

# Normal Male Reproductive Hormones And Sperm Parameters In Adult-Onset Still's Disease- A Case Report And Literature Review

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**Abstract:** Adult-onset Still's disease (AOSD) is an uncommon systemic auto-inflammatory disease. It can affect multiple body organs. Herein, we report the reproductive hormone and semen profiles in a male with AOSD. A 23-year-old male with already diagnosed and controlled AOSD requested a premarital check-up on his fertility potential. He was kept on a maintenance treatment protocol for the disease including prednisolone, methotrexate, folic acid, and vitamin D3. His reproductive hormones and semen profiles were found normal. The questionable enhancing effects of the different elements of the treatment protocol on the tested reproductive indices were discussed and refuted. To the best of our knowledge, this is the first case report describing the impact of AOSD on male fertility potential which was not deleterious in the reported case.

**Keywords:** Still's disease, semen, reproduction

## Introduction

Adult-onset Still's disease (AOSD) is a rare systemic auto-inflammatory disease with idiopathic etiology. The commonest manifestations of the disease are poly-arthritis, hectic fever, usually at night, and transient salmon-pink rash. The disease can affect various body organs. Some common features may include lymphadenopathy, leukocytosis, and sore throat. Its direct diagnosis is difficult due to the presence of many non-characteristic signs and symptoms as well as the lack of pathognomonic laboratory markers. Therefore, it is usually diagnosed after exclusion of other diseases with similar manifestations like malignancies, infections and other rheumatologic disorders<sup>1,2</sup> Epidemiological reports on AOSD are very limited. Its incidence in the general population has been registered to reach 0.16–0.4 per 100.000.<sup>2</sup> About 70% of the patients with this disease are females.<sup>1</sup> The most familiar medications used successfully to ameliorate the disease complaints and prevent its complications are corticosteroids and methotrexate.<sup>2</sup>

A literature review showed many clinical studies investigating the impact of the disease on many body systems and physiological functions.<sup>1,2</sup> In addition, a significant number of case reports have shown the conjoined existence of the disease with a huge number of exceptional pathologies.<sup>3</sup> However, nothing was found in the literature about the impact of the disease on the male fertility potential and reproductive hormones, although the median age of the disease has been reported to be around 36 years,<sup>2</sup> an age within the golden years to establishing a

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family. This motivated us to describe the sperm parameters and reproductive hormonal profile of a man with AOSD.

## Case Report

A 23-year-old Caucasian male teacher presented to the Andrology Clinic, Alexandria University Hospital, Alexandria, Egypt for a pre-marital check-up on his reproductive potential. He was 116 kg body weight, 172 cm length, and 39.2 body mass index. He was a non-smoker and with no history of the intake of recreational drugs. He was practicing masturbation on regular basis and denied any sexual partnership. He had no history of scrotal trauma or testicular pain. Male secondary sexual characters were intact. Scrotal examination showed normally placed testes in the scrotum with normal configuration of both epididymides and vasa deferentia. Testicular volumes were equal on either side, 15 cc, as detected by Prader orchidometer. No clinically detectable varicocele or hydrocele was existent. However, a deep exploration of the medical history indicated the past existence of AOSD for 30 months, based on the major diagnostic criteria of Yamaguchi<sup>1</sup> which included spiking fever (39°C), skin rash, arthralgia >2 weeks and neutrophilic leukocytosis. Prednisolone (12.5 mg/d), methotrexate (MXT) (10 mg/w), folic acid (5 mg/w), and vitamin D3 (25-Hydroxy Cholecalciferol) (5000 IU/d) were given during the early days of the disease and kept until the moment. The patient at the current presentation was symptom-free. His lipid profile, fasting and post-prandial blood sugars, glycosylated hemoglobin (HbA1c), liver enzymes, renal function, blood proteins, serum ferritin (4580 then 77.47 ng/mL - N:17.9–464 ng/mL), C-reactive protein (24 mg/L then negative - Negative <5 mg/L), anti-streptolysin O (ASO) titer (200 IU/L then negative - Negative <200 IU/L), erythrocyte sedimentation rate (ESR) (80 then 20 mm/h - N: 0–15 mm/h) and WBC (13.3 then 7 K/mL - N: 4–11 K/mL) were within normal ranges. Vitamin D3 was 38.3ng/mL (Sufficiency: 30–100 ng/mL). Abdominal ultrasonography was irrelevant. No history of intake of any medications was given like non-steroidal anti-inflammatory or salicylates for joint pains during the early days of the disease.

Male reproductive hormones, testosterone (T), luteinizing hormone (LH), follicle-stimulating hormone (FSH), and prolactin (PRL) were ordered. The patient gave a peripheral venous blood sample at 9:00 AM. The hormonal assay was expedited using an automated analyzer (Cobas e411, Roche Diagnostics, Mannheim, Germany). The results showed normal levels of all requested hormones [T: 2.75 ng/mL

(N: 2.49–8.36 ng/mL), LH: 4.19 mIU/mL (N: 2.4–12.6 mIU/mL), FSH: 4.7 mIU/mL (N: 3.5–12.5 mIU/mL), and PRL: 288.7 mIU/mL (N: 86–324 mIU/mL)]. Semen analysis was also requested after abstinence for 3 days and the sample was retrieved by masturbation in the laboratory. The analysis was repeated three times. At the first time, the analysis was done manually. The data showed normal semen parameters where the volume was 5cc (N: >1.5 cc), pH was 8 (N: 7.2–8), liquefaction happened after 30 mins (N: within 60 mins), viscosity was normal, white blood cells 3-5/HPF (N: 0-5/HPF), sperm count was 31 M/cc (N: ≥20M/cc), total sperm per ejaculate was 155 M (N: ≥39/ejaculate), motility was (rapid progression: 25%, N: ≥25%, total motility: 60%, N: ≥50%), and normal forms were 63% (N: ≥30%). Seven months later, the second semen analysis was done followed by the third check-up with 3 weeks interval in between. These two assessments were expedited using computer-assisted analysis (Mira 9000 sperm analyzer, Mira Laboratory, Cairo, Egypt) as based on WHO criteria.<sup>4</sup> The semen parameters of these two analyses showed normal values. The averages of these values were as follows: volume (3.9cc), pH (7.8), count (34.16 M/cc), normal forms (5.68%) and white blood cells (0-2/HPF). Both liquefaction and viscosity in these last two tests were normal. Regarding motility, the second semen analysis revealed normal forward progression (51.88%), total motility (69.12%) and total motile spermatozoa (156.41/ejaculate). In the third semen analysis, motility could not be assessed as the patient was away from the automated semen machine. An aliquot of semen was taken, kept refrigerated and sent by express mail in association with fixed semen smears to assess the other semen parameters.

## Ethical Considerations

A written informed consent was obtained from the patient for publication of this case report.

## Discussion

AOSD is not a common disease. Information about the epidemiology of AOSD is lacking in many areas in around the globe.<sup>2</sup> The provisional diagnosis of AOSD comes after exclusion from the other medical disorders which have the similar non-specific clinical picture.<sup>1,2</sup> Then, the diagnosis can be reinforced by laboratory testing for the existence of hyperferritinemia.<sup>2</sup>

In this report, we have described the reproductive hormones and semen profiles in a young man with already diagnosed adult-onset Still's disease. To the best of our

knowledge, this is the first case study which reports these male reproductive potentials in such disease. The literature review, irrespective of language, did not show any study or even case report describing any data about the fertility status of men with AOSD.

In this case report, there were normal male reproductive hormone (T, LH, FSH & PRL) and semen profiles. Although the patient was under a multi-medication treatment regimen, however, we think that AOSD activity per se has no deleterious impact on the male reproductive hormone and sperm profiles. There were important data in the patient to support this suggestion. First, the patient was kept on MXT, as the sole cytotoxic drug, in a small dose (10 mg/w). MXT in low doses (<0.4 mg/kg/w), not in combination with other cytotoxic medications, does not affect the quality of sperm or testosterone level,<sup>5</sup> particularly in absence of the risk factors which potentiate its toxicity like renal insufficiency, hypoalbuminemia, concurrent use of drugs known to interact with MTX.<sup>6</sup> These latter risks were not existent in our patient whose kidney function and blood proteins were normal. In addition, the patient denied the intake of medications which may potentiate TXT toxicity like salicylates.<sup>6</sup> Second, the patient received folic acid in small dose (5 mg/w). Folic acid alone, particularly in small doses, has an effect not different from placebo on sperm parameters and testosterone.<sup>7</sup> Third, the patient received prednisolone (12.5 mg/d). Other studies which used similar doses like our patient reported no change in testosterone<sup>8</sup> or spermogram.<sup>9</sup> Fourth, the patient was given vitamin D3 in reasonable dosing (5000 IU/d). Vitamin D3 supplementation, even in high doses (30.000 IU initially and then maintained on 1200 IU/d for 5 months) was not associated with any significant enhancement of sperm parameters or alteration in male reproductive hormones (T, FSH & LH).<sup>10</sup> Fifth, the increased ferritin, in the reported patient, was not associated with iron overload as the cause was not related to repeated blood transfusion or iron supplementation intake.<sup>11</sup> Therefore, no deposition of iron in the pituitary gland to cause secondary hypogonadism or in the testis to trigger primary hypogonadism occurred.<sup>12</sup> As a result, the patient presented with normal testosterone and pituitary-released hormones.

Rheumatic diseases have diverse pathogenic mechanisms to affect male fertility. The literature showed that some rheumatic diseases like systemic lupus, dermatomyositis and rheumatoid arthritis have negative impacts on male fertility affecting both sperm and reproductive hormones due to the disease activity itself and the treating alkylating medications.<sup>13</sup> Other diseases like Behcet disease and ankylosing spondylitis

have been demonstrated not to have deleterious effects on male fertility<sup>13</sup> like our patient with AOSD in this case report.

## Conclusion

AOSD may not have a negative impact on male reproductive hormone and semen profiles.

## Author Contributions

All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

## Disclosure

The authors report no conflicts of interest in this work. This study has received no financial support.

## References

1. Yamaguchi M, Ohta A, Tsunematsu T, et al. Preliminary criteria for classification of adult still's disease. *J Rheumatol*. 1992;19:424–430.
2. Gerfaud-Valentin M, Jamilloux Y, Iwaz J, Sève P. Adult-onset still's disease. *Autoimmun Rev*. 2014;13:708–722. doi:10.1016/j.autrev.2014.01.058
3. Yilmaz S, Karakas A, Cinar M, et al. Adult onset still's disease as a paraneoplastic syndrome—a case report and review of the literature. *Bull Hosp Jt Dis*. 2013;71:156–160.
4. World Health Organization. *WHO Laboratory Manual for the Examination of the Human Semen and Sperm-Cervical Mucus Interaction*. Cambridge: Cambridge University Press; 2010.
5. Pectasides D, Pectasides E, Papaxoinis G, et al. Testicular function in poor-risk nonseminomatous germ cell tumors treated with methotrexate, paclitaxel, ifosfamide, and cisplatin combination chemotherapy. *J Androl*. 2009;30:280–286. doi:10.2164/jandrol.108.006437
6. Kivity S, Zafirir Y, Loebstein R, Puzner R, Mouallem M, Mayan H. Clinical characteristics and risk factors for low dose methotrexate toxicity: a cohort of 28 patients. *Autoimmun Rev*. 2014;13:1109–1113. doi:10.1016/j.autrev.2014.08.027
7. Irani M, Amirian M, Sadeghi R, Lez JL, Latifnejad Roudsari R. The effect of folate and folate plus zinc supplementation on endocrine parameters and sperm characteristics in sub-fertile men: a systematic review and meta-analysis. *Urol J*. 2017;14:4069–4078.
8. Mateo L, Nolla JM, Bonnin MR, Navarro MA, Roig-Escofet D. Sex hormone status and bone mineral density in men with rheumatoid arthritis. *J Rheumatol*. 1995;22:1455–1460.
9. Mancini RE, Lavieri JC, Muller F, Andrada JA, Saraceni DJ. Effect of prednisolone upon normal and pathologic human spermatogenesis. *Fertil Steril*. 1966;17:500–513. doi:10.1016/s0015-0282(16)36008-3
10. Blomberg Jensen M, Lawaetz JG, Petersen JH, Juul A, Jørgensen N. Effects of vitamin D supplementation on semen quality, reproductive hormones, and live birth rate: a randomized clinical trial. *J Clin Endocrinol Metab*. 2018;103:870–881. doi:10.1210/jc.2017-01656
11. Koperdanova M, Cullis JO. Interpreting raised serum ferritin levels. *Br Med J*. 2015;351:h3692. doi:10.1136/bmj.h3692
12. Pelusi C, Gasparini DI, Bianchi N, Pasquali R. Endocrine dysfunction in hereditary hemochromatosis. *J Endocrinol Invest*. 2016;39:837–847. doi:10.1007/s40618-016-0451-7
13. Tiseo BC, Cocuzza M, Bonfa E, Srougi M, Silva CA. Male fertility potential alteration in rheumatic diseases: a systematic review. *Int Braz J Urol*. 2016;42:11–21. doi:10.1590/S1677-5538.IBJU.2014.05.95

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