CASE REPORT

Infertile Males with Muscle Weakness: Keep Your Eyes Open for Myotonic Dystrophy

Partha P. Chakraborty¹ · Sugata N. Biswas¹ · Shinjan Patra¹ · Gouranga Santra¹

Received: 31 January 2016 / Accepted: 12 April 2016 / Published online: 3 May 2016
© Federation of Obstetric & Gynecological Societies of India 2016

About the Author

Partha P. Chakraborty is a consultant endocrinologist of repute with interest in male factor infertility. He has more than 50 publications in various national and international journals to his credit. He is into West Bengal Medical Education Service since 2006, and currently, he holds the post of Assistant Professor, Department of Medicine, Midnapore Medical College and Hospital.

Introduction

Male factor infertility affects approximately 1 in 20 men and is the responsible factor in almost half of the couples undergoing assisted reproductive treatments (ARTs). The most common presentation is oligozoospermia, as defined by a sperm concentration less than 15 million/ml [1]. Though idiopathic spermatogenetic disorders are the underlying cause of oligozoospermia in majority, it may occur in a variety of reproductive or systemic diseases. A

detailed history and thorough clinical examination may at times identify treatable causes of oligozoospermia. In case effective treatment is unavailable for a particular disorder, a precise diagnosis can identify associated systemic comorbidities, which may have profound implications for general health. Last but not the least, underlying genetic disorders may potentially influence treatment of the reproductive disorder and transmission of the disease to the offspring. In this article, we discuss two patients of myotonic dystrophy (MD), in whom a careful questioning and appropriate clinical examination revealed the diagnosis.

Partha P. Chakraborty, Assistant Professor; Sugata N. Biswas, Postgraduate trainee; Shinjan Patra, Postgraduate trainee; Gouranga Santra, Associate Professor.

✉ Partha P. Chakraborty
docparthapc@yahoo.co.in

¹ Department of Medicine, Midnapore Medical College and Hospital, Midnapore, Paschim Medinipur, West Bengal 721101, India

Case report

Case: 1

A 23-year-old male, married for 2 years attended our clinic seeking medical advice for primary male factor infertility.

Fig. 1 Elongated face with bilateral ptosis and atrophy of temporalis muscles: the 'hatchet facies'

He had normal libido, preserved spontaneous erections and satisfactory tumescence. However, a detailed history revealed mild distal muscle weakness and difficulty in releasing objects from his handgrip, which he had been experiencing for the past 2 years. His face appeared hatchet-shaped with bilateral ptosis and visible atrophy of masseter and temporalis muscles (Fig. 1) and with movements of neck against resistance, sternocleidomastoids were found to be atrophied bilaterally (Fig. 2). He was adequately virilised, but the testes were soft and atrophied, measuring 8 and 10 ml on right and left, respectively. Bilaterally, vas deferens and epididymes were normal on palpation. Neurological examination revealed moderate weakness of the distal muscles of all four extremities with percussion myotonia over the thenar eminences and tongue. Semen analysis was identical in three successive samples separated by a month each with oligospermia (concentration: less than 5 million/ml), average ejaculate volume of 1.5 ml and pH between 7.3 and 7.5 with normal seminal fluid fructose. Early morning serum testosterone, FSH, LH and serum creatine kinase were found to be 895 ng/dl (300–1200 ng/dl), 28.2 mIU/ml (1.0–13.0 mIU/ml), 7.4 mIU/ml (1.0–9.0 mIU/ml) and 182 U/L (50–200 U/L), respectively. Electromyography (EMG) of distal extremity muscles revealed myotonic discharges with a waxing–waning frequency, amplitude and a characteristic 'engine revving' sound (Fig. 3). A diagnosis of MD was thus arrived at.

Case: 2

A 26-year-old husband of an infertile couple was referred for evaluation of intermittent erectile dysfunction and severe oligospermia (sperm concentration: <1 million/ml).

Fig. 2 Thinned out bilateral sternocleidomastoids seen on movement of the neck against resistance

Fig. 3 Electromyography of one of the hand muscles showing characteristic myotonic discharges

They had been married for 3 years without an issue, despite engaging in regular sexual activities. The patient had suffered from four episodes of spontaneous bilateral temporomandibular joint dislocations while chewing food over the previous 2 years and also noticed progressive weakness of the small muscles of his extremities. On examination, temporal hollowing with atrophy of temporal and masseter muscles and thinning of the sternocleidomastoids were noted. Neurological examination revealed myotonia which was confirmed subsequently by EMG.

The testes were soft and atrophied, measuring 6 ml on right and 4 ml on left side. Secondary sexual characteristics were normal with palpable vas deferens bilaterally. Serum testosterone, FSH, LH and serum creatine kinase were estimated to be 130 ng/dl, 68.0 mIU/ml, 22.4 mIU/ml and 190 U/L, respectively. Apart from severe oligospermia, the seminograms were normal. In the light of these evidences, a diagnosis of MD was made.

Both the couples were counselled regarding the very poor probability of spontaneous pregnancy, the inheritance pattern of the disease and available treatment options with ARTs. However, the first couple did not avail any of the suggested techniques for reproductive assistance, in knowledge of dominant inheritance pattern of the disease

and declined ART using donor sperms. The second couple refused assisted reproduction citing financial restraints.

Discussions

MD is a multisystem disease with an autosomal dominant inheritance. The underlying defect is an unstable repeat expansion of CTG in the 3'-untranslated region of dystrophin myotonia protein kinase gene (DMPK) (MD type 1) and CCHC-type zinc finger, nucleic acid-binding protein gene (CNBP) (MD type 2). MD type 1, which accounts for 98 % of cases, is associated with more severe clinical manifestations. The numbers of trinucleotide repeats vary normally from 5 to 35, above which the disease manifests. Genetic anticipation, defined as increased severity of phenotype in successive generations, is a distinctive finding of this disease. Muscle weakness is the predominant presenting feature in majority of patients with early involvement of distal limb and neck muscles including the sternocleidomastoids. Patients have a characteristic facial appearance, the so-called hatchet facies as noticed in our patients. The clinical presentations may include cardiac conduction defects, intellectual impairment, posterior subcapsular cataracts, insulin resistance and diabetes, type 2 pseudohypoparathyroidism, difficulty in swallowing, decreased gastrointestinal motility and testicular atrophy with impaired spermatogenesis. MD as a cause of male infertility, although well recognised, is rarely sought after in clinical practice. Primary hypogonadism, which occurs in approximately 80 % of young to middle-aged males, may not be evident till adulthood. Most of these men have isolated impairment of sperm production or function and atrophy with hyalinisation and fibrosis of the seminiferous tubules is observed on testicular biopsy [2]. Moreover, capacitation and acrosome reaction in the spermatozoa may be defective and may account for infertility in MD patients with relatively higher sperm counts [3]. Approximately 20–40 % of men with MD have variable degree of testosterone deficiency. Both of our patients had oligospermia, and one of them had low early morning serum testosterone. Poor secondary sexual characteristics, low muscle mass and diminished bone mineral density may also be found. Serum gonadotropins are high with disproportionate elevation of FSH compared to LH levels, which was also evident in our patients. Elevated FSH levels alter estradiol-to-testosterone ratio and may cause gynaecomastia. Several studies have reported oligospermia and azoospermia in patients with myotonic dystrophy type 1

[2]. An association of larger CTG repeat alleles (in DMPK gene) with idiopathic azoospermia has been variably observed [4]. In congenital form of the disease, larger trinucleotide repeats are observed with increased disease severity.

Presently testicular sperm extraction (TESE) or testicular sperm aspiration (TESA) or microsurgical epididymal sperm aspiration (MESA) with subsequent intra cytoplasmic sperm injection (ICSI) has become a successful ART for male factor infertility due to wide variety of spermatogenetic disorders, precise diagnosis of the underlying disorder and prior genetic counselling is of utmost importance to avoid transmission of such heritable diseases among the offspring.

Acknowledgments The study was not funded by anybody. The patients themselves bore the cost of suggested investigations.

Author Contributions PPC, SNB, SP, GS were involved in evaluation and management of both patients. PPC, SNB and SP were involved in the literature search and writing the manuscript. GS checked and finalised the manuscript.

Compliance with Ethical Standards

Conflict of interest Disclosure of potential conflicts of interest if any: none. All the authors (PPC, SNB, SP, GS) declare that they have no conflict of interest.

Ethical Approval This article contains case report only. The patients were evaluated according to their presentations. They were not included in any study protocol by any of the authors. The institute approves publication of case series.

Informed Consent Informed consents were obtained from all individual patients.

References

1. World Health Organization. World health organization laboratory manual for the evaluation and processing of human semen. 5th ed. Cambridge: Cambridge University Press; 2010.
2. Vasquez JA, Pinies JA, Martul P, et al. Hypothalamic-pituitary-testicular function in 70 patients with myotonic dystrophy. *J Endocrinol Invest.* 1996;13:375–9.
3. Hortas ML, Castilla JA, Gil MT, et al. Decreased sperm function of patients with myotonic muscular dystrophy. *Hum Reprod.* 2000;15(2):445–8.
4. Pan H, Li YY, Li TC, et al. Increased (CTG/CAG)(n) lengths in myotonic dystrophy type 1 and Machado-Joseph disease genes in idiopathic azoospermia patients. *Hum Reprod.* 2002;17:1578–83.