Successful pregnancy in a woman with Kartagener's syndrome who had aggravation of lung disease during pregnancy: A case report

Goro Kuramoto[1], Jun Kakogawa[1], Akira Nakabayashi[1], and Naoki Masaoka[1]

[1]Tokyo Women's Medical University

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Abstract

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Title page

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Authors: Goro Kuramoto, M.D., Ph.D., Akira Nakabayashi, M.D., Ph.D., Naoki Masaoka, M.D., Ph.D., Jun Kakogawa, M.D., Ph.D.

Affrication: Department of Obstetrics and Gynecology, Tokyo Women's Medical University, Tokyo, Japan.

Corresponding to: Jun Kakogawa, M.D., Ph.D

8-1, Kawada-cho, Shinjuku-ku, Tokyo, Japan, 1628666.

Department of Obstetrics and Gynecology, Tokyo Women's Medical University.

Tel: +81-3-3353-8111

Fax: +81-3-5269-7619

E-mail: kakogawa.jun@twmu.ac.jp

Conflicts of Interest notification

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Key words

Kartagener's syndrome; infertility; in vitro fertilization and embryo transfer; lung transplantation.

Key Clinical Message:

We describe a case of successful pregnancy in a patient with Kartagener's syndrome who had been offered an indication for lung transplantation before conception, despite aggravation of the lung disease during pregnancy.

Abbreviations

KS: Kartagener's syndrome, IVF-ET: in vitro fertilization and embryo transfer.

Abstract

Lung transplantation is an option for end-stage lung disease in Kartagener's syndrome patients. We describe a case of successful pregnancy in a patient with Kartagener's syndrome who had been offered an indication for lung transplantation before conception, despite aggravation of the lung disease during pregnancy.

Main document

Introduction

Kartagener's syndrome (KS) is an autosomal recessive genetic disorder characterized by a triad syndrome: chronic sinusitis, bronchiectasis and situs inversus. KS results from congenital ciliary dysfunctions and has an incidence of 1 in 25,000 [1]. Congenital ciliary dysfunctions in the respiratory tract, fallopian tube and flagella of spermatozoa can cause chronic or recurrent upper respiratory diseases and infertility. Gene mutations such as *DNAI1* and *DNAH5* have been indicated in KS patients [2]. Therapeutic strategies in KS patients are primarily focused on the control of respiratory infection, and lung transplantation is an option for end-stage lung disease.

Females with KS are not necessarily infertile, although males with KS are infertile due to abnormal sperm motility [1]. Previous reports have presented courses of pregnancies in females with KS without aggravation of the lung disease after natural conception [3] as well as in vitro fertilization and embryo transfer (IVF-ET) [4, 5]. Regarding pregnancy following lung transplantation, careful management is essential for contraception, timing of conception, maintenance of immunosuppression, adverse perinatal complications and risk of breastfeeding by neonatal exposure to immunosuppressants [6].

In this report, we describe a case of successful pregnancy in a patient with KS with *DNAH5* mutations who had been offered an indication for lung transplantation before conception, despite aggravation of the lung disease during pregnancy, by a multidisciplinary approach.

Case presentation

A 35-year-old Japanese woman with KS was referred to our department with a desire to achieve pregnancy. She married a 47-year-old healthy Japanese male 9 months before her first visit. She had been found to have situs inversus at 5 years old. She was diagnosed with KS at 27 years old, and her clinical and imaging findings revealed chronic sinusitis, bronchiectasis and situs inversus on electron microscopic examination of bronchial cilia. She had heterozygous mutations in*DNAH5* at 33 years old [7]. She was offered an indication for lung transplantation at 34 years old. In her family history, her sister had KS.

Infertility examinations were performed, including basal body temperature charts, hysterosalpingography, semen analysis, antisperm antibodies and assays of serum thyroxine, prolactin and follicle-stimulating hormone, and all the data were within normal limits. Considering her offer of lung transplantation and the advanced age of her husband, IVF-ET was planned. She had conceived by the first cycle of IVF at 36 years old and attended antenatal care visits in our department. During the pregnancy, she was examined by a respiratory specialist at our hospital every month.

She noticed frequent exacerbation of cough with copious purulent sputum at 33 weeks of gestation. At 35 weeks and 1 day of gestation, she was admitted to our hospital because of exacerbation of cough and progressive dyspnea that made it difficult to maintain her supine position. On admission, a physical examination revealed a blood pressure of 94/60 mmHg, regular pulse rate of 94 beats per minute, respiratory rate of 24 breaths per minute, body temperature of 36.9 °C and SpO_2 of 96% at room air. Auscultation of the chest revealed coarse crackles in both lungs, and the heartbeat was audible on the right side of the chest. The chest radiograph showed a cardiac shadow on the right side and bronchiectasis with fibrotic bands in the lower field on both sides, which was an unremarkable change from before pregnancy (Figure 1). Laboratory findings revealed a white cell count of 11,470/μL, hemoglobin of 11.1 g/dl, and C-reactive protein level of 1.84 mg/dL. The echocardiogram demonstrated normal cardiac function, and there was no evidence of systemic inflammatory disease. Ultrasound evaluation confirmed an appropriate date and viable fetus.

The timing and mode of delivery, as well as the potential pulmonary impact of continuing pregnancy, were discussed with combined input from the obstetrician, respiratory specialist and neonatologist. After a joint multidisciplinary team meeting, a decision was made to perform a preterm cesarean section under epidural and spinal anesthesia to avoid further exacerbation of the respiratory function due to diaphragmatic elevation by the gravid uterus. The cesarean section was performed at 35 weeks and 5 days of gestation under epidural and spinal anesthesia. The operating table was placed in a slight reverse Trendelenburg position (head up position at a 30° angle) during the operation (Figure 2). A healthy, female neonate weighing 2,633 g with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively, was delivered with no gross anomalies.

Following the operation, the patient was transferred to the intensive care unit (ICU), and supplemental oxygen was continued. In the ICU, chest physiotherapy by postural drainage was initiated to facilitate the drainage of bronchopulmonary secretions from the tracheobronchial tree. On the 1st postoperative day, supplemental oxygen was discontinued, and she was moved to the obstetrics ward. Her cough and dyspnea gradually improved, and she was discharged from our hospital on the 6th postoperative day. One month after delivery, the patient's respiratory function was restored to prepregnancy values.

Discussion

In KS, gene mutations in *DNAI1* and *DNAH5* lead to impaired ciliary motility, which predisposes patients to recurrent sinopulmonary infections, infertility and errors with left-right body orientation. The mutated genes *DNAI1* and *DNAH5* cause the cilia to be the wrong size or shape or move in the wrong way, making ciliary motility defective [2]. The current case had heterozygous mutations of*DNAH5* before conception [7].

Abnormal ciliary motility leads to infertility in both males and females [1]. Male infertility is due to the immotility of sperm, while in females, cilial movement may be absent in the fallopian tubes [8]. Females with KS have a variable degree of fertility. IVF is necessary for some females with KS who desire children, although spontaneous pregnancy is not impossible [1].

In the current case, lung transplantation was offered at the first visit to our department. Pregnancy should be avoided for at least 1-2 years posttransplantation to minimize the risks to allograft function [9]. Transplant patients have an increased risk of maternal and neonatal complications, such as preterm birth, low birth weight and postpartum graft loss [6]. In the current case, the patient's husband was 47 years old at her first visit to our department. Thus, we considered that earlier pregnancy by IVF was preferred considering potential adverse outcomes associated with posttransplant conception and childcare burden due to advanced age, although she might have had a possibility of spontaneous conception.

The physiological reduction in lung volume and the increase in oxygen consumption during pregnancy may impair respiratory function. It has been reported that a woman with KS had three consecutive spontaneous conceptions that resulted in full-term vaginal deliveries without exacerbation of respiratory function [3]. Another report showed a woman with KS with a twin pregnancy who did not exhibit impaired respiratory status during pregnancy and delivered healthy neonates by cesarean section under spinal anesthesia [5]. To the best of our knowledge, there have been no reports of impaired maternal respiratory function during pregnancy in KS females. In the current case, one reason for impaired respiratory function during pregnancy was that the patient's respiratory function had been at a level that would be considered an indication of lung transplantation even before conception. Another reason was that the increased size of the gravid uterus and splinting of the diaphragm caused a decrease in lung expansion, which affected her respiratory function.

In the perinatal management of KS females, the mode of delivery and anesthetic technique should be planned with a multidisciplinary team to assess the characteristics and to determine the best approach for preserving maternal and fetal wellbeing. Combined epidural and spinal anesthesia can be used, as it produces post-operative pain relief, optimizing respiratory function. Our case underwent cesarean section under epidural and spinal anesthesia in a slight reverse Trendelenburg position based on a multidisciplinary discussion. Positioning the patient on the operating table might be challenging. It has been considered that early chest physiotherapy in the ICU could contribute to the early improvement of respiratory function.

In conclusion, we stress that appropriate assessment and management by a multidisciplinary team from preconception to the postpartum period are essential to achieve a good pregnancy outcome for females with KS, especially for those with aggravation of the lung disease during pregnancy. Our case provides valuable information for preconception care and perinatal management in females with KS.

Author Contributions

Study conception: G Kuramoto, A Nakabayashi, J Kakogawa. Data collection: G Kuramoto, A Nakabayashi, J Kakogawa. Analysis: all authors. Investigation: all authors. Writing: J Kakogawa. Critical review and revision: A Nakabayashi, J Kakogawa. Supervision: N Masaoka. Final approval of the article: all authors. Accountability for all aspects of the work: all authors.

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Conflict of Interest Statement

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Date Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Consent

Informed consent was obtained from the patient for publication of this case report and accompanying image in accordance with the journal's patient consent policy.

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Figure legends

Figure 1

The chest radiograph showed a cardiac shadow on the right side (arrow head) and bronchiectasis with fibrotic bands in the lower field on both sides (arrows), which was an unremarkable change from before pregnancy

Figure 2

The operating table was placed in a slight reverse Trendelenburg position (head up position at a 30° angle) during the operation (arrow).

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