ABSTRACT

Scarlet fever is a term used for an infection caused by a Group A Streptococcal bacteria. The early treatment of scarlet fever is strongly essential either to prevent further spreading of infection or to prevent the risk of complications consisting of peritonsillar and retropharyngeal abscess, sepsis, hepatitis, acute rheumatic fever, glomerulonephritis, pneumonia, endocarditis, and meningitis. We present a case of scarlet fever with sepsis, hepatitis, and severe acute malnutrition in a 15 year and 6 months old female adolescent. Since the patient had specific clinical features of scarlet fever with continuous fever, sore throat, and productive cough since 4 days, followed by general red maculopapular rash initially from the head and progressively spreading to the rest of her body. The patient also diagnosed with sepsis, hepatitis, and severe acute malnutrition. Erythromycin, ursodioxycolic acid, vitamin C, folic acid, and vitamin b complex were given to the patient.

Rapid diagnosis and prompt treatment are important to prevent other potential complications such as sepsis, abscess, and acute rheumatic fever. Early diagnosis of scarlet fever simultaneously with adequate treatment will prevent the complications of the disease and its spreading among other children.

Keywords: Scarlet fever; sepsis; hepatitis; severe acute malnutrition; adolescent
Introduction

Scarlet fever is a term used for an infection caused by a Group A Streptococcal bacteria presenting with exudative pharyngitis and maculo-papular rash.\textsuperscript{1} Outbreak of the disease has been noted in 2009 in Vietnam and China figuring for 23,000 cases and 100,000 cases; respectively. Report of the outbreak was also documented in the UK covering 12,906 cases between September 2015 and April 2016.\textsuperscript{2–5} The characteristic of ‘strawberry tongue’ or a ‘raspberry tongue’ accompanied by fever and maculo-papular rash is a common symptom of scarlet fever.\textsuperscript{6,7} The early treatment of scarlet fever is strongly essential either to prevent further spreading of infection or to prevent the risk of complications consisting of peritonsillar and retropharyngeal abscess, sepsis, hepatitis, acute rheumatic fever, glomerulonephritis, pneumonia, endocarditis, and meningitis.\textsuperscript{1,8–10}

The term ‘severe acute malnutrition (SAM) has been used to diagnose children with severe wasting and kwashiorkor (also known as nutritional edema) and replaced the previous term of ‘protein-energy malnutrition’.\textsuperscript{11} In 2013, an estimated 2.9 million children under five were admitted globally for treatment of SAM. Children with SAM are nine times more likely to die than well-nourished children.\textsuperscript{12} Children with malnutrition are at significantly higher risk of more severe disease and suffer significantly more acute and long-term morbidity and mortality when infected, including scarlet fever.\textsuperscript{13} This report is to highlight the importance of early diagnosis and prompt treatment of scarlet fever in a malnourished child to prevent either risk of complications or the spreading of the disease among other children.

Case

A –15 years and 6 month-old female adolescent was referred on April 24, 2021 to Wahidin Sudirohusodo Hospital Makassar due to a general red rash spreading over her whole body one day before referring (Figure1). She complained of continuous fever, sore throat, and productive cough for 4 days, followed by a general red maculopapular rash initially from the head and progressively spreading to the rest of her body one day before admission. There was a previous history of amputation of her right leg due to osteosarcoma at the orthopedic of the Wahidin Sudirohusodo Hospital Makasar. There was no exposure to patients with Kawasaki syndrome as well as typhoid fever. The other history of illness was unremarkable.
Fig 1. The patient and her strawberry tongue and general red maculopapular rash (black arrow)

The physical findings showed a severely ill, malnourished, and conscious female adolescent with the fever of 38.5°C, blood pressure 90/60mmHg, pulse 104/min, respiration rate 24/min, SpO2: 99% room air, capillary refill time < 3 secs and pain scale 0. There were signs and symptoms of general maculopapular rash over the whole body, enlarged tonsils, pharyngeal hyperemic, strawberry tongue, absent of lymphadenopathy, ribs xylophone, wasting, and right leg amputation. The further examination of the abdomen, heart, and lungs documented normal findings. The nutritional status demonstrated a severe malnutrition adolescent with normal stature. (Fig1) The Center score for this patient was three consisting of fever 1, enlarged tonsils 1, and cough 1.

Laboratory examination showed Hb 14.3 g/dl, WBC 17.100/mm³, platelet 247.000, blood glucose 123 mg/dl, ureum 18 mg/dl, creatinine 0.54 mg/dl, albumin 3.5 gr/dl, sodium 137 mmol/l, potassium 4.7 mmol/l, chloride 105 mmol/l, CRP 32.5 mg/l, procalcitonin 2.8 ng/ml, SGOT 806 U/L, SGPT 554 U/L, direct bilirubin 4.03 mg/dl, total bilirubin 5.62 mg/dl, alkali fosfatese 162 IU/L, gamma GT 90 IU/L and ASTO 328 IU/ml. Hepatitis examination: HbsAg, anti Hbs AG and anti HCV non-reactive. Blood culture: Klebsiella Pneumonia. Chest x ray and electrocardiograph showed normal impression.

Definitive diagnosis: Scarlet fever, hepatitis, sepsis and severe acute malnutrition. The patient was admitted with working diagnosis of scarlet fever based on examination and increased Anti-streptolysin O titer). The treatment for scarlet fever was erythromycin 250 mg/ 6 hours for streptococcus eradication because benzathine penicillin was not available. The patient had malnutrition, so she also received malnutrition management according to WHO guideline by giving F75 / 3 hours, vitamin C 50 mg / 12 hours, folic acid 1 mg / 24 hours, vitamin B complex 1 tablet / day. Sepsis resulted in blood culture results with Klebsiella pneumonia infection, therefore antibiotic ceftriaxone 1 gram / 12 hours was administered. The patient also had hepatitis resulting in jaundice and elevation of transaminase enzyme and bilirubin, so she also received ursodeoxycholic acid 250 mg/8 hours.

On the 9th day of treatment, her general condition was still weak but the rash decreased progressively
day by day. On the 22nd day of treatment, the general condition was good, the rash almost disappeared and signs of hepatitis were reduced. On day 26 of treatment, the patient recovered clinically with no more signs and symptoms of scarlatina, sepsis and hepatitis, she was discharged after completing the antibiotic therapy and further follow up was conducted at the child health policlinics of the Wahidin Sudirohusodo Hospital Makassar. The prognosis: Quo ad Vitam (survival), Quo ad sanationam (cured): Quo ad functionam (functional): bonam.

Discussion

Since our case presented with scarlet fever, SAM complicated with sepsis and hepatitis based on the clinic and laboratory features, therefore different from Kawasaki syndrome and typhoid fever. Our case presented with a history of 4 days of fever, sore throat, strawberry tongue, cough without mucous membrane exchanges, bilateral conjunctival injection, or cervical lymphadenopathy, which surely did not fulfill the criteria of Kawasaki syndrome. Although Kawasaki syndrome may be accompanied by elevation of serum transaminase and hyperbilirubinemia but without pyuria and thrombocytosis on admission, we can ruled out the Kawasaki syndrome. Typhoid fever was also ruled out due to no signs and symptoms of characteristic salmon-colored spots on trunk and abdomen, bradycardia, or exposure to patients with typhoid fever. Hepatitis is a rare complication of scarlet fever in the pediatric population. The pathophysiological mechanism is unclear. Direct bacterial injury, toxicity and immunologic mediation have been proposed. Liver biopsies in patients with scarlet fever have shown granulocytic infiltration of the portal areas and hepatocytic degeneration. Diagnosis of Scarlet fever was mostly based on the clinical features and supported by the elevated ASO titer. Since our patient presented with 4 days of fever, sore throat, cough, characteristic general maculopapular rash, and elevated ASO titer, the hepatitis was surely following the clinical presentation of Scarlet fever. On further follow-up, the liver transaminases were reduced day by day up to normal.

Malnutrition should be considered as a silent killer due to malnutrition potentially leading to the death of children every day as supported by one study estimating around 20 million severely acute malnourished children in the whole world and the report also showed approximately one million children die from severe acute malnutrition every year in the developing countries, more than 25% of children under five are undernourished that accounts about 143 million children. Globally, 55 million children under the age of five are estimated to be wasted, of whom 19 million (35%) are severely wasted or severely malnourished. Major contributing factors for severe malnutrition are poor child-feeding practices, infectious disease, poor hygiene and sanitation. Co-existing infection increases the risk of death among severely malnourished children. Wasting is an important indicator of acute malnutrition which impairs the immune response and predispose to invasive infection. Comorbidity of malnutrition
makes the child more vulnerable to invasive infection. Several previous studies have been shown to have a significant association between severe acute malnutrition with Klebsiella bacteremia.\textsuperscript{21} The relationship between scarlet fever and malnutrition may be a mere coincidence or it may suggest that those weakened by some level of nutritional deficiency were particularly liable to be among victims of the disease.\textsuperscript{22} In this patient, sepsis due to klebsiella infection and scarlet fever could be easily acquired due to the patient's malnourished condition which lowered the patient's immunity. Fortunately, our patient were diagnosed early and prompt adequate measurements was given to her to prevent the risk of other severe complications and especially death.

The physicians should be focusing on early recognition of scarlet fever and prompt treatment to prevent the complications due to a delay of diagnosis among older children were which frequency 2.8 times as likely when a sore throat was present at onset, with symptoms often resembled any viral infection.\textsuperscript{23}

To the best of our knowledge, this case was the first case of scarlet fever and SAM complicated by sepsis and hepatitis in female adolescent in the Wahidin Sudirohusodo Hospital Makassar.

**Conclusion**

Early diagnosis and rapid treatment of scarlet fever are strongly important to prevent the potentially severe complications such as sepsis, hepatitis, acute rheumatic fever, glomerulonephritis, pneumonia, endocarditis, and meningitis. Early diagnosis of scarlet fever simultaneous with adequate treatment will prevent the complications of the disease and its spreading among other children. The physicians should be focusing on early recognition of scarlet fever and rapid treatment to prevent the potentially severe complications.

**Declaration**

**Ethics Approval and Consent to Participate**

DR Wahidin Sudirohusodo Hospital’s ethics committee and review board has approved this study.

**Consent for Publication**

Written informed consent was obtained from the patient’s legal guardian for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

**Authors’ contributions**

ANF, NMP and HA were responsible for the management of our patient; ANF, NMP and HA participated in the study design and coordination and helped draft the manuscript. All authors read and approved the final manuscript.
Conflict of Interests

The authors declare that they have no competing interests.

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1. Wessels MR. Pharyngitis and Scarlet Fever. In: Ferretti JJ, Stevens DL, Fischetti VA, editors. Streptococcus pyogenes: Basic Biology to Clinical Manifestations. Oklahoma City (OK): 2016.

2. Lu Q, Wu H, Ding Z, Wu C, Lin J. Analysis of Epidemiological Characteristics of Scarlet Fever in Zhejiang Province, China, 2004-2018. Int J Environ Res Public Health. 2019 Sep;16(18).

3. Ben Zakour NL, Davies MR, You Y, Chen JHK, Forde BM, Stanton-Cook M, et al. Transfer of scarlet fever-associated elements into the group A Streptococcus M1T1 clone. Sci Rep [Internet]. 2015;5(1):15877. Available from: https://doi.org/10.1038/srep15877

4. Basetti S, Hodgson J, Rawson TM, Majeed A. Scarlet fever: a guide for general practitioners. London J Prim Care (Abingdon) [Internet]. 2017 Aug 11;9(5):77–9. Available from: https://pubmed.ncbi.nlm.nih.gov/29081840

5. Sayers DR, Bova ML, Clark LL. Brief report: Diagnoses of scarlet fever in Military Health System (MHS) beneficiaries under 17 years of age across the MHS and in England, 2013-2018. MSMR. 2020 Feb;27(2):26–8.

6. Huang Y, Wen Y, Jia Q, Wang L, Cheng Q, Liu W, et al. Genome analysis of a multidrug-resistant Streptococcus sanguis isolated from a throat swab of a child with scarlet fever. J Glob Antimicrob Resist. 2020 Mar;20:1–3.

7. Muzumdar S, Rothe MJ, Grant-Kels JM. The rash with maculopapules and fever in children. Clin Dermatol. 2019;37(2):119–28.

8. Turner CE, Pyzio M, Song B, Lamagni T, Meltzer M, Chow JY, et al. Scarlet Fever Upsurge in England and Molecular-Genetic Analysis in North-West London, 2014. Emerg Infect Dis. 2016 Jun;22(6):1075–8.

9. Wong SSY, You Y, Chen JHK, Forde BM, Stanton-Cook M, et al. Transfer of scarlet fever-associated elements into the group A Streptococcus M1T1 clone. Sci Rep [Internet]. 2015;5(1):15877. Available from: https://doi.org/10.1038/srep15877

10. Bassetti S, Hodgson J, Rawson TM, Majeed A. Scarlet fever: a guide for general practitioners. London J Prim Care (Abingdon) [Internet]. 2017 Aug 11;9(5):77–9. Available from: https://pubmed.ncbi.nlm.nih.gov/29081840

11. Sayers DR, Bova ML, Clark LL. Brief report: Diagnoses of scarlet fever in Military Health System (MHS) beneficiaries under 17 years of age across the MHS and in England, 2013-2018. MSMR. 2020 Feb;27(2):26–8.

12. Huang Y, Wen Y, Jia Q, Wang L, Cheng Q, Liu W, et al. Genome analysis of a multidrug-resistant Streptococcus sanguis isolated from a throat swab of a child with scarlet fever. J Glob Antimicrob Resist. 2020 Mar;20:1–3.

13. Muzumdar S, Rothe MJ, Grant-Kels JM. The rash with maculopapules and fever in children. Clin Dermatol. 2019;37(2):119–28.

14. Turner CE, Pyzio M, Song B, Lamagni T, Meltzer M, Chow JY, et al. Scarlet Fever Upsurge in England and Molecular-Genetic Analysis in North-West London, 2014. Emerg Infect Dis. 2016 Jun;22(6):1075–8.

15. Wong SSY, You Y, Chen JHK, Forde BM, Stanton-Cook M, et al. Transfer of scarlet fever-associated elements into the group A Streptococcus M1T1 clone. Sci Rep [Internet]. 2015;5(1):15877. Available from: https://doi.org/10.1038/srep15877

16. Bassetti S, Hodgson J, Rawson TM, Majeed A. Scarlet fever: a guide for general practitioners. London J Prim Care (Abingdon) [Internet]. 2017 Aug 11;9(5):77–9. Available from: https://pubmed.ncbi.nlm.nih.gov/29081840

17. Sayers DR, Bova ML, Clark LL. Brief report: Diagnoses of scarlet fever in Military Health System (MHS) beneficiaries under 17 years of age across the MHS and in England, 2013-2018. MSMR. 2020 Feb;27(2):26–8.

18. Huang Y, Wen Y, Jia Q, Wang L, Cheng Q, Liu W, et al. Genome analysis of a multidrug-resistant Streptococcus sanguis isolated from a throat swab of a child with scarlet fever. J Glob Antimicrob Resist. 2020 Mar;20:1–3.

19. Muzumdar S, Rothe MJ, Grant-Kels JM. The rash with maculopapules and fever in children. Clin Dermatol. 2019;37(2):119–28.

20. Turner CE, Pyzio M, Song B, Lamagni T, Meltzer M, Chow JY, et al. Scarlet Fever Upsurge in England and Molecular-Genetic Analysis in North-West London, 2014. Emerg Infect Dis. 2016 Jun;22(6):1075–8.

21. Wong SSY, You Y, Chen JHK, Forde BM, Stanton-Cook M, et al. Transfer of scarlet fever-associated elements into the group A Streptococcus M1T1 clone. Sci Rep [Internet]. 2015;5(1):15877. Available from: https://doi.org/10.1038/srep15877

22. Bassetti S, Hodgson J, Rawson TM, Majeed A. Scarlet fever: a guide for general practitioners. London J Prim Care (Abingdon) [Internet]. 2017 Aug 11;9(5):77–9. Available from: https://pubmed.ncbi.nlm.nih.gov/29081840

23. Sayers DR, Bova ML, Clark LL. Brief report: Diagnoses of scarlet fever in Military Health System (MHS) beneficiaries under 17 years of age across the MHS and in England, 2013-2018. MSMR. 2020 Feb;27(2):26–8.