CASE REPORT

Testicular toxoplasmosis in a 26-year-old immunocompetent man

Vincent Wong,¹ Channa Amarasekera,² Shilajit Kundu²

¹Department of Urology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

²McGaw Medical Center of Northwestern University, Chicago, Illinois, USA

Correspondence to
Dr Channa Amarasekera,
channa.amarasekera@northwestern.edu

Accepted 12 May 2018

SUMMARY

Testicular toxoplasmosis is a very rare presentation of *Toxoplasma gondii*. A 26-year-old immunocompetent man presented to us with right testicular pain and a right epididymal mass. Ultrasound was concerning for malignancy and a radical orchiectomy was performed. Surgical pathology revealed chronic granulomatous inflammation which stained positive for *T. gondii*.

BACKGROUND

Toxoplasma gondii is a protozoon that can infect a wide range of birds and animals. It is highly prevalent in humans, with 25%–30% of the world's population estimated to be infected.¹ There are multiple methods of transmission, with the most common being consumption of cysts in undercooked meat, faecal-oral transmission of oocytes in faeces of infected animals such as cats and congenital transplacental transfer. *T. gondii* infection is typically asymptomatic, but can be symptomatic in congenitally infected infants, immunosuppressed patients and occasionally in immunocompetent patients. In the rare instances of symptomatic infection in immunocompetent persons, it presents as an acute systemic infection that is benign and self-limited. Patients often experience mild fever, chills, sweats and bilateral, symmetrical non-tender cervical lymphadenopathy. In immunocompromised patients, symptoms are mainly neurological, with patients presenting with encephalitis and ring-enhancing lesions on brain MRI. Toxoplasmosis can also have extracerebral manifestations, such as pulmonary toxoplasma as well as ocular toxoplasmosis which occurs in about 2% of cases of acquired toxoplasmosis.² Even more rare is testicular toxoplasmosis, which after an extensive literature search has been reported in only a few patients, all of whom were immunocompromised.^{3–6} We describe a case of testicular toxoplasmosis in an immunocompetent 26-year-old patient.

CASE PRESENTATION

A 26-year-old immunocompetent man with no past medical history presented with right testicular pain. On physical examination, there was a 1 cm area of fullness on the right epididymal head associated with mild diffuse epididymal tenderness.

INVESTIGATIONS

Testicular tumour markers alpha-fetoprotein, beta-human chorionic gonadotropin and lactate

dehydrogenase were within normal limits. Serological tests for HIV and syphilis were negative. Testicular ultrasound showed a focal area of hypoechogenicity with mild heterogeneity in the right testis and increased vascularity and enlargement of the right epididymis concerning for right epididymitis with focal orchitis versus an underlying malignancy. On follow-up 8 weeks later, the pain and the palpable epididymal mass had resolved with non-steroidal anti-inflammatory drugs but follow-up testicular ultrasound images showed new diffuse heterogeneous hypoechoic lesions in the right testis (figure 1). CT scan of the abdomen and pelvis did not show metastatic lesions or significant adenopathy.

DIFFERENTIAL DIAGNOSIS

Our differential diagnosis included:

- ▶ Primary versus secondary testicular malignancy.
- ▶ Lymphoma.
- ▶ Granulomatous or chronic orchitis.

TREATMENT

Due to concerns surrounding the risk of upstaging with testicular biopsy in the event of malignancy, the patient elected for a right radical orchiectomy from which he recovered well with minimal discomfort. Prior to orchiectomy, he had his sperm cryopreserved because he currently does not have children but may desire them in the future. Semen analysis did not show any abnormalities in sperm concentration, motility, number and morphology or in semen volume or pH. Pathology of the surgical specimen revealed necrotising and non-necrotising granulomas. Special stains for acid fast bacilli and Gomori Methenamine-Silver Nitrate were negative for mycobacteria and fungal organisms and Treponema staining was negative.

Postoperatively, the patient recalled developing cervical lymphadenopathy and oral ulcers several weeks after travelling to South America (where he had frequent cat exposure) 8 months prior to presenting to us. He was diagnosed with toxoplasmosis at the time and had not received treatment for his symptoms as he was immunocompetent. The cervical lymphadenopathy and oral ulcers resolved spontaneously. He noted being in his usual state of health in the intervening months between his toxoplasmosis diagnosis and the onset of right testicular pain which led to his current presentation. Given the new concern for testicular toxoplasmosis, infectious disease specialists were consulted, and

To cite: Wong V, Amarasekera C, Kundu S. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2018-224962

Figure 1 Right testicular ultrasound with and without Doppler.

a review of his surgical pathology with immunohistochemistry staining on testicular tissue using rabbit anti-*T. gondii* polyclonal antibodies with standard immunohistochemical techniques was performed. This revealed isolated cysts approximately 20 µm in diameter, confirming a diagnosis of testicular toxoplasmosis (figure 2). DNA detection of toxoplasma in the removed testes was not performed.

Serum Toxoplasma IgG and IgM antibodies were positive on ELISA, with no titres reported, while serum Toxoplasma DNA was not detected by PCR. Serological and urinary tests for fungi, tuberculosis, blastomycosis and Histoplasma were negative. The testicular ultrasound was re-reviewed and microlithiasis was noted in his left testicle. Due to concern for early toxoplasmosis of the left testicle, systemic toxoplasmosis treatment with pyrimethamine and sulfadiazine with leucovorin was started. His immune system was evaluated given this unusual presentation of toxoplasmosis and he was confirmed to be immunocompetent.

OUTCOME AND FOLLOW-UP

He has been in good health since his right orchiectomy and several repeat ultrasounds have revealed persistent microlithiasis of the left testis without further changes. Fertility of the patient was not evaluated after orchiectomy.

DISCUSSION

Toxoplasmosis is highly prevalent, infecting up to 30% of the world's population. It usually presents symptomatically in congenitally infected infants and immunocompromised patients, mainly affecting the neurological system. There have been

Figure 2 Testicular tissue at 600× magnification with Toxoplasma immunohistochemical staining with large red arrow indicating the Toxoplasma cyst and small blue arrow indicating bradyzoites inside the cyst.

studies suggesting that systemic *T. gondii* infection can reduce fertility in immunocompetent men, but how exactly this systemic *T. gondii* infection does so is not entirely understood. Studies in rat models have found that infection can lead to decreased luteinizing hormone levels and worsening of sperm parameters, including sperm count, motility, concentration and increased sperm abnormalities.^{7,8} According to two systemic reviews of protozoa infection and fertility, the mechanism for how this occurs is hypothesised to be due to changes in the hypothalamic-pituitary axis leading to secondary hypogonadism and subsequently decrease in sperm quality.^{9,10} Another systemic review on how *T. gondii* affects hormone levels found varying results, with some studies reporting increased testosterone with infection, while others found decreased testosterone, as compared with uninfected individuals.¹¹ The few studies of fertility in humans infected with *T. gondii* have also shown varying results. A cross-sectional, observational study of 60 immunocompetent men found no statistically significant difference in follicle stimulating hormone and testosterone levels or in sperm count, motility, morphology or ejaculate quantity.¹² On the other hand, a case control study of 100 sterile male patients in China found an increased association between sterile males and anti-*T. gondii* antibodies as compared with controls.¹³ At least for our patient, it appears that his fertility was not affected by the Toxoplasma infection given his normal semen parameters on semen analysis.

In regard to testicular toxoplasmosis, there have only been a few cases reported in the literature. These have all been in immunocompromised patients, either with AIDS or on immunosuppression after organ transplantation. The testicular toxoplasmosis was either asymptomatic and discovered on autopsy or was discovered after the patient presented with a tender testicular mass, similar to how our patient presented.³⁻⁶ Our case is unique in that it is the only reported case of testicular toxoplasmosis in an immunocompetent patient. In our patient, following findings of hypoechoic lesions on testicular ultrasound, high on the differential diagnosis were cancer or granulomatous infection.

A radical orchiectomy was performed. Even after surgical pathology revealed granulomatous inflammation, the aetiology remained unclear as the usual stains for mycobacteria, fungi and *Treponema* were negative. Only after the patient revealed his history of toxoplasmosis, which prompted a referral to infectious diseases specialists, was the diagnosis made.

Extensive literature review suggests this is a unique presentation of toxoplasmosis. There have been no previous case reports of testicular toxoplasmosis in an immunocompetent host.

Learning points

- ▶ This is a very rare presentation of toxoplasmosis.
- ▶ Previous cases of testicular toxoplasmosis have all been reported in immunocompromised hosts.
- ▶ This is the first case to show that immunocompetent men can also develop testicular toxoplasmosis, and a high index of suspicion is required to make the diagnosis.

Contributors VW made substantial contributions to the conception or design of the work and interpretation of data. CA contributed by revising the critically for important intellectual content. Final approval of the version published was made by SK. All authors are in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2018. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Montoya JG, Liesenfeld O. Toxoplasmosis. *The Lancet* 2004;363:1965–76.
- 2 Holland GN. Ocular toxoplasmosis: a global reassessment. Part I: epidemiology and course of disease. *Am J Ophthalmol* 2003;136:973–88.
- 3 Crider SR, Horstman WG, Massey GS. Toxoplasma orchitis: report of a case and a review of the literature. *Am J Med* 1988;85:421–4.
- 4 Hofmann A, Zaharatos G, Miller M. Case report and review of the literature: toxoplasma gondii encephalitis in a 40-year-old woman with common variable immunodeficiency and a new diagnosis of large granular lymphocytic leukemia. *Can J Infect Dis Med Microbiol* 2008;19:309–10.
- 5 Barreto F, Hering F, Dall'oglio MF, et al. [Testicular toxoplasmosis: a rare case of a testicular mass]. *Actas Urol Esp* 2008;32:666–8.
- 6 Nistal M, Santana A, Paniaqua R, et al. Testicular toxoplasmosis in two men with the acquired immunodeficiency syndrome (AIDS). *Arch Pathol Lab Med* 1986;110:744–6.
- 7 Dvorakova-Hortova K, Sidlova A, Ded L, et al. Toxoplasma gondii decreases the reproductive fitness in mice. *PLoS One* 2014;9:e96770.
- 8 Terpsidis KI, Papazahariadou MG, Taitzoglou IA, et al. Toxoplasma gondii: reproductive parameters in experimentally infected male rats. *Exp Parasitol* 2009;121:238–41.
- 9 Shiadeh MN, Niyyati M, Fallahi S, et al. Human parasitic protozoan infection to infertility: a systematic review. *Parasitol Res* 2016;115:469–77.
- 10 Martínez-García F, Regadera J, Mayer R, et al. Protozoan infections in the male genital tract. *J Urol* 1996;156:340–9.
- 11 Galván-Ramírez ML, Gutiérrez-Maldonado AF, Verduzco-Grijalva F, et al. The role of hormones on Toxoplasma gondii infection: a systematic review. *Front Microbiol* 2014;5.
- 12 Colosi HA, Jalali-Zadeh B, Colosi IA, et al. Influence of toxoplasma gondii infection on male fertility: a pilot study on immunocompetent human volunteers. *Iran J Parasitol* 2015;10:402–9.
- 13 Qi R, Su XP, Gao XL, et al. [Toxoplasma infection in males with sterility in Shenyang, China]. *Zhonghua Nan Ke Xue* 2005;11:503–4.

Copyright 2018 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow