Case report

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Hormone disbalance in patient with hypogonadism and cranial base toxoplasmosis

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Toxoplasmosis represents a globally prevalent infection caused by the protozoan parasite Toxoplasma gondii (T. gondii), and it is known as an adaptable and widespread parasitic organism. This report examines alterations in endocrine function in a patient with T. gondii infection. A 45-year-old man was examined by a neurosurgeon because of visual impairment and intermittent headaches, while the magnetic resonance imaging of the brain revealed an extracranial presentation of symmetrical subcentimeter cystic lesions in the skull base. There were no signs of intracranial involvement, nor in the sela turcica. Although our patient had secondary hypogonadism, with low both LH and FSH values, T. gondii did not lead to an increase in testosterone levels. This rare case of a patient with T. gondii infection and hypogonadism emphasizes the requirement for further research to better understand the pathophysiological mechanisms underlying the infection with this parasite.

Keywords: *toxoplasmosis, hypogonadism, skull base*

Prikaz slučaja

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Hormonski disbalans kod pacijenta sa hipogonadizmom i toksoplazmozom baze lobanje

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Toksoplazmoza predstavlja globalno rasprostranjenu infekciju koju izaziva parazit Toksoplazma gondii (T. gondii), prilagodljiv i široko rasprostranjen organizam. Ovaj prikaz slučaja ispituje promene u hormonskom disbalansu kod pacijenta sa infekcijom T. gondii. Muškarac star 45 godina sagledan je od strane neurohirurga zbog problema sa vidom i povremenih glavobolja, dok je magnetnom rezonancom mozga utvrđeno prisustvo ekstrakranijalnih simetričnih subsantimetarskih cističnih lezija u bazi lobanje. Nije bilo znakova intrakranijalnog zahvatanja, kao ni zahvatanje u selarnoj regiji. Iako je naš pacijent imao sekundarni hipogonadizam, sa niskim vrednostima i LH i FSH, T. gondii nije dovela do povećanja nivoa testosterona. Ovaj redak slučaj pacijenta sa infekcijom T. gondii i hipogonadizmom naglašava potrebu za daljim istraživanjem kako bi se bolje razumeli patofiziološki mehanizmi koji leže u osnovi infekcije ovim parazitom.

Ključne reči: toksoplazmoza, hipogonadizam, baza lobanje

Introduction

Toxoplasmosis represents a globally prevalent infection caused by the protozoan parasite Toxoplasma gondii (T. gondii), and it is known as an adaptable and widespread parasitic organism (1). This germ is able to infect people as but is more common in certain species, with rates above 50% in dogs, rabbits, along with sea otters, exceeding 60% in rodents as well as wild birds, in addition to rates as high as 70% in felines, bears, and deer (2, 3). Based on epidemiological assessments, it is highly likely that more than a third of all people worldwide have been exposed to the parasite (4). Hypogonadism in men involves reduced or absent secretion of sex hormones and impaired reproductive function of the testicles, and is divided into primary hypogonadism due to dysfunction of the gonadal tissue, or as central (secondary) hypogonadism (CH), due to dysfunction of the hypothalamic-pituitary axis. These patients have reduced serum testosterone levels, with variable levels of gonadotropins. Clinically, it can be manifested with infertility, reproductive dysfunction, bone density loss, reduced libido, emotional fluctuations and fatigue (5). Some new evidence suggests that infection with T. gondii might influence human behavior by affecting hormonal regulation, such as changing testosterone levels. This report examines alterations in endocrine function in a patient with T. gondii infection.

Case Report

A 45-year-old man was examined by a neurosurgeon because of visual impairment and intermittent headaches. Magnetic resonance imaging (MRI) of the pituitary gland confirmed the presence of a microadenoma in the left lateral aspect of the pituitary gland (Figure 1).

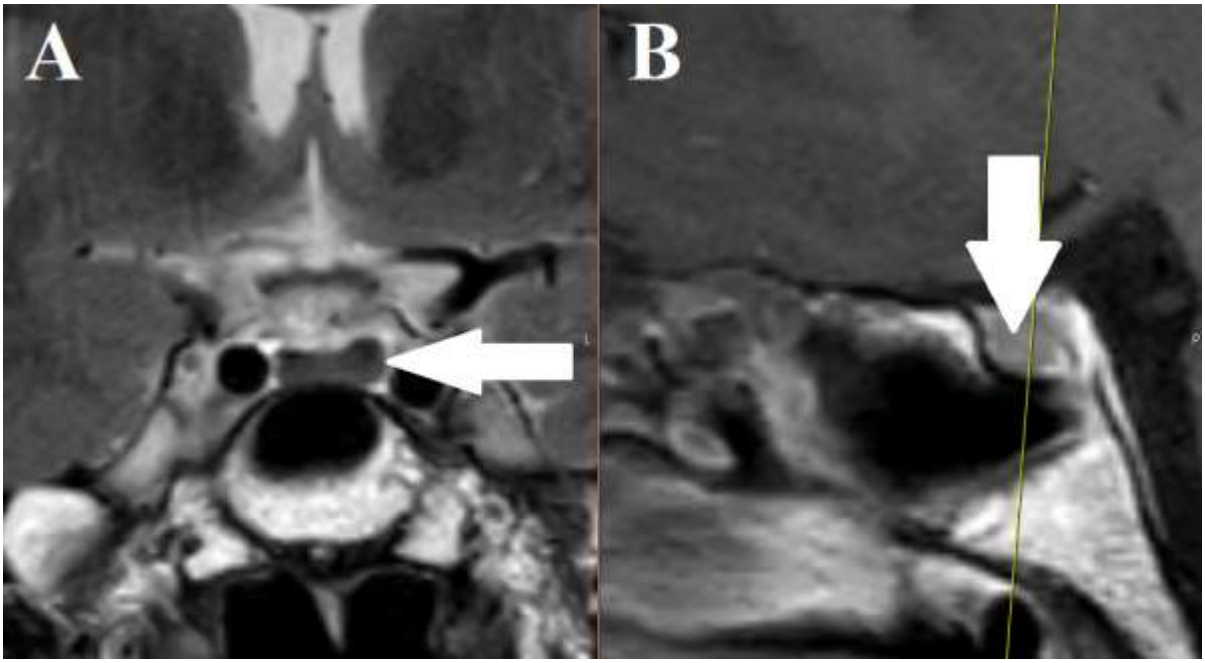

Figure 1 In the left lateral aspect of the adenohypophysis (A, B), an irregular T2W hyposignal mass (white arrows), measuring 3x5 mm, is observed, which lags behind in post-contrast enhancement and corresponds to a microadenoma

MRI of the brain revealed an extracranial presentation of symmetrical subcentimeter cystic lesions in both sphenoid bones retromaxillary, in the right medial and superior rectus muscles, as well as in both infratemporal fossae adjacent to the parotid glands (Figure 2, 3). There were no signs of intracranial involvement, nor in the sela turcica.

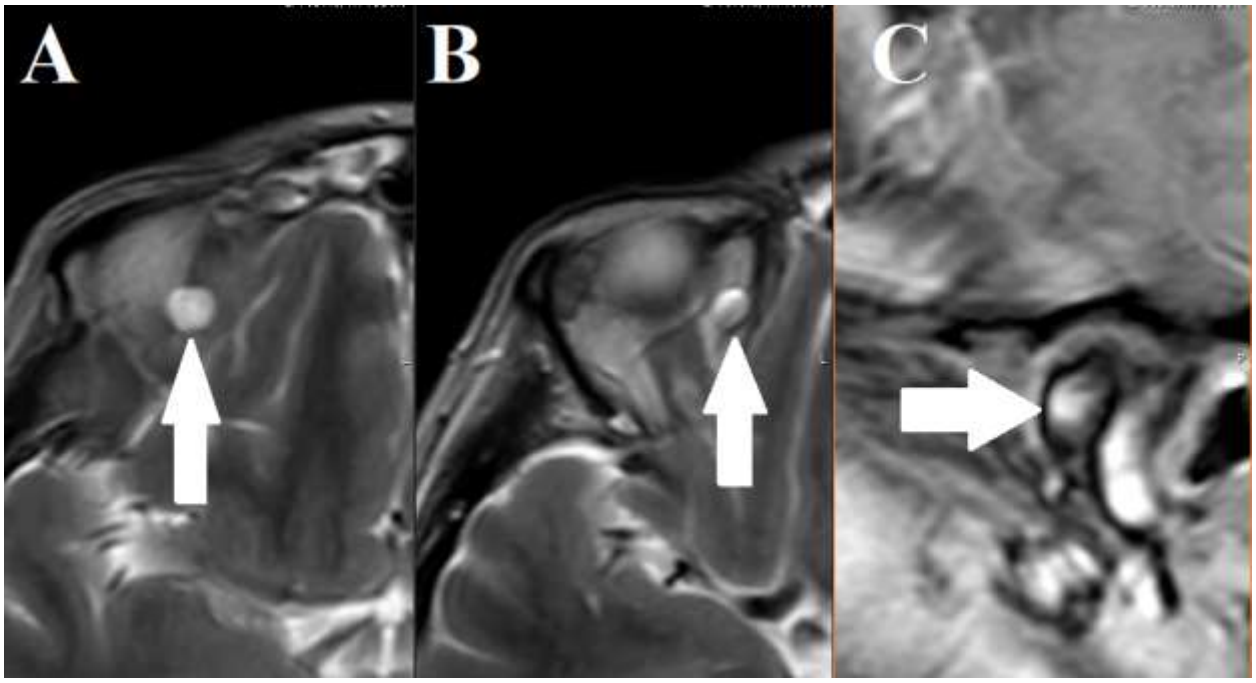

Figure 2 Multiple cystic changes localized along the superior (A) and internal (B) rectus muscles in the right orbit, as well as in the deep lobes of the left parotid gland (C), which are marked by the white arrows.

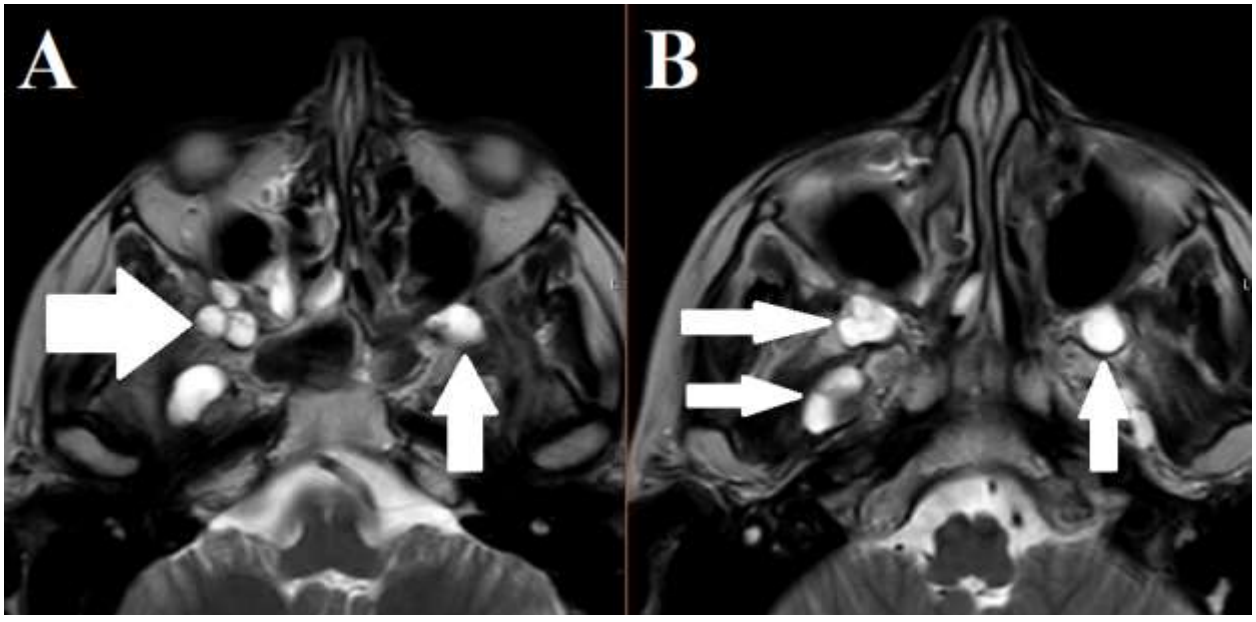

Figure 3 Multiple cystic lesions localized bilaterally retromaxillary (A, B), marked by the white arrows.

The physical appearance of the patent was specific. The patient exhibited a tall stature, a delicate physique, pale skin, and an absence of facial hair. Additionally, the patient had no children, nor previous marriages or long-lasting relationships. For the last 20 years, he has lived with several cats. A complete neurological exam exhibited normal findings.

Since the brain MRI showed no findings of surgical significance, so the patient was referred to infectious disease specialist. The Western Blot Toxoplasmosis IgG and IgM test was positive, so conservative treatment was started with albendazole (400mg twice per day, for seven days) and prednisone (20mg once a day) for four weeks. Additionally, gastroprotective agents, probiotics, and analgesic medication were prescribed. A follow-up examination was performed after a year, while control brain MRI demonstrated no progression of the disease.

Hormonal assessments were conducted with ELISA test, with the following results: growth hormone values were 3.40 ng/ml (reference values <2.47), S-oxytocin were 248.88 pg/ml (reference values 15.0-242), luteinizing hormone values were 0.2 IU/L (reference values 1.2-8.6), follicle stimulating hormone values were 0.4 IU/L (reference values 1.3-19.3), testosterone value was 2.9 nmol/l (reference values 9.9–27.8). The values of ACTH, FT4, TSH and prolactin were within the normal range. The patient was referred for further assessment and treatment by an endocrinologist because of the secondary hypogonadism.

The next follow-up examination was scheduled after 12 months, with a control brain MRI revealing no significant changes regarding the number and size of the cystic lesions as well as the size of microadenoma. Hormonal evaluations were carried out again using the ELISA test, yielding the following results: growth hormone values were 2.97 ng/ml (reference values <2.47), S-oxytocin were 165.1 pg/ml (reference values 15.0-242), luteinizing hormone values were 0.1 IU/L (reference values 1.2-8.6), follicle stimulating hormone values were 0.3 IU/L (reference values 1.3-19.3), testosterone value was 1.22 nmol/l

(reference values 9.9–27.8). The values of ACTH, FT4, TSH and prolactin were within the normal range. Conservative treatment by neurosurgery was continued with analgesic therapy when needed for occasional headaches.

Discussion

It has been estimated that circa 20–60% of Eastern European population is infected with T. gondii (6). The parasite is most commonly acquired through consumption of undercooked food containing cysts, contact with infected feline feces, or intrauterine transmission during pregnancy. In symptomatic patients, the most common symptoms are flu-like symptoms, headache, enlarged lymph nodes, fever, chills, malaise, and fatigue (7). In more severe cases, such as in immunocompromised patients and neonates, encephalitis, chorioretinitis, and mental retardation develop (8). Abortions and congenital anomalies are common. However, in most cases, T. gondii infection is asymptomatic, whereas latent toxoplasmosis can cause sex hormone imbalance and hypogonadism (9).

Furthermore, Toxoplasma gondii infection has been associated with various mental and psychological alterations in patients (10). It is known that the sexual reproduction of this parasite is linked to the cat as a host, and selective pressures have evolved for Toxoplasma to perfect mechanisms of transmission from the intermediate host (rodents) to the definitive host (feline host), thus completing its life cycle. The affinity of T. gondii for the central nervous system of the intermediate host has evolved to induce such manipulation (11). Additional studies have elaborated on these hypotheses, examining whether T. gondii affects the perception of risk of the cat's danger to the mouse (12, 13). An experimental study analyzed how rodents react to cat odors, as cat odor is known to induce a strong aversion, even in laboratory rodents after many generations. The results showed that uninfected rats clearly avoided areas with cat odor, while infected rats showed a pathological, potentially suicidal, attraction to areas marked with cat urine (14). Some authors (15) have indicated an increase in attraction between uninfected female and infected male rats, resulting in a higher number of matings between them, which is one of the confirmed modes of transmission of this parasite.

Other authors have studied the pathophysiology of behavioral changes in rats and have demonstrated a positive correlation between behavioral changes and the expression of genes involved in testosterone synthesis in experimentally infected male rats (16).

Behavioral alterations of infected patients may be preceded by encephalitis, with different predilection sites depending on the T. gondii strains (17). Some authors have analyzed the effects of T. gondii infection on libido and attractiveness in men and women, obtaining confirmatory results of increased libido and attractiveness in infected patients (18). Some of the results are that

infected patients had lower fluctuating facial asymmetry, while women with T. gondii infection had lower body mass index, a higher number of sexual partners, and higher levels of self-rated attractiveness compared to uninfected controls.

On the other hand, one study showed that both infected men and women were rated as attractive and healthy by uninfected individuals (17). One potential route of interhuman transmission of the infection could be unprotected sexual intercourse and oral sex (19). These hypotheses are supported by studies on the female sex workers (20) and individuals with a history of sexual promiscuity (21) in Latin America. On the other hand, seropositive men with T. gondii are significantly more promiscuous than uninfected men (21). Furthermore, T. gondii may play a role in the development of schizophrenia (10), depression, anxiety disorders, obsessive-compulsive disorder (OCD) (21), and autism spectrum disorder (ASD) (10, 22, 23, 24).

Numerous studies have shown a positive correlation between the presence of T. gondii and increased testosterone levels (9). Most human studies have shown increased testosterone levels after latent toxoplasmosis in men, while three studies have noted a decrease in levels, and two have not observed significant changes. This discrepancy in results could be explained by the incompletely understood pathophysiological mechanisms of T. gondii infection in humans, selectively stimulating libido and sexual activity to enhance its sexual transmission. Could secondary hypogonadism and low libido be influenced by the presence of T. gondii? As anticipated, our case report demonstrated that this was not the case. Although our patient had secondary (central) hypogonadism and pituitary microadenoma, with low both LH and FSH values, T. gondii did not lead to an increase in testosterone levels. The patient remained with identical appearance and sex hormone levels for a 2 year of follow-up. His serological findings showed the persistence of infection despite being given therapy, but no increase in testosterone levels was noted.

Additionally, lower testosterone levels in infected humans and animals may cause infertility and lower libido. A potential explanation could be that different strains and intensity of infection, detected by serological tests, PCR, and microscopic methods, play an important role in the variation in testosterone levels (25).

Conclusion

This rare case of a patient with T. gondii infection and hypogonadism emphasizes the requirement for further research to better understand the pathophysiological mechanisms underlying the infection with this parasite.

References

1. Boothroyd JC, Grigg ME. Population biology of Toxoplasma gondii and its relevance to human infection: do different strains cause different disease? Curr Opin Microbiol 2002;5:438-42. doi: 10.1016/s1369-5274(02)00349-1

2. Lafferty KD. Can the common brain parasite, Toxoplasma gondii, influence human culture? Proc R Soc B 2006;273:2749-55. doi: 10.1098/rspb.2006.3641

3. Webster JP. Prevalence and transmission of Toxoplasma gondii in wild brown rats, Rattus norvegicus. Parasitology 1994;108:407-11. doi: 10.1017/s0031182000075958

4. Tenter AM, Heckeroth AR, Weiss LM. *Toxoplasma gondii*: from animals to humans. Int J Parasitol 2000;30(12):1217-58. doi: 10.1016/S0020-7519(00)00124-7

5. Barber TM, Kyrou I, Kaltsas G, Grossman AB, Randeva HS, Weickert MO. Mechanisms of Central Hypogonadism. Int J Mol Sci 2021;22(15):8217. doi: 10.3390/ijms22158217

6. Pappas G, Roussos N, Falagas ME. Toxoplasmosis snapshots: global status of Toxoplasma gondii seroprevalence and implications for pregnancy and congenital toxoplasmosis. Int J Parasitol 2009;39(12):1385-94. doi: 10.1016/j.ijpara.2009.04.003

7. Dubey JP, Jones JL. *Toxoplasma gondii* infection in humans and animals in the United States. Int J Parasitol 2008;38(11):1257-78. doi:10.1016/j.ijpara.2008.03.007

8. Flegr Jaroslav. Effects of *Toxoplasma* on human behavior. Schizophr Bull 2007;33(3): 757-60. doi: 10.1093/schbul/sbl074

9. Abdoli A, Ghaffarifar F, Sharifi Z, Taghipour A. Toxoplasma gondii infection and testosterone alteration: A systematic review and meta-analyses. PLoS One 2024;19(4):e0297362. doi: 10.1371/journal.pone.0297362

10. Webster JP. The effect of Toxoplasma gondii on animal behavior: playing cat and mouse. Schizophr Bull 2007;33(3):752-6. doi: 10.1093/schbul/sbl073

11. Werner H, Masihi KN, Senk U. Latent Toxoplasma infection as a possible risk factor for CNS disorders. Zentralbl Bakteriol Mikrobiol Hyg A 1981;250:368-75 doi: 10.1016/S0174-3031(81)80129-1

12. Berdoy M, Webster JP, Macdonald DW. Fatal attraction in Toxoplasma-infected rats: a case of parasite manipulation of its mammalian host. Proc R Soc B 2000;267:1591–4. doi: 10.1098/rspb.2000.1182.

13. Webster JP, Lamberton PHL, Donnelly CA, Torrey EF. Parasites as causative agents of human affective disorders? The impact of anti-psychotic, mood-stabilizer and anti-protozoan medication on T. gondii's ability to alter host behaviour. Proc Biol Sci 2006;273:1023-30. doi: 10.1098/rspb.2005.3413

14. Webster JP, Lamberton PHL, Donnelly CA, Torrey EF. Parasites as causative agents of human affective disorders? The impact of anti-psychotic, mood-stabilizer and anti-protozoan medication on T. gondii's ability to alter host behaviour. Proc Biol Sci 2006;273:1023-30. doi: 10.1098/rspb.2005.3413

15. Dass SAH, Vasudevan A, Dutta D, Soh LJT, Sapolsky RM, Vyas A. Protozoan parasite *Toxoplasma gondii* manipulates mate choice in rats by enhancing attractiveness of males. PloS One 2011;6(11):e27229. doi: 10.1371/journal.pone.0027229

16. Lim A, Kumar V, Hari Dass SA, Vyas A. Toxoplasma gondii infection enhances testicular steroidogenesis in rats. Mol Ecol 2013;22(1):102-10. doi: 10.1111/mec.12042

17. Borráz-León JI, Rantala MJ, Krams IA, Cerda-Molina AL, Contreras-Garduño J. Are *Toxoplasma*-infected subjects more attractive, symmetrical, or healthier than non-infected ones? Evidence from subjective and objective measurements. PeerJ 2022;10:e13122. doi: 10.7717/peerj.13122

18. Lim A, Kumar V, Hari Dass SA, Vyas A. *Toxoplasma gondii* infection enhances testicular steroidogenesis in rats. Mol Ecol 2013;22(1):102-10 doi: 10.1111/mec.12042

19. Flegr J, Klapilová K, Kaňková Š. Toxoplasmosis can be a sexually transmitted infection with serious clinical consequences. Not all routes of infection are created equal. Med Hypotheses 2014;83(3):286-9. doi: 10.1016/j.mehy.2014.05.019

20. Alvarado-Esquivel C, Sánchez-Anguiano LF, Hernández-Tinoco J, Arreola-Cháidez E, López J, Salcido-Meraz KI, et al. High seroprevalence of *Toxoplasma gondii* infection in female sex workers: a case-control study. Eur J Microbiol Immunol 2015;5(4):285-92 doi: 10.1556/1886.2015.00039

21. Alvarado-Esquivel C, Estrada-Martínez S, Ramos-Nevárez A, Pérez-Álamos AR, Beristain-Garcia I, Alvarado-Félix ÁO, et al. Is *Toxoplasma gondii* Infection Associated with Sexual Promiscuity? A Cross-Sectional Study. Pathogens 2021;10(11):[1393 p]. doi: 10.3390/pathogens10111393

22. Groër MW, Yolken RH, Xiao JC, Beckstead JW, Fuchs D, Mohapatra SS, et al. Prenatal depression and anxiety in *Toxoplasma gondii*–positive women. Am J Obstet Gynecol 2011;204(5):433. doi: 10.1016/j.ajog.2011.01.004

23. Nayeri Chegeni T, Sarvi S, Amouei A, Moosazadeh M, Hosseininejad Z, A. Aghayan S, et al. Relationship between toxoplasmosis and obsessive compulsive disorder: A systematic review and meta-analysis. PLoS Negl Trop Dis 2019;13(4):e0007306 doi: 10.1371/journal.pntd.0007306

24. Al Malki JS, Hussien NA, Al Malki F. Maternal toxoplasmosis and the risk of childhood autism: serological and molecular small-scale studies. BMC Pediatr 2021;21(1):133. doi: 10.1186/s12887-021-02604-4

25. Abdoli A. *Toxoplasma*, testosterone, and behavior manipulation: the role of parasite strain, host variations, and intensity of infection*. Front Biol* 2014;9(2):151–60 doi: 10.1007/s11515-014-1291-5