






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

 Ayşe Selda TEKİNER^a,
 Hafize YEĞİN^a,
 Ayşe Gülsen CEYHUN PEKER^a,
 Makbule ÇAYLAK^b,
 Ayşe ÇÖLGEÇEN^a

^aDepartment of Family Medicine,
 Ankara University Faculty of Medicine,
^bClinic of Radiology,
 Dr. Abdurrahman Yurtaslan Ankara
 Oncology Training and Research Hospital,
 Ankara, TURKEY

Received: 06 Dec 2018
 Received in revised form: 28 Feb 2019
 Accepted: 14 Mar 2019
 Available online: 18 Mar 2019

Correspondence:
 Ayşe Selda TEKİNER
 Ankara University Faculty of Medicine,
 Department of Family Medicine,
 Ankara, TURKEY
 seldatekiner@gmail.com

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 thrombocytopenia. 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.¹ 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%.² The bacterial cause of sore throat is mainly group A β -hemolytic streptococci (GA β HS), and can be cultured in 5% to 17% of adults with sore throat.³ 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.^{4,5} A study exploring patients with tonsillitis showed that those whose tests were positive for GA β HS and treated with penicillin had relieved symptoms about 16 hours earlier than those whose tests were negative for GA β HS.⁴ Treated or not, 85% of patients became completely free of symptoms after one week.⁶ The host immunity and the aggressivity of the etiological agent effects 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 subside. Nevertheless, he didn't improve and his complaints continued to increase.

He was weak and pale at the time of admittance, 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 5cm below the costal margin.

Laboratory examinations were as follows: white blood cell count: $125,000 \times 10^9 / L$ (4.5 to 11.0×10^9 cells /L), hemoglobin: 8.6 g/dL (13.1-17.2g/dl), thrombocyte count: $17 \times 10^9 / L$ (150 to $450 \times 10^9 / L$), 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.^{7,8} 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.^{4,9} 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%.¹⁰⁻¹² 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 GAβHS is the only common reason requiring antibiotherapy.¹

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.² 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 malign neoplasms, 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 65 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 bruisability. 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 blastic 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.

To conclude, although it is believed to be uncommon to have an incidental diagnosis of leukemia we were able to discover such a patient in 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

Idea/Concept: Hafize Yeğin, Makbule Çaylak, Ayşe Gülsen Ceyhun Peker; **Design:** Ayşe Selda Tekiner, Ayşe Gülsen Ceyhun Peker; **Control/Supervision:** Ayşe Selda Tekiner, Hafize Yeğin, Makbule Çaylak; **Data Collection and/or Processing:** Ayşe Selda Tekiner, Hafize Yeğin, Makbule Çaylak, Ayşe Çölgeçen; **Analysis and/or Interpretation:** Ayşe Selda Tekiner, Ayşe Gülsen Ceyhun Peker; **Literature Review:** Makbule Çaylak, Ayşe Çölgeçen, Hafize Yeğin, Ayşe Selda Tekiner; **Writing the Article:** Ayşe Selda Tekiner, Hafize Yeğin, Makbule Çaylak; **Critical Review:** Ayşe Selda Tekiner, Ayşe Gülsen Ceyhun Peker.

REFERENCES

- Bisno AL. Acute pharyngitis. N Eng J Med. 2001;344(3):205-11. [Crossref] [PubMed]
- Worrall G, Huthsinson J, Sherman G, Griffiths J. Diagnosing streptococcal sore throats in adults: randomized controlled trial of in-office aids. Can Fam Physician. 2007;53(4):666-71.
- Linder JA, Stafford RS. Antibiotic treatment of adults with sore throat by community primary care physicians: a national survey, 1989-1999. JAMA. 2001;286(10):1181-6. [Crossref] [PubMed]
- Johnson BC, Alvi A. Cost effective workup for tonsillitis. Testing, treatment, and potential complications. Postgrad Med. 2003;113(3):115-8. [Crossref] [PubMed]
- Schwaab M, Gurr A, Hansen S, Minovi AM, Thomas JP, Sudhoff H, et al. Human beta-defensins in different states of diseases of the tonsilla palatina. Eur Arch Otorhinolaryngol. 2010;267(5):821-30. [Crossref] [PubMed]
- Touw-Otten FW, Johansen KS. Diagnosis, antibiotic treatment and outcome of tonsillitis: report of a WHO Regional Office for Europe study in 17 European countries. Fam Pract. 1992;9(3):255-62. [Crossref] [PubMed]
- Worrall G. Acute sore throat. Can Fam Physician. 2011;57(7):791-4.
- Little P, Stuart B, Hobbs FD, Butler CC, Hay AD, Delaney B, et al. Antibiotic prescription strategies for acute sore throat: a prospective observational cohort study. Lancet Infect Dis. 2014;14(3):213-9. [Crossref]
- Quinn J, Ruoff GE, Ziter PS. Efficacy and tolerability of 5-day, once-daily telithromycin compared with 10-day, twice-daily clarithromycin for the treatment of group A beta-hemolytic streptococcal tonsillitis/pharyngitis: a multicenter, randomized, double-blind, parallel-group study. Clin Ther. 2003;25(2):422-43. [Crossref]
- Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. JAMA. 1997;278(11):901-4. [Crossref] [PubMed]
- Şencan M. [Acute leukemias: epidemiology, etiology and pathogenesis]. Türkiye Klinikleri J Hem Onc-Special Topics. 2010;3(2):1-4.
- Pelucchi C, Grigoryan L, Galeone C, Esposito S, Huovinen P, Little P, et al; ESCMID Sore Throat Guideline Group. Guideline for the management of acute sore throat. Clin Microbiol Infect. 2012;18 Suppl 1:1-28. [Crossref] [PubMed]
- Saultz JN, Garzon R. Acute myeloid leukemia: a concise review. J Clin Med. 2016;5(3):1-17. [Crossref] [PubMed] [PMC]
- Dechler B, Lübbert M. Acute myeloid leukemia: epidemiology and etiology. Cancer. 2006;107(9):2099-107. [Crossref] [PubMed]
- Özkalemkaş F, Özkocaman V, Özçelik T, Ozan Ü, Tunali A. [Epidemiological characteristics of acute myelogenous leukemia in Southern Marmara Region of Türkiye]. Journal of Uludag University Medical Faculty. 2002;28(2):33-7.
- Davis AS, Viera AJ, Mead MD. Leukemia: an overview for primary care. Am Fam Physician. 2014;89(9):731-8.
- De Kouchkovsky I, Abdul-Hay M. 'Acute myeloid leukemia: a comprehensive review and 2016 update'. Blood Cancer J. 2016;6(7):e441. [Crossref] [PubMed] [PMC]
- Forman D, Stockton D, Møller H, Quinn M, Babb P, De Angelis R, et al. Cancer prevalence in the UK: results from the EURO-PREVAL study. Ann Oncol. 2003;14(4):648-54. [Crossref] [PubMed]
- Şencan İ, Keskinlik B. [2014]. Türkiye Kanser İstatistikleri. 1. Baskı. Ankara: T.C. Sağlık Bakanlığı Türkiye Halk Sağlığı Kurumu; 2017. p.16-40.
- 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]