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Case Report

Myotonic Dystrophy Type 1 Presenting as Male Infertility

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Myotonic dystrophy 1 (DM1) is a multi-system disorder characterized by endocrine defects that include testicular and tubular atrophy, oligospermia and azoospermia, and increased follicle-stimulating hormone levels. We describe a rare case of DM1 presenting as infertility in a 29-year-old man.

Key Words: *Infertility; Myotonic dystrophy*

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Myotonic dystrophy 1 (DM1) is defined as a hereditary, autosomal dominant multi-system disorder characterized by the development of structural and functional abnormalities in the muscle membrane protein associated with muscular dystrophy, cardiac conduction disorders, cataracts, mental retardation, and endocrine and reproductive defects [1]. The genetic mutation in DM1 is the expansion of a CTG repeat sequence found in the 3'-untranslated region of the myotonic dystrophy protein kinase (*DMPK*) gene located on chromosome 19q13.3 [2,3]. Reproductive abnormalities are a well-recognized finding in DM1. Progressive testicular atrophy is a prominent feature and occurs with an incidence of approximately 80%. Histological abnormalities include hyalinization, atrophy, fibrosis of seminiferous tubules, and reduced sperm numbers [1]. Oligospermia and azoospermia are reported in approximately 73% of DM1 patients [4]. Herein, we report a case of a patient with azoospermia associated with DM1 and review the literature.

CASE REPORT

A 29-year-old man was seen in our clinic over a 2-year duration for infertility. His medical history did not include cryptorchidism, herniorrhaphies, orchitis, mumps, or drug ingestion. He appeared healthy, and his height and body weight were 171 cm and 70 kg, respectively. However, the patient complained of progressive, mild distal extremities weakness for the past 3 years. He could not endure a heavy burden of more than 10 kg. The physical exam revealed soft, atrophied testicle on palpation, measuring 5 ml, bilaterally, with preserved epididymis and vas. The size of the penis and pubic hair growth were unremarkable. He did not complain of any erectile problems. Neurologic examination demonstrated 4-4+/5 strength at the proximal extremities and 3-3+/5 strength at the distal extremities. Semen analysis performed 2 times after an appropriate abstinence period demonstrated a low ejaculate volume (< 1 ml) with azoospermia. Post-ejaculate urinalysis also showed no sperm. Endocrine evaluation revealed a plasma leutenizing hormone level of 2.97 mIU/ml (0.4 to 5.7) and testosterone level of 668.80 ng/ml (241 to 827), but his plasma follicle stimulating hormone level was elevated at 30.33 mIU/ml (1.1 to 13.5). A testicular biopsy was performed given concerns for primary testicular failure. The biopsy results revealed hypospermatogenesis (Fig. 1A), atrophy, and marked hyalization of the seminiferous tubules (Fig. 1B). Needle electromyography demonstrated an early interference pattern and myotonic discharge at the distal extremities, which is a pathognomonic finding for DM1 (Fig. 2). Gene analysis revealed an expansion of the CTG repeat sequence of up to 833 copies, thus confirming classic DM1.

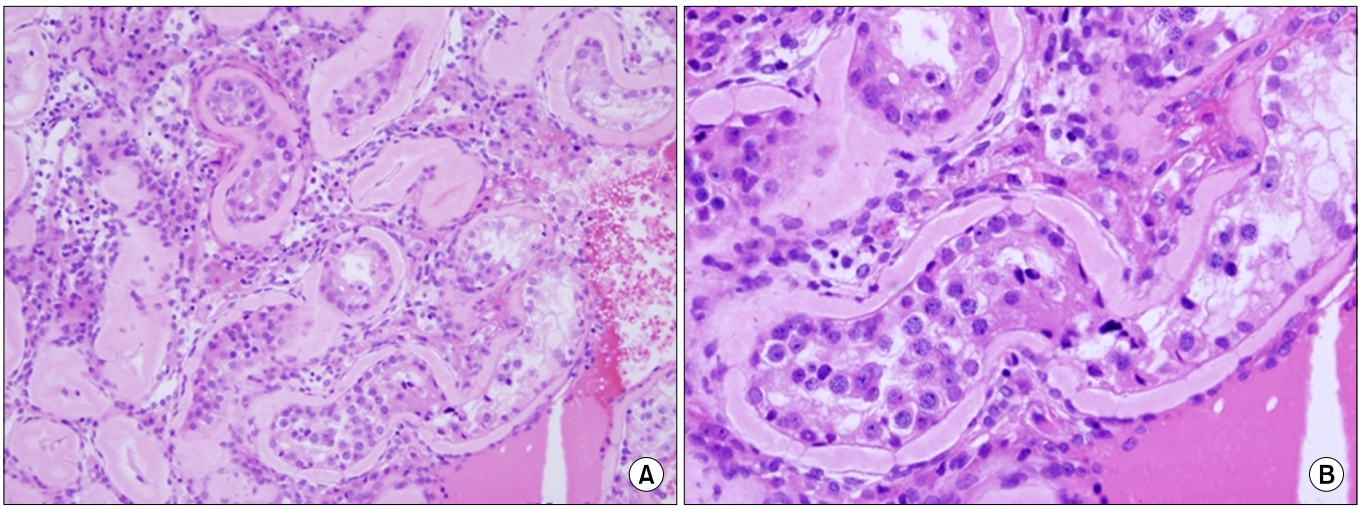

FIG. 1. (A) Testicular biopsy revealed hypospermatogenesis (H&E, x100), (B) atrophy, and marked hyalization of the seminiferous tubules (H&E, x400).

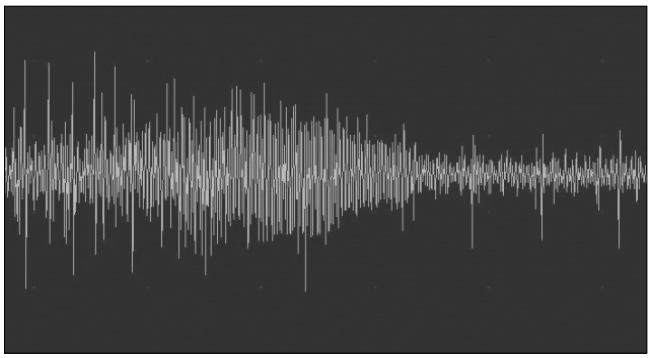

FIG. 2. Needle electromyography demonstrated myotonic discharge at the distal extremities.

The patient was informed that having a baby might be possible by intracytoplasmic sperm injection (ICSI); however, it would result in the heritable disease among his offspring.

DISCUSSION

DM1 is the most common cause of an inherited, adult-onset, muscular dystrophy [5]. Symptoms include muscle atrophy, cataracts, male infertility, and endocrinopathies. The disease is caused by an expansion of an unstable CTG trinucleotide repeat on chromosome 19q13.3 of a gene that codes for a serine-threonine kinase. The size of the unstable repeat appears to be related to the age at onset and to the severity of the disease; the largest repeat sizes are seen in persons with congenital DM1 [5]. In the normal population, the number of CTG repeats is polymorphic, ranging from 5 to 37 copies [3]. A minimal amplification of the repeat, ranging from 42 to 80 copies, designates mild DM1, which is characterized by no or only mild manifestations of the disease. In classic DM1, the copy number of CTG repeats is usually >80, which causes a more severe phenotype [6]. Our patient had 833 copies and belonged to this category.

To our knowledge, this is the first case of male infertility associated with DM1 in Korea. Although there are no data on the prevalence of DM1 in Korea, the Japanese, an ethnicity similar to Koreans, have a comparable or higher prevalence of DM1 (5.5/100,000) compared with West Europeans (2.5 to 5.5/100,000) [7]. Reproductive abnormalities are a well-recognized finding in DM1. Nearly two thirds of men have testicular atrophy and many will have oligospermia or azoospermia [5]. Although ICSI has become a powerful technology for men with various spermatogenic disorders to increase their prospects of parenthood, genetic consultation with these infertile patients is of great concern. Recent studies have suggested that many of the so-called idiopathic azoospermia may have a genetic basis [8]. It has been proposed that larger CTG repeat alleles in the *DMPK* gene might be associated with idiopathic azoospermia [9]. This implies that some patients with idiopathic azoospermia may be carriers of larger trinucleotide repeat alleles, ultimately leading to increased incidences of heritable diseases among their offspring [9]. Genetic diseases that do not primarily affect the genitourinary tract may have hidden urologic manifestations such as infertility. Thus, the practicing urologist should have knowledge of these diseases.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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