JOMH
Journal of Men's Health

J. Mens. Health **2022**; 18(3): 058
http://doi.org/10.31083/jomh.2021.114

Case Report

Retrograde ejaculation as an initial presenting symptom of type 2 diabetes mellitus: a case report and literature review

Yu-Shan Mao[1,*], Ning-Jun Fang[2], Zhi-Ren Sheng[1], Yi-Feng Mai[1]

[1]Department of Endocrinology, the Affiliated Hospital of Medical School, Ningbo University, 315020 Ningbo, Zhejiang, China
[2]Department of Urology, the Affiliated Hospital of Medical School, Ningbo University, 315020 Ningbo, Zhejiang, China
*Correspondence: maoyushan@nbu.edu.cn (Yu-Shan Mao)
Submitted: 13 July 2021 Accepted: 25 August 2021 Available online: 10 September 2021 Published: 28 February 2022

Abstract

Retrograde ejaculation (RE), known as one of the late complications of diabetes mellitus, is rarely a presenting symptom in the diagnosis of diabetes. A 30-year-old male presented with a progressive decline in ejaculate over 2-month. Lab results revealed a high random blood glucose level (425 mg/dL). A substantial number of sperm were found in the post-ejaculate urine specimens, confirming a diagnosis of RE. Further lab tests revealed an hemoglobin-A1c (HbA1c) of 12.7%, with negative results for antibodies to glutamic acid decarboxylase, insulin antigen-2, insulin receptor and islet cell, consistent with a diagnosis of type 2 diabetes mellitus (T2DM). Insulin glargine and oral anti-hyperglycemic agents were initiated. Also, imipramine and pseudoephedrine were prescribed for 4-week and then discontinued, as no positive effect on ejaculation was seen. At the 36-month follow-up, the patient had a normal glucose level with HbA1c <6.5%. However, RE persisted. RE is commonly seen as a late-stage complication among T2DM. We presented a rare case where RE was the first referred symptom of T2DM and RE persisted even after adequate control of glycemia.

Keywords: Retrograde ejaculation; Type 2 diabetes mellitus; Complication; Case report

1. Introduction

Retrograde ejaculation (RE) is defined as misdirected propulsion of semen from the posterior urethra into the bladder after orgasm. The improper ejaculation is associated with dysfunctional contraction of the internal vesicle sphincter, the muscle that seals off the bladder during ejaculation and forces semen to exit through the urethral [1]. The diagnosis of RE is confirmed by the detection of substantial number of sperm in the urine after ejaculation. Long-standing diabetes mellitus (DM) can cause extensive autonomic neuropathy, which could result in RE that is typically a late-onset complication of type 2 diabetes mellitus (T2DM). We reported a rare case where RE was seen as the initial presenting symptom of T2DM.

2. Case presentation

A 30-year-old male presented to our outpatient clinic with a progressive decline in ejaculation volume for more than 2-month, followed by a complete absence of ejaculation emission over 3-week. The patient had a normal sensation of orgasm and no indication of erectile dysfunction or decrease in libido. He had a 2-year history of primary hypertension but was well-controlled by treatment with valsartan/amlodipine 80/5 mg single-pill combination daily. No prior history of tobacco or alcohol use, hematuria, outlet obstruction symptoms or urinary tract infections was noted. Lab tests revealed that his random blood glucose level was 425 mg/dL, and therefore he was admitted on the same day. The patient has a family history of hypertension and diabetes mellitus.

His physical examination and laboratory results at admission were shown in Table 1. Of note, his fasting plasma glucose level was 331 mg/dL, and his hemoglobin-A1c (HbA1c) level was 12.6%. Given the rapid onset of hyperglycemia and a negative ketone urine test, autoimmune pathology testing was done, which returned negative results for glutamic acid decarboxylase (GAD) antibodies, insulin antigen-2 (IA2) antibodies, insulin receptor antibodies and islet cell antibodies, confirming a diagnosis of T2DM. The semen analysis indicated a total absence of ejaculate, but a substantial number of sperm were found in the post-ejaculate urine specimens, which were collected following masturbation, and therefore confirmed a diagnosis of RE. A comprehensive eye exam was performed to exclude diabetic retinopathy and the patient had a normal urinary albumin/creatinine ratio at diagnosis. A written informed consent was obtained from the patient. Formal ethics approval was waived, because this is a case report.

The patient was initially treated for T2DM with a basal regiment of insulin glargine combined with oral anti-hyperglycemic agents (metformin and acarbose) for T2DM during his hospital stay. At discharge from 1-week hospitalization, insulin glargine was discontinued and acarbose was replaced with sitagliptin due to the gastrointestinal side effects of acarbose reported by the patient. After discussion with the multidisciplinary team and the patient, imipramine 25 mg and pseudoephedrine 120 mg twice daily were prescribed for 4-week for the treatment of RE. However, no positive treatment effect on ejaculation was observed and therefore imipramine and pseudoephedrine were discontinued.

Table 1. Physical examination and clinical laboratory results at admission.

Parameter	Value	Reference range
Height (cm)	186	
Weight (kg)	100	
BMI (kg/m^2)	28.9	
Waist circumference (cm)	101	
Systolic blood pressure (mmHg)	135	
Diastolic blood pressure (mmHg)	82	
Post-ejaculatory urine microscopy	Spermatozoa present	
Fasting serum glucose (mg/dL)	331	70–110
2-hr postprandial serum glucose (mg/dL)	481	70–140
HbA1c (%)	12.6	4.0–6.0
Fasting insulin (pmol/L)	68.8	18.1–173.4
2-hr postprandial insulin (pmol/L)	249.5	182.5–629.5
Fasting C-peptide (nmol/L)	0.42	0.26–0.63
2-hr postprandial C-peptide (nmol/L)	1.33	1.33–2.50
GAD antibodies	Negative	
IA-2 antibodies	Negative	
Insulinreceptor antibodies	Negative	
Islet cell antibodies	Negative	
Creatinine (μmol/L)	59.5	58.3–106.0
Uric acid (μmol/L)	368.0	208.0–428.0
Alanine aminotransferase (U/L)	23.0	9.0–50.0
Aspartate aminotransferase (U/L)	14.0	15.0–40.0
Triglyceride (mmol/L)	4.90	0.30–1.70
TC (mmol/L)	5.61	2.70–5.20
LDL-C (mmol/L)	3.19	1.00–3.12
HDL-C (mmol/L)	0.88	1.16–1.42
White-cell count (10^9/L)	4.5	3.5–9.5
Red-cell count (10^{12}/L)	5.17	4.30–5.80
Hemoglobin (g/L)	149.0	130.0–175.0
Platelet count (10^9/L)	179	125–350
Luteinizing hormone (IU/L)	5.0	1.24–8.62
Follicle stimulating hormone (IU/L)	3.24	1.21–19.26
Prolactin (mIU/L)	180.87	56.00–274.80
Total testosterone (nmol/L)	13.23	6.07–27.10
Progesterone (nmol/L)	1.09	0.32–2.67
Estradiol (pmol/L)	166.67	73.4–172.49
Urine tests		
Glucose	4+	
Protein	Negative	
Blood	Negative	
Ketone	Negative	
Albumin/creatinine ratio (mg/g)	22	$<$30

BMI, body mass index; MRI, magnetic resonance imaging; GAD, glutamic acid decarboxylase; IA2, insulin antigen-2; TC, total cholesterol; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol.

The patient was seen at 1-month after discharge and was followed every 3-month since then. During each follow up visit, the patient maintained normal glucose levels with HbA1c <6.5%, but had no improvement in RE. At 36-month follow up, RE persisted even after glycemic status was well-controlled.

3. Discussion

The normal ejaculation process depends upon the anatomical and functional integrity of the urinary bladder neck and posterior urethra. However, in patients with RE, the neck of the bladder does not close in the expulsion phase, so, as a result, the semen flows into the bladder instead of being ejaculated from the external urethral meatus. RE can manifest itself in varying degrees, ranging from decreases in ejaculated semen to a complete absence. In the latter case, a dry ejaculation followed by cloudy urine when voiding has been observed [1].

The causes of RE are multifactorial, including a variety of disease conditions and pharmaceuticals. DM is one of the most common causes of autonomic neuropathy [2,3], which is associated with genitourinary tract disturbances including bladder and/or sexual dysfunction [4]. In a case-control study, the liquid profilometric technique was used to examine 3 groups of men: 8 diabetic patients with RE; 5 patients with DM without ejaculatory disorders; and 7 healthy subjects. Only the group of diabetic patients with RE had no elevation of intraureteral pressure in the area of the inner sphincter of the urinary bladder, which evidenced its atony [5]. This phenomenon revealed sympathic nervous dysfunction may impair bladder neck closure during ejaculation that results in RE.

Although RE has a strong association with diabetes, the true prevalence of RE in diabetics is unknown. In a prospective case-control study comparing diabetic men with matched controls according to RE and erectile dysfunction, RE was observed in 34.6% of diabetic men aged between 35 and 55 years, whereas none of the controls exhibited RE ($P < 0.01$) [2]. Meanwhile, other studies of young male diabetics have estimated RE to be present in only 6% of patients [6]. Furthermore, there are no studies comparing the rates of RE in Type 1 vs Type 2 diabetes mellitus.

RE is an uncommon presenting symptom of T2DM. The mean duration of DM was longer for DM patients with RE compared with DM patients without RE (20 years vs 13 years), which indicated that RE due to diabetic autonomic neuropathy tends to be a late-onset complication [2]. Kam J *et al.* [7] have presented a case report which described a 19-year-old male with RE being the primary presenting symptom of T1DM. To our knowledge, this is the first case report of RE as an initial presentation of T2DM.

Medical treatment of RE in T2DM is based on either increasing the sympathetic tone of the bladder or decreasing the parasympathetic activity. A study that consisted of 33 diabetic men with RE has examined different therapeutic approaches, including imipramine 25 mg twice/day, pseudoephedrine 120 mg twice/day, or combination of the two drugs, which resulted in 38.5%, 47.8% and 61.5% success rates, respectively [8]. It is also worth noting that in the previous case report of a patient with T1DM, correction of RE was achieved after adequate glycemic control [7]. In contrast, correction of RE was not observed in this patient with T2DM. Future studies are needed in order to have a better understanding of the factors associated with treatment efficacy of RE in T2DM.

4. Conclusions

To the best of our knowledge, we report a rare case where RE is an initial presenting symptom in a newly diagnosed type 2 diabetic patient. While previous studies have shown that RE tends to be a late-onset complication in diabetic men, the early onset of RE is difficult to explain in the context of diabetes mellitus. Our case has shed light upon the importance of screening for diabetes in patients presenting with RE in order to achieve a proper treatment for both T2DM and associated RE.

Abbreviations

BMI, body mass index; GAD, glutamic acid decarboxylase; HDL-C, high density lipoprotein cholesterol; IA2, insulin antigen-2; LDL-C, low density lipoprotein cholesterol; MRI, magnetic resonance imaging; RE, retrograde ejaculation; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; TC, total cholesterol.

Author contributions

Conception and design—YSM. Administrative support—ZRS and YFM. Collection of materials of patients—NJF and YSM. Collection of literatures—YFM and YSM. Manuscript writing—YSM and ZRS. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This case report was conducted in accordance with the Declaration of Helsinki. Informed written consent was obtained from the patient for publication of this report.

Acknowledgment

The authors thank Jingyan Yang, Institute for Social and Economic Research and Policy (ISERP), Columbia University, New York, for the English-editing. Thanks to all the peer reviewers for their opinions and suggestions.

Funding

This work was supported by the Natural Science Foundation in Ningbo, China (No. 2018A610248), Grant of Zhejiang Medicine and Health Technology Project, China

(No. 2018ZH029, 2020KY871), the Major Project for Science & Technology Innovation 2025 in Ningbo, China (No. 2019B10035), and Grant of Ningbo Social Development, China (No. 2019C50080).

Conflict of interest

The authors declare no conflict of interest.

References

[1] Parnham A, Serefoglu EC. Retrograde ejaculation, painful ejaculation and hematospermia. Translational Andrology and Urology. 2016; 5: 592–601.

[2] Fedder J, Kaspersen MD, Brandslund I, Højgaard A. Retrograde ejaculation and sexual dysfunction in men with diabetes mellitus: a prospective, controlled study. Andrology. 2013; 1: 602–606.

[3] Verrotti A, Prezioso G, Scattoni R, Chiarelli F. Autonomic neuropathy in diabetes mellitus. Frontiers in Endocrinology. 2014; 5: 205.

[4] Mostafa T, Abdel-Hamid IA. Ejaculatory dysfunction in men with diabetes mellitus. World Journal of Diabetes. 2021; 12: 954–974.

[5] Ibragimov AZ, Aliev TA, AbdullaevKI, Mirza-Zade VA. The function of the closure apparatus of the bladder in retrograde ejaculation in diabetics. Urologiia i Nefrologiia. 1990; 3: 65–68.

[6] Gaunay G, Nagler HM, Stember DS. Reproductive Sequelae of Diabetes in Male Patients. Endocrinology and Metabolism Clinics of North America. 2013; 42: 899–914.

[7] Kam J, Tsang VH, Chalasani V. Retrograde Ejaculation: a Rare Presenting Symptom of Type 1 Diabetes Mellitus. Urology Case Reports. 2016; 10: 9–10.

[8] Arafa M, El Tabie O. Medical Treatment of Retrograde Ejaculation in Diabetic Patients: a Hope for Spontaneous Pregnancy. The Journal of Sexual Medicine. 2008; 5: 194–198.