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Transient azoospermia following rosuvastatin medication for hypercholesterolemia

Y. Tada, K. Kitaya, T. Hayashi, Y. Iwaki, M. Karita, S. Taguchi, M. Funabiki, Y. Nakamura

IVF Center, Oak Clinic, Nishinari-ku, Osaka (Japan)

Summary

The authors report a case of transient azoospermia following hydroxymethylglutaryl-coenzyme A reductase (HMGCR) inhibitor rosuvastatin medication for hypercholesterolemia. While a primary infertile couple with oligoasthenospermia was preparing for an in vitro fertilization program, the male partner had been diagnosed with hypercholesterolemia in a medical check-up and prescribed four-week oral administration of rosuvastatin. No motile spermatozoa were found in the ejaculated semen and urine on the day of follicular aspiration. Azoospermia was confirmed by re-examination in weeks 3 and 7. Spermatozoa appeared in the ejaculated semen in two weeks of drug withdrawal. In week 16, the sperm count and motility increased to the level where intracytoplasmic sperm injection was available.

Key words: Azoospermia; Rosuvastatin; Hypercholesterolemia; In vitro fertilization.

Introduction

Rosuvastatin is a competitive inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR), the rate-limiting enzyme in cholesterol biosynthesis. The adverse events associated with rosuvastatin are uncommon and widely used for treatment of hypercholesterolemia, dyslipidemia, and hypertriglyceridemia. In addition, rosuvastatin was found to lower the relative risk of heart attack and stroke uniquely and therefore also utilized for prevention of cardiovascular diseases in the high risk cohort [1, 2].

As cholesterol is a substrate for steroid biosynthesis, administration of HMGCR inhibitor may possibly trigger some endocrine disorders including hypogonadism. However, to the authors' best knowledge, there are only one article that reported a case of oligospermia in a secondary infertile man who was taking a HMGCR inhibitor lovastatin for hypercholesterolemia and its recovery after drug withdrawal [3]. Meanwhile, there are no reports regarding the relationship between rosuvastatin and male infertility. The authors here report a case of primary infertile man who developed transient azoospermia following four-week administration of rosuvastatin for hypercholesterolemia and its recovery after drug withdrawal.

Case Report

A primary infertile couple of 46-year-old man and 40-year-old woman with infertility period for nine months visited the infertility care unit. Screening examinations revealed that the male partner had oligoasthenospermia (sperm count 8×10^6 per ml semen; motility 12 %) with elevated serum follicle-stimulating hormone level (14.6 IU/L). Serum luteinizing hormone (5.3 IU/L), free testosterone (8.8 pg/ml), and prolactin (5.0 IU/L) levels measured within the normal ranges. The estimated bilateral testicular volumes were normal (the left testis 15 ml and the right testis 12 ml with orchidometer). Physical examinations and ultrasonogram did not show any pathological findings including varicocele, testicular tumors, and pelvic/urinary/seminal tract inflammation. The couple had seven failed cycles of in vitro fertilization (IVF) cycles using short gonadotropin releasing hormone agonist protocol [4, 5], intracytoplasmic sperm injection, and blastocyst transfer.

On the day of oocyte pickup in the eighth IVF cycle, motile spermatozoa were not found in the fresh ejaculated semen as well as in the urine. IVF was cancelled and the retrieved oocytes were immediately subjected to vitrification. The results of the physical and endocrinological examinations were similar to those at the first visit. No spermatozoa were found in the ejaculated semen and urine in following three weeks. A detailed interview disclosed that the male partner was diagnosed with hypercholesterolemia in a periodic medical check-up and prescribed oral rosuvastatin (2.5 mg/tablet, one tablet per day) for approximately four weeks. Magnetic resonance and physical reexamination did not demonstrate marked abnormal findings regarding testis, seminal tract, seminal vesicle, prostate, and penis. In reference to previous report [3], the authors suggested the consultation with the physician in charge regarding withdrawal or change of medication if possible. The male partner immediately stopped taking medicine following consultation, but semen analysis in weeks 4, 6, and 8 proved azoospermia.

Spermatozoa, however, appeared in the ejaculated semen in week 12 after drug withdrawal. In week 16, the sperm count (73×10^6 per ml semen) and motility (17 %) increased to the level where intracytoplasmic sperm injection was available. In week 18, intracytoplasmic sperm injection was performed using thawed oocytes and fresh spermatozoa.

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Discussion

Several reports documented the cases of drug-associated azoospermia/cryptozoospermia including colchicine, cyclophosphamide, clomiphene citrate, hormone/steroids, antibiotics, α-blockers, 5α-reductase inhibitors, pesticides, and recreational drugs [6, 7]. The authors here present a case of transient azoospermia developed in the male partner of an infertile couple following weeks of oral HMGCR inhibitor rosuvastatin administration.

As androgens are synthesized from cholesterol and play an essential role in spermatogenesis, it is conceivable that inhibition of cholesterol biosynthesis by rosuvastatin potentially deteriorated the sperm quantity and quality. Indeed, recent investigations demonstrated that treatment of hypercholesterolemia with HMGCR inhibitors reduced testicular volume and serum total and free testosterone concentration and increased serum follicle-stimulating hormone concentration and the onset of hypogonadism-related symptoms [8]. Following 16 weeks of drug withdrawal, the sperm count and motility improved to the level where intracytoplasmic sperm injection was available, suggesting a reversible cause-effect relationship between rosuvastatin administration and azoospermia in this patient.

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Address reprint requests to:
K. KITAYA, M.D.
IVF Center, Oak Clinic,
2-7-9 Tamade-Nishi, Nishinari-ku,
Osaka 557-0045 (Japan)
e-mail: kitaya_k@oakclinic-group.com