A Rare Cause of Nonresponsive Tonsillitis in the Primary Care Setting: Acute Myeloid Leukemia

ABSTRACT We present a 51-year-old man with sore throat, headache, high fever, and weakness for two weeks. He had been diagnosed cryptic tonsillitis and given antibiotic treatment. Although he adhered to the therapy, he got worse. At the time of admittance he was weak and pale, pharynx, tonsils and buccal mucosa were hyperemic and inflamed, pus was present in tonsil area. The liver was extending about 5cm below the costal margin. He had substantial increase in leukocyte count, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels. He had lymphopenia, neutropenia and trombocytopenia. After suspicion of a hematologic malignancy, the patient was referred to the Department of Haematology and he was diagnosed with acute myeloid leukemia after bone marrow aspiration. We wanted to emphasize the importance of a detailed anamnesis and an extensive physical examination for nonresponsive tonsillitis in order not to overlook underlying pathologies such as leukemia in primary care.

Keywords: Primary health care; tonsillitis; leukemia myeloid acute

Sore throat is among the most common causes of admission in primary care. A sore throat is predominantly a disease of adolescents and those in their early school years. In adults, the most common reason for sore throat is an upper respiratory tract virus infection including rhinovirus, coronavirus and adenovirus with a ratio of 85% to 90%. The bacterial cause of sore throat is mainly group A β-hemolytic streptococci (GAβHS), and can be cultured in 5% to 17% of adults with sore throat. Acute tonsillitis is an acute inflammatory disorder of the tonsils manifested usually by swollen tonsillar structures associated with the symptoms of a sore throat. Tonsillitis may represent as an isolated disease or it can be associated with systemic diseases such as infections and neoplastic disorders. A study exploring patients with tonsillitis showed that those whose tests were positive for GAβHS and treated with penicillin had relieved symptoms about 16 hours earlier than those whose tests were negative for GAβHS. Treated or not, 85% of patients became completely free of symptoms after one week. The host immunity and the aggressivity of the etiological agent affects the severity and course of acute tonsillitis.

Herein we present an adult who had been complaining about a sore throat, headache, high fever, and weakness for two weeks and, after being suspected of having leukemia by the primary health care professionals, was
diagnosed with “acute myeloid leukemia” (AML) at the Hematology Department.

CASE REPORT

A 51-year-old man was admitted to Department of Family Medicine of İbni Sina Hospital with a sore throat, headache, high fever, and weakness. He reported that his complaints had begun two weeks before and then had been diagnosed with cryptic tonsillitis. He did not agree for a throat swab for a culture or a rapid antigen test. He was treated with oral amoxicillin-clavulanate for the first five days. Then, an intramuscular administration of another antibiotic commenced as his complaints did not supersede. Nevertheless, he didn’t improve and his complaints continued to increase.

He was weak and pale at the time of admission, his tympanic temperature was 38.2°C, his pulse rate was 90 bpm, his arterial blood pressure was 110/80 mmHg, and his respiratory rate was 18/min. His pharynx, tonsils and buccal mucosa were hyperemic and inflamed, and yellow pus was present in the tonsil area. There were follicular-like crusted lesions behind the right ear and on the middle section of the right clavicle. His liver edge was firm, easily felt and extending about 5 cm below the costal margin.

Laboratory examinations were as follows: white blood cell count: 125,000x10⁹/L (4.5 to 11.0 x 10⁹ cells /L), hemoglobin: 8.6 g/dL (13.1-17.2g/dl), thrombocyte count: 17x10⁹/L (150 to 450 x10⁹/L), CRP: 148 mg/dL (less than 5.0 milligrams per liter, or mg/L), 82.5% monocyte (3%-9%), 9.7% neutrophile (40%-70%), 7.5% lymphocyte (20%-45%), hematocrit 25.8% (39%-50%), erythrocyte sedimentation rate 144 mm/h, Epstein-barr virus IgM (-), Cytomegalovirus IgM (-), Toxoplasma IgM (-), HbsAg(-), anti HCV (-), and anti HIV (-). Throat swabs were not taken, neither for culture nor for rapid test, due to his previous antibiotic treatment.

Abiding by the laboratory test results, we requested consultation from the Department of Hematologic Diseases. The patient was suspected to have a hematologic malignancy and hospitalized at the Hematology Clinic. A peripheral blood smear showed immature white cells, so a bone marrow aspiration was done and showed hyper-cellular marrow with blastic infiltration consistent with AML. The treatment started immediately.

Verbal informed consent was obtained from the patient.

DISCUSSION

An acute sore throat is a symptom often caused by an inflammatory process in the pharynx, tonsils or nasopharynx, and these infections are among the most common infectious diseases seen by family physicians. In the United States, acute throat infection cases account for about 40 million primary care physician visits on a yearly basis, making it one of the most common respiratory infections. Acute tonsillitis usually manifests with the classic sore throat. Symptoms of inflammation include fever and chills, odynophagia, dysphagia, and tender cervical lymphadenopathy. In adults, the viruses are the most common agent of pharyngeal tonsillitis in the ratio of 85% to 90%. Perhaps, based on this knowledge, when this patient was admitted to the health center with a sore throat for the first time, no throat swab or rapid test was implemented, but, regardless, he was given an oral antibiotic treatment, whereas GA βHS is the only common reason requiring antibiotherapy. In medical practice, bacteriae are clinically the most important and most microbiologically identified agents of acute tonsillitis and of them the most frequent type is the streptococcal infection. The main bacterial cause of a sore throat is GAβHS, which is cultured in 5% to 17% of adults with a sore throat. So, the physician might decide visually that the sore throat has arisen from Group A β-hemolytic streptococci.

Rhinoviruses, echoviruses, adenoviruses, and, less frequently, respiratory syncytial viruses, among other species, are the determinants of a virus. On the other hand, the Herpes simplex virus or Coxsackie virus, may cause angina vesiculosa. In exceptional circumstances, the Epstein Barr virus can cause exudative tonsillitis which resembles a bacterial infection. Spirochetes and fusiform bac-
teria are the other causes of the painful ulcerating inflammation of the tonsils, mouth, and oropharynx. In immunologically deprived persons, microbial opportunists may be involved.4

Acute myeloid leukemia (AML) is a heterogeneous clonal disorder characterized by immature myeloid cell proliferation and bone marrow failure.13 While “Acute myeloid leukemias” are infrequent malignancies, they are responsible for a great number of deaths related with cancer. Acute myeloid leukemia is the most common type of leukemia in adults, accounting for about 80% of cases, and it has the lowest survival rate among all types of leukemia.14-16 The incidence of the disease is highest in the USA, Australia, and Western Europe, and lower in Asian countries.14,15 Its incidence increases progressively with age and is primarily a disease of later adulthood. The incidence is 1.3 per 100,000 persons in patients younger than 65 years, and 12.2 cases per 100,000 persons in patients over 65 years.17 Patients newly diagnosed with AML have a median life expectancy of 6 years. In adults, it has a slight male predominance in most countries.14 In the UK, the total prevalence rates per 100,000 persons were 35 in males aged 45-64 years, and 124 in males aged 65 or more years, whereas the prevalence rates were 25 and 73 in females respectively.18 According to 2014 cancer statistics of Turkey, the age-standardized rate distribution for myeloid leukemia is 2 per 100,000 persons in women and 2.6 per 100,000 persons in men.19 The patient presented here was a 51 year old man.

If the disease is untreated, it is uniformly fatal. Patients ultimately die of bone marrow failure complications, such as infections and hemorrhage, even if they can be supported for a certain period of time (normally about 11-20 weeks). In a certain study it was reported that while the survival rate was 23% for those who are younger than 55 years old, the rate was 11% for those older than 55 years old.14

Although it is believed that several risk factors play a role in the development of AML, generally the causes of the disease are unknown. Age, previous hematologic diseases, and genetic disorders are the known risk factors which account for a small number of cases. Besides, previous chemotherapy, certain occupational hazards, exposure to viruses, radiation or chemicals are the other risk factors.14 In our case, there were none of the known risk factors listed above. The symptoms of anemia, infection, or bleeding require medical attention and usually immediate therapeutic interventions. The diagnosis of acute leukemia usually starts as a clinical suspicion. Patients with AML are often diagnosed in the case of an intensive infection with fever, or the acute onset of a bleeding problem with petechiae or easy bruisingability. Patients also relate symptoms of profound weakness, fatigue resulting from exercise, dizziness resulting from exertion, fever with or without infection, and bleeding diathesis.14 Adults with AML are less likely to have bone pain. Hepatosplenomegaly and lymphadenopathy are rare in adults with AML.16 This patient didn’t indicate any bone pain, and we didn’t determine any lymphadenopathy or splenomegaly during the physical examination. The liver was enlarged about 5 cm below the costal margin.

When the patient is suspected to have AML, a bone marrow aspiration should be done for a definitive diagnosis. For the diagnosis, a marrow or blood blast count of 20% or more is needed.11 We followed up on the patient’s further laboratory examinations, and explored a hyper-cellular marrow aspirate and peripheral smear showing diffuse leukaemic infiltration and morphologic changes compatible with AML.

Although a few cases of leukemia with exudative tonsillitis, are available in literature none of them was coming from a primary care setting.20 Acute myeloid leukemia is a disease which must be diagnosed quickly and treated as early on in the process as possible. Therefore, primary care physicians should be able to recognize the common presentations of leukemia and perform the initial diagnostic evaluation. Clinical suspicion is important, especially in the case of long
lasting and nonresponsive tonsillitis. In the research literature, there are a few cases of leukemia with exudative tonsillitis but none of them was from the primary care setting. Because of this, we wanted to emphasize the importance of a detailed anamnesis and an extensive physical examination for nonresponsive tonsillitis in order not to overlook the underlying pathologies such as leukemia in primary care setting.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and/or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

_Idia/Concept_: Hafize Yeğin, Makkube Çaylak, Ayşe Gülşen Ceyhun Peker; _Design_: Ayşe Selda Tekiner, Ayşe Gülşen Ceyhun Peker; _Control/Supervision_: Ayşe Selda Tekiner, Hafize Yeğin, Makkube Çaylak; _Data Collection and/or Processing_: Ayşe Selda Tekiner, Hafize Yeğin, Makkube Çaylak, Ayşe Çölgeçen; _Analysis and/or Interpretation_: Ayşe Selda Tekiner, Ayşe Gülşen Ceyhun Peker; _Literature Review_: Makkube Çaylak, Ayşe Çölgeçen, Hafize Yeğin, Ayşe Selda Tekiner; _Writing the Article_: Ayşe Selda Tekiner, Hafize Yeğin, Makkube Çaylak; _Critical Review_: Ayşe Selda Tekiner, Ayşe Gülşen Ceyhun Peker.

REFERENCES

20. Bain JB. The nature of leukaemia, cytology, cytochemistry and the morphological classification of acute leukaemia. Leukaemia Diagnosis. 5th ed. Hoboken NJ: John Wiley & Sons; 2017. p.1-68. [Crossref] [PMC]