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Letter to the Editor

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Streptococcal Infection Can Be the Trigger for Thyroid Storm

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To the Editor

Thyroid storm is a life-threatening medical condition with a high mortality rate of 8-25% [1, 2]. This condition occurs in thyrotoxic patients and is manifested by the decompensation of multiple organs such as congestive heart failure and respiratory failure [3].Thyroid storm is a very rare disorder with an incidence of 0.2 per 100,000 person-years in Japan, and the incidence of thyroid storm in patients who were admitted to hospital due to thyrotoxicosis is 1-5% [1, 3, 4]. An apparent trigger could be identified in about 70% of thyroid storm cases: irregular use or discontinuation of anti-thyroid drugs, followed by infection [3]. Although infection is the second most crucial trigger of thyroid storm, it has been unknown what infectious agent can be the trigger of thyroid storm. We experienced two patients with thyroid storm which might have been triggered by streptococcal infection. Here, we discuss a possible mechanism for streptococcal infection-triggered thyroid storm, by the analysis of our patients.

Our two middle-aged female patients showed thyrotoxicosis (decreased serum thyroid stimulating hormone (TSH), and elevated serum free T3 (fT3) and free T4 (fT4) levels), fever, tachycardia and gastrointestinal symptoms and restlessness. According to the guideline by Japan Thyroid Association, they were diagnosed as having thyroid storm [3]. Interestingly, both patients developed sore throat and fever before the onset of thyroid storm. On admission, both patients showed swelling of bilateral palatine tonsils and thyroid, and the rapid antigen detection test for group A beta-hemolytic streptococci (GAS) by swab of palatine tonsil was positive. In both patients, the third-generation TSH-receptor antibody (TRAb) levels were remarkably elevated to > 30 IU/L (normal range, < 2.0 IU/L). The intensive treatment by using antibiotics, hydrocortisone, potassium iodide, propylthiouracil and beta-blocker promptly improved patients' symptoms and data.

An apparent trigger was identified in about 70% of thyroid storm cases [3]. The highest trigger of thyroid storm was the irregular use or discontinuation of anti-thyroid drugs (40%), and the second highest trigger was infection (29%), particularly the upper respiratory tract infection [3]. However, the detail of upper respiratory tract infection was not shown [3]. Further, it has been unknown what infectious agent can be the trigger for thyroid storm.

We experienced two patients with thyroid storm which might have been triggered by streptococcal infection which was confirmed by the rapid antigen detection test for GAS by swab of palatine tonsil, suggesting an association of GAS infection with thyroid storm. Further, an association between thyroid storm and acute tonsillitis was reported in a case report written in Japanese [5]. Bacterial tonsillitis has been reported to be most commonly caused by GAS [6], supporting an association between GAS infection and thyroid storm.

The characteristic finding observed in our thyroid storm patients was remarkably elevated titer of the third-generation TRAb. The third-generation TRAb can specifically identify patients with Graves' disease [7]. In the study that investigated performance of the third-generation TRAb, medical records of 200 consecutive patients with thyroid disorders who had TRAb measured since the introduction of the assay, and sera and medical records of 44 patients with newly identified hyperthyroidism were used [7]. In these patients, the maximal titer of the third-generation TRAb was 30 IU/L, and only two patients showed 30 IU/L [7]. Further, receiver operating characteristic analysis determined an optimal cut-off point of TRAb ≥ 3.5 IU/L with a 100% specificity to exclude patients without Graves' disease [7]. These results show that the titer of the third-generation TRAb in our thyroid storm cases is strikingly high. Serum fT3 and fT4 concentrations in thyroid storm patients were similar to those in thyrotoxicosis patients without thyroid storm in the Japanese nationwide surveys [3], suggesting that the development of thyroid storm cannot be explained by only thyrotoxicosis. Streptococcal infection has been reported to induce autoimmune diseases such as acute rheumatic fever, Sydenham's chorea and pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections (PANDAS) [8, 9].

We think that streptococcal infection may trigger the development of thyroid storm via over-induction of TRAb.

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Conflict of Interest

The authors declare that they have no conflict of interest concerning this article.

Informed Consent

Not applicable.

Author Contributions

MH, HK, SK, AK, and HH treated patients. MH and HK collected data. HY analyzed data, and HY wrote the paper. All authors read and approved the final paper.

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