

## A CASE OF ADULT TOURETTE SYNDROME: IRON ADMINISTRATION REDUCES TIC SEVERITY

Yusuke Arai<sup>1,2</sup>, Daimei Sasayama<sup>1</sup>, Yoshitaka Takeuchi<sup>2</sup>, Shihoko Inada<sup>2</sup>, Nobuteru Usuda<sup>2</sup>,  
Akira Tanaka<sup>1,2</sup>, Shiho Murata<sup>2</sup>, Kazuaki Kuraishi<sup>2</sup> & Shinsuke Washizuka<sup>1</sup>

<sup>1</sup>Department of Psychiatry, Shinshu University School of Medicine, Matsumoto-City, Nagano, Japan

<sup>2</sup>Department of Psychiatry, Kurita Hospital, Nagano-City, Nagano, Japan

received: 7.9.2022;

revised: 21.10.2022;

accepted: 31.10.2022

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### INTRODUCTION

Tourette syndrome (TS) is characterized by multiple motor tics and one or more vocal tics. According to the Diagnostic and Statistical Manual of Mental Disorders, 5<sup>th</sup> Edition (DSM-5) (American Psychiatric Association 2013), TS is classified under the neurodevelopmental disorders group and frequently co-occurs with other disorders within this group. Typically, tics develop between 4 and 6 years of age and reach their greatest severity between the ages of 10-12 years. However, by early adulthood, roughly three-quarters of children with TS will have greatly diminished tic symptoms and over one-third will be tic free. (Bloch & Leckman 2009). Additionally, patients with TS often have tic urges, which are uncomfortable sensations preceding the tics. Patients are compelled to perform the tics to control their urges; however, the urges reappear shortly after the tics, creating a vicious cycle. Abnormal dopamine and gamma-aminobutyric acid (GABA) functions are thought to be etiological factors for TS (Hallet 2015); however, its pathophysiology remains unclear. Here, we report a case of TS in which iron administration was effective in relieving tic symptoms. This finding has important implications for the pathophysiology and management of TS.

### CASE REPORT

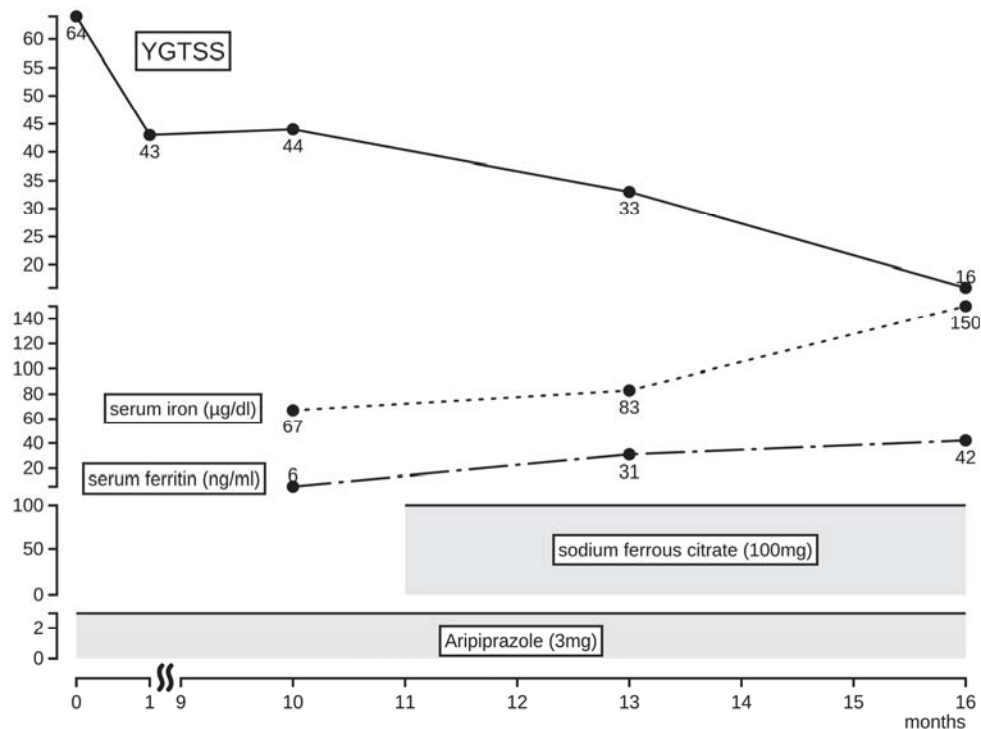
A 21-year-old woman diagnosed with a tic disorder by a pediatrician at the age of 11 years recently visited a psychiatrist because her tics persisted. These included motor tics such as blinking; facial frowns; abdominal tension; movements of the nose, mouth, head, and limbs; as well as vocal tics such as clearing the throat and repeating the following sounds: "ouch," "shih," and "kuh." The urge to carry out these behaviors was higher at night. She had no family history of mental illness and was diagnosed with TS according to DSM-5. Furthermore, she was also diagnosed with a specific learning disability in mathematics. We administered the Yale Global Tic Severity Scale (YGTSS) (Storch et al. 2005) to assess tic symptom severity; the score was 64 points at the first visit. We prescribed

aripiprazole 3 mg/d. Treatment was continued on an outpatient basis, and she was followed up at our hospital once a month.

Figure 1 shows the clinical course of the patient over 16 months after the prescribed treatment was initiated. As a result of oral administration of aripiprazole for 1 month, her YGTSS score decreased from 64 to 43 points. Subsequently, the patient continued the same treatment for 9 months. However, further improvement was insignificant and her YGTSS score remained at 44 points. We wondered if there was any additional therapy, other than antipsychotic treatment, that might improve her tic symptoms. We noticed that her tics worsened at night, resembling the clinical manifestations of Restless Legs Syndrome (RLS). It is known that, in some cases, RLS is caused by iron deficiency (Aurora et al. 2012). Thus, although the symptoms displayed by our patient did not strictly correspond to RLS, we considered the possibility that iron deficiency may have a role as they worsened at night. As expected, the patient's serum ferritin levels (6 ng/ml) as well as serum iron levels (67 µg/dl) were low; therefore, we prescribed an iron supplement (sodium-ferrous-citrate) at 100 mg/d. Two months later, serum ferritin levels increased to 31 ng/ml, and serum iron level was 83 µg/dl. Moreover, her YGTSS score decreased to 33 points. She continued taking the iron supplement; after 5 months, her serum ferritin levels increased to 42 ng/ml, serum iron levels to 150 µg/dl, and the YGTSS score further improved, reducing to 16 points. Furthermore, the patient declared that she experienced days without tic symptoms. There was no stress-induced worsening of tic symptoms or adverse events during this period. Since the aforementioned treatment, the severity of tic symptoms has remained static.

### DISCUSSION

Our report has two important clinical implications. One is that administration of antipsychotic drugs is indeed effective for TS; however, the addition of iron supplements may further improve outcomes. Second, some of the symptoms present in TS may be triggered by latent iron deficiency.



One month of aripiprazole treatment improved the YGTSS score from 64 to 43 points, but further improvement was not significant in the next 9 months. After that, 2 months add-on treatment of iron supplement (sodium-ferrous-citrate) improved YGTSS score to 33 points. In addition, the patient continued taking iron supplements for the next 3 months; her YGTSS score improved to 16 points with increasing serum ferritin and serum iron levels

**Figure 1.** Clinical course of the patient

Aripiprazole treatment improved tic symptoms to an appreciable extent during the first month but did not lead to further improvement. This is possibly due to the stabilization of aripiprazole levels in the blood and the partial agonist action of dopamine. Treatment with the iron supplement was initiated while continuing with aripiprazole, and the tic symptoms improved corresponding with increases in serum iron and ferritin levels. This improvement is most likely due to treatment with iron, although natural course of improvement and placebo effect cannot be ruled out. To our best knowledge, this is the first reported case of iron treatment being effective for residual TS in adulthood. Administration of iron was effective for up to 5 months after initiation. Normal levels of serum ferritin and iron were reestablished during the last 5 months, suggesting that tic symptoms may be associated with systemic iron deficiency. The efficacy of iron treatment for TS in children has been reported. Ghosh & Burkman (2017) reported that iron administration in children with TS improved tic symptoms regardless of pretreatment serum ferritin levels. Furthermore, when classified according to serum ferritin levels before intervention using a cut-off level of 50 ng/ml, the group with serum ferritin levels lower than 50 ng/ml showed higher YGTSS scores. This suggests that latent iron deficiency contributes to the pathophysiology of TS and that reduced serum ferritin levels are associated with greater severity of tic

symptoms. The clinical management of this case suggests that iron supplements, often effective in alleviating RLS symptoms, may also be effective for some patients with TS. Therefore, it appears that iron may work as an additional treatment for TS with low serum ferritin levels, regardless of age.

## CONCLUSION

This is the first report of a case where iron administration reduced tic severity in an adult with TS. The present findings show that latent iron deficiency may contribute to the pathophysiology of TS, which has clinical features similar to RLS, such as nocturnal exacerbations. Further research is warranted to investigate the involvement of iron in the pathophysiology of TS.

**Acknowledgements:** None.

**Conflict of interest:** None to declare.

### Contribution of individual authors:

Yusuke Arai: manuscript writing, literature search.

Daimei Sasayama, Yoshitaka Takeuchi, Shihoko Inada, Nobuteru Usuda, Akira Tanaka, Shiho Murata, Kazuaki Kuraishi & Shinsuke Washizuka: manuscript writing, supervising of the writing of the paper.

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Correspondence:

Yusuke Arai, MD

Department of Psychiatry, Shinshu University School of Medicine

3-1-1 Asahi, Matsumoto-City, Nagano, 390-8621, Japan

E-mail: 19hm101k@shinshu-u.ac.jp