetic rather than totally immotile. These observations support the hypothesis that dyskinetic ciliary activity in the reproductive tract explains the fertility in women with KS. That is, fertility depends on the degree and efficiency of the ciliary beat in the fallopian tubes, which is variable in women with the syndrome. Although women with KS have a variable degree of fertility, they definitely have an increased risk for sterility [5].

KS patients should be encouraged for the possibility of natural conception and normal gestational course [2]. McLean and Claman demonstrated that intrauterine insemination does not help infertile female patients with PCD to conceive [3]. Among the seven cases in Table I, four cases attempted and failed super-ovulation and intrauterine insemination before IVF-ET was used. The optimum treatment of choice for infertile women with PCD should be IVF-ET [4]. Once a woman has successfully conceived, PCD is unlikely to adversely affect the course and outcome of pregnancy [6]. However, with the diaphragm pressed upward due to the enlargement of the uterus during the gestational course, the underlying respiratory symptoms will become worse. The patient may suffer from aggregated and increased frequency of episodes of dyspnea and cough during gestation, which may increase obstetrical risk during delivery. The present patient had classic KS triad and conceived with the help of IVF-ET procedure. During the gestational course, she had worsened respiratory symptoms including productive cough and difficulty in clearing the sputum, which required antibiotics. Under the circumstances of poorly controlled respiratory function and patient's requirement, performing a cesarean section would be a better course of action rather than vaginal delivery for this patient.

In conclusion, PCD could affect female infertility to various degrees. For women with primary infertility associated with chronic respiratory symptoms, PCD should be highly suspected and more diagnostic tests should be conducted. Intrauterine insemination cannot not assist an infertile woman with PCD to conceive; IVF-ET is considered to be the optimum treatment of choice in an infertile woman with PCD. The mode of delivery should be considered carefully in a complicated gestational course according to the individual circumstances of each patient.

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