A Case of Sore Throat and Fever

Masayuki Amano, MD\(^1\) and Taro Shimizu, MD, MPH, MBA\(^2\)

\(^1\) Department of Internal Medicine Nara Prefectural Gojo Hospital, Nara, Japan
\(^2\) Department of General Internal Medicine, Tokyo Joto Hospital, Tokyo, Japan

A previously healthy 41-year-old man presented to his primary care physician because of sore throat. He noticed the symptom two days ago, that was sixteen days before his admission. He had not had rhinorrhea or a cough, and his temperature was normal. He had mild erythema on his pharynges, and mild tenderness of the anterior neck. His primary care doctor performed laryngoscopy, which denied the swelling of his epiglottis. He was diagnosed as pharyngitis, and an antibiotic and an anodyne were prescribed. His symptoms subsided after four days, but mild soreness of his throat persisted. Seven days before his admission, he developed headache and high grade fever (39°C). Two days before his admission, he visited another primary care doctor. Cefcapene pivoxil hydrochloride was prescribed but it didn’t help him. The day before his admission, the antibiotic was changed to amoxicillin/clavulanate potassium. However, his sore throat, headache, fever, fatigue got worsen, so he decided to consult our hospital. At first, he visited to the Department of Neurology, in afraid of meningitis. Lumbar puncture was performed, and meningitis was denied. Focus of fever was unknown at this time, so he was admitted and consulted to the internal medicine team.

He was married and worked as system engineer. He denied any use of alcohol, cigarettes, or illicit drugs. He had no remarkable past medical history, and took no medications. He had not recently traveled outside Japan, and had not had any recent contact with sick persons or animals.

Sore throat is one of the common symptoms physicians encounter on daily basis. Differential diagnosis of sore throat is broad, and coexisting symptoms help us to narrow the possibilities. When sore throat involves cough and rhinorrhea, that can be common cold. There is usually no need to treat them with antibiotics nor do any further testing.

When a patient has swelling tonsils with exudates, he/she may have acute bacterial pharyngitis. We should be aware of group A streptococcal infection, since treatment can shorten the duration of the symptoms. The presence of the symptoms listed in Centor’s score is highly suggestive of streptococcal pharyngitis; high fever, anterior cervical adenopathy with tender, tonsillar exudates, and absence of cough. A pharyngitis patient with a trismus should be checked the displacement of the uvula because it implies peritonsillar abscess. Another bacterial infection for young patient includes gonococcal pharyngitis. It is pivotal to ask sexual
history for young patients with acute pharyngitis. When we encounter severe sore throat with little pharyngeal lesion, it should be carefully examined since it could be life-threatening infection or the pain from the outside of the throat; severe odynophagia, drooling or stridor suggest the acute epiglottitis; neck pain without odynophagia could be thyroiditis or Kikuchi-Fujimoto disease; sudden onset of discomfort of the throat could be radiation pain coming from myocardial infarction or aortic dissection. In patients with sore throat but clear throat, differential diagnosis should include subacute thyroiditis (SAT), epiglottitis, and deep neck infection. If such patient has severe pain and poor dental hygiene, Lemierre’s disease should be considered. The condition of the patient’s teeth should be evaluated as well as throat. Differential diagnosis of viral pharyngitis is broad. Infectious mononucleosis and infectious mononucleosis-like syndrome is an important consideration for this patient. This condition may be caused by Epstein-Barr virus, human immunodeficiency virus, cytomegalovirus (CMV) and other viruses, although CMV does not usually cause sore throat. Posterior cervical lymphadenopathy may imply the infection of these viruses. This case is a previously healthy middle-aged man with fever and sore throat. Through the intuitive diagnostic process (System 1), most available diagnosis could be viral pharyngitis. However, the duration of his symptom was longer and more severe than the typical clinical course of pharyngitis. We need to be aware of the spreading of inflammation to the deep neck space or presence of the entirely different diseases. In order to avoid the interference of biases, we need to go through analytical diagnostic process, what we call System 2 diagnostic process, by taking Review of Systems (ROS) and listed up the differential diagnosis.

ROS and further questioning revealed that his expression of “sore throat” actually meant “neck pain”. In fact, there was no relation between soreness and swallowing. The neck pain occurred acutely, and it was at first localized in left side of neck with palpable nodule. The painful nodule moved to the right side of the neck along time course. His headache was localized in right auricle area. He also remembered that lost his weight and he had more sweat than usual. Those changes occurred from two weeks before his admission. It is important to clarify patient’s history. For the purpose of gathering the patient’s medical problems, open-ended questions and ROS are effective. The physicians picked up the pertinent key pieces of information for the diagnosis, and then polish and clarify them by using close-ended questions. In this case, patient’s problem was not “sore throat”, rather, “anterior neck pain”. We decided to go through the System 2 again, listed up the differential diagnosis of anterior neck pain; cardiovascular event, acute epiglottitis, deep neck space infections, thyroiditis, and lymphadenopathy. In addition, we decided to go through the process of lateral thinking (System 3) as asking the patient’s explanatory model. He shared with that he had been worried about meningitis, and, he was also worried about his painful creeping nodule on his neck. This information drove us to take focused physical examination of thyroid.

On physical examination, he was alert and in severe distress due to general fatigue. His pulse was 122 beats per minute, blood pressure was 110/70 mmHg, SpO2 was 96% in room air, respiratory rate was normal, and body temperature was 38.0°C. His height was 171 cm and weight was 53.0 kg. Jolt accentuation was negative, temporal artery was non-tender on palpation. No lesions were noted on the mouth, oropharynx, or ear. There was no palpable lymph node on his whole body. Cardiovascular examination revealed a regular tachycardia with normal heart sounds and no murmurs. Examination of the pulmonary, abdominal and musculoskeletal systems was unremarkable. His thyroid gland was slightly diffuse enlarged, firm on palpation, slightly tender on right lobe but no palpable nodules. There was no exophthalmos or lid lag. His skin was moist and warm. Brisk reflexes were noted, and slight tremor on both hands was elicited by holding a piece of paper on the outstretched hand.

We found no signs strongly suggesting of cardiovas-
cular event, acute epiglottis, deep neck space infections or systemic lymphadenopathy. We did not find thyroid nodules on palpation, but found slight enlargement of thyroid which implied the tenderness was from thyroid. There are some characteristic findings on physical examination of the hyperthyroidism. Three eye findings including Grave’s ophthalmopathy, eyelid lag, and eyelid retraction are useful for making diagnosis of hyperthyroidism. Grave’s ophthalmopathy occurs only with Graves’s disease, while the others are found in patients with hyperthyroidism from any etiology. Sensitivity, specificity and positive likelihood ratio are 34%, 99%, 33.2 in eyelid retraction, and 19%, 99%, 18.6 in eyelid lag. Neuromuscular findings in hyperthyroidism are also famous, such as fine finger tremor, brisk reflex, and diminished exercise tolerance. Positive likelihood ratio of tremor is 11.5. To detect mild tremor, it is useful to tell patients to hold a piece of paper. The tremor is amplified by the paper so that we can see the tremor through the movement of paper.

The laboratory data are shown in Table 1. The leukocyte count was 12500/mm³; erythrocyte sedimentation rate was 89 mm/2 hr; C-reactive protein was 10.4 mg/dl; Alanine aminotransferase was 25 IU/l; Aspartate aminotransferase was 15 IU/l. Free T3 was 18.05 pg/ml, Free T4 was over 7.77 pg/ml (too high to measure), Thyroid-stimulating hormone was 0.020 µIU/ml. Two sets of blood culture were obtained. The urinalysis showed no leukocyte, and urine culture was negative. An electrocardiogram only revealed sinus tachycardia. A chest radiograph showed a normal-size heart and no pulmonary consolidation in both lungs.

The result of blood test came up to our expectation. Hyperthyroidism was confirmed. The elevation of C-reactive protein and erythrocyte sedimentation rate was compatible with SAT. There was no sign of arrhythmia and heart failure. The differential diagnosis of hyperthyroidism with thyroid pain includes SAT, acute infectious thyroiditis, hemorrhage into a thyroid nodule, carcinoma, Grave’s disease and acute exacerbation of Hashimoto disease. In order to confirm diagnosis, anti-thyroid hormone level determination and cervical ultrasonography should be performed.

The results of additional blood test were as follows: anti-thyroid peroxydase antibody was 25 IU/ml, Thyroid stimulating hormone receptor antibody was undetectable. Ultrasonography showed normal sized, heterogeneity hypoechogenic thyroid with normal blood flow on color Doppler ultrasonography. There were no signs of abscess, hemorrhage or malignancy. Technetium imaging showed low uptake (0.012%). The diagnosis of SAT was confirmed, and oral loxoprofen sodium (60 mg, three times a day after every meal) was initiated on the second hospital day. The medication stabilized his vital signs including temperature, and helped his neck pain and headache on the third hospital day. He was discharged on the seventh hospital day with additional loxoprofen for seven days. He was planned to have follow up visit by his family physician for monitoring his thyroid.

### Discussion

SAT is a self-limited inflammatory disorder of thyroid. The epidemiology of SAT in Japan is these; the female-male ratio was 7:1, developed most often in patients aged 40 to 50 years, highest incidence in summer. Although the exact etiology of SAT is still unclear, viral infection is considered to be a trigger of SAT. In addition, an association between SAT and HLA B35 has been reported in many ethnic groups.

A quarter of SAT begins with an upper respiratory

<table>
<thead>
<tr>
<th>Table 1.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb 13.4 mg/dl, WBC 12500 µl, Plt 47.4 × 10⁴/µl, ESR 89 mm/2 hr, Glc 102 mg/dl, TSH 0.020 µIU/ml, Free T3 18.05 pg/ml, Free T4 over 7.77 pg/ml (too high to measure)</td>
</tr>
<tr>
<td>TP 7.3 mg/dl, BUN 16.7 mg/dl, Cr 0.74 mg/dl, T-Bil 0.89 mg/dl, AST 15 IU/l,</td>
</tr>
<tr>
<td>ALT 25 IU/l, LD 122 IU/l, ALP 393 IU/l, CK 29 IU/l, Na 141 mEq/l,</td>
</tr>
<tr>
<td>K 4.5 mEq/l, Cl 101 mEq/l, CRP 10.42 mg/dl,</td>
</tr>
</tbody>
</table>

---

65
infection followed by fever and severe neck pain.\textsuperscript{6} At the time of the onset, approximately 60\% of patients have fever, and half of them have temperatures of greater than 38°C.\textsuperscript{4} Almost all of the patients have neck pain. The pain may be limited to the region of the thyroid but it can radiate to the neck, jaw, throat, upper chest, and ears. A painful nodule appears on one side initially, and then 30\% of the patients experience spreading of painful nodule to the other side in days or weeks. This phenomenon is called “creeping”, in the sense sometimes SAT is called as creeping thyroiditis.\textsuperscript{6} On physical examination, thyroid usually slightly enlarges unilaterally or diffusely. Almost all patients have tender on thyroid. Approximately 60\% of patients have symptoms and signs of thyrotoxicosis. The hyperthyroidism is usually mild and transient, so that focused and detailed physical examination is required to detect the sign.\textsuperscript{4}

On laboratory test, hyperthyroidism can be confirmed by blood test; high serum free T4, T3 and low serum TSH concentrations. Serum antithyroid peroxidase or antithyroglobulin antibodies are usually undetectable or present at low titer, and these findings are different from those of Hashimoto disease.\textsuperscript{7} Inflammatory changes can also be observed; leukocytosis, elevation of the erythrocyte sedimentation rate and C-reactive protein.\textsuperscript{8} Liver function tests can be abnormal, and it return to normal without treatment over the next one to two months as the disease improves.\textsuperscript{9}

On imaging studies, ultrasonography and scintigraphy are useful to determine the diagnosis of SAT. On ultrasonography, the thyroid is focally or diffusely hypoechoogenic regardless of its size.\textsuperscript{10} A hypoechoogenic area may be the focus of inflammation. The occurrence of the hypoechoogenic area on the intact side of the thyroid suggests the spreading of inflammation.\textsuperscript{4} Color-flow Doppler ultrasonography shows low-to-normal vascularity in hyperthyroid phase of SAT, while that of Grave’s disease shows hyper vascularity.\textsuperscript{10} On scintigraphy, the uptake of I 123 or technetium will show low, distinguishing SAT from Graves’ disease.\textsuperscript{11}

The main purpose of the treatment for SAT is to alleviate the thyroid pain and tenderness. Nonsteroidal anti-inflammatory medication can remove mild pain, while severe pain needs high doses of glucocorticoids (e.g., 40 mg of prednisone daily) to relieve the symptoms.\textsuperscript{11} Some patients need treatment for hyperthyroidism, and beta blockers may be useful to relieve symptoms. Thyroid function will be normal after several weeks. Hypothyroidism, usually asymptomatic, will develop subsequently. It will last four to six months, and many patients recover spontaneously.

Recurrence of SAT can occur in 2 to 5 percent of patients.\textsuperscript{4} In this case, the gender and season were uncommon (the patient presented on winter), but the time course of disease was so typical. His “headache” was localized in periauricular area and diminished as the patient recovers. This patient had such mild signs of hyperthyroidism that the patient could not note them. Careful history and physical examination helped physicians to detect the presence of hyperthyroidism. The laboratory and imaging findings were consistent with SAT. For the treatment, loxoprofen worked well and there was no need to proceed to corticosteroids therapy.

In view of diagnosis, it was difficult to consider the diagnosis of SAT through system 1 on first presentation; SAT is not too common disease per se, and this patient had the uncommon background (gender and season); the medical history of his upper respiratory infection could evoke a premature closure. Careful history and detailed physical examination based on System 2 shed light on his true medical problem. And then, System 3 as asking his explanatory model led us straight forward to the diagnosis.

\section*{Conclusion}

We encountered a case of SAT. His history of illness and signs of hyperthyroidism enabled us to make accurate diagnosis. This case told us again the importance of the basics of history taking and physical examination.

\section*{References}