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Case Report

Cervical abscess caused by methicillin-susceptible Staphylococcus aureus in an infant infected with SARS-CoV-2: Diagnostic dilemma

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A B S T R A C T

A new inflammatory disease has emerged in children after the COVID-19 disease and has been named multisystem inflammatory syndrome in children (MIS-C). We report a case of cervical abscess in an infant with COVID-19 who was first considered to have MIS-C due to persistent fever, high inflammatory markers.

A 10-month-old boy was admitted to the emergency department due to a 3-day fever and cervical lymphadenopathy. SARS-CoV-2 RNA was detected by a real-time reverse transcriptase-polymerase chain reaction in the nasopharyngeal swab specimen of the patient. Regarding initial clinical and laboratory findings, the patient was diagnosed to have MIS-C and bacterial co-infection. Clindamycin and ceftriaxone treatments were initiated for bacterial co-infection. Despite treatment, his fever persisted and acute phase reactants compatible with MIS-C were elevated and intravenous immunoglobulin (IVIG) was administered. After IVIG treatment, his fever persisted and the patient developed local inflammatory signs including erythema, tenderness, fluctuation developed. Cervical ultrasonography and magnetic resonance imaging demonstrated the findings compatible with the cervical abscess. Drainage of the cervical abscess was performed by an otolaryngologist. Methicillin-susceptible Staphylococcus aureus was isolated from the abscess culture. After abscess drainage, fever and acute phase reactants declined. His nasopharyngeal swab was negative for SARS-CoV-2 on the 7th day. He was discharged on the 21st day of hospitalization with full recovery.

To the best of our knowledge, no cases of COVID-19 with cervical abscess caused by Staphylococcus aureus in children had been reported previously. Bacterial co-infection should be kept in mind in children infected with SARS-CoV-2 and showing MIS-C findings.

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1. Introduction

Coronavirus disease 2019 (COVID-19) was first reported in Wuhan, China in December 2019. Then, COVID-19 spread rapidly all over the world and became a global threat. On 11 March 2020, the WHO declared COVID-19 as a pandemic [1,2]. COVID-19 affects all age groups, and clinical presentation of COVID-19 can vary from completely asymptomatic to mild or moderate in 90% of pediatric cases [2].

Acute unilateral cervical lymphadenitis is usually caused by Staphylococcus aureus, Group A Streptococcus, and anaerobic pathogens. Antimicrobial therapy concomitant with drainage of abscess has been recommended for children those having severe symptoms including fever, fluctuant nodes, and concomitant cellulitis. Aerosol-generating procedures in COVID-19 patients can create aerosols with high viral loads and may lead to increased risk of infection for healthcare workers. It can be challenging for the clinicians to decide about the time of surgery during a pandemic particularly in patients having concomitant COVID-19.

Unlike adults, a new inflammatory disease has emerged in children 2–4 weeks after COVID-19 disease and this new inflammatory disease has been named multisystem inflammatory syndrome in children (MIS-C). This syndrome has similar symptoms which also can be observed in Kawasaki disease and toxic shock
syndrome. The clinical presentation of MIS-C includes persistent fever, gastrointestinal symptoms, rash, conjunctivitis, and lymphadenopathy [3–5]. Patients typically present with three to five days of fever, followed by the development of shock or multisystem involvement. Laboratory findings include elevated inflammatory markers, and elevated cardiac markers [3–5].

Here, we present a case of cervical abscess in a child with COVID-19 who was considered to have MIS-C due to the characteristic persistent fever and high inflammatory marker.

2. Case report

A 10-month-old male infant who was born via spontaneous vaginal delivery at 39 weeks of gestation was admitted to our emergency department with cervical swelling and a history of 3-day fever with a maximum peak temperature of 39.0 °C. The patient was previously healthy and fully immunized. The child was treated with 1 day of azithromycin for fever in the rural hospital before he was admitted to our hospital. His mother was diagnosed to have COVID-19 in another hospital 3 days ago and advised to be self-quarantined. On the second examination at the pediatric emergency department, the patient was febrile, tachycardic (heart rate, 140/min), peripheral capillary oxygen saturation 100% (ambient air) and, not tachypneic (respiratory rate 32/min). Physical examination showed unilaterally, multiple, painful, sized 30 × 30 mm lymph nodes in the right cervical area (Fig. 1A). Laboratory tests were as follows: total leukocyte count: 28.1 × 10^3/μL (neutrophil 61%, monocyte 7.1%, lymphocyte 31%), hemoglobin 10g/dL, platelet count: 457 × 10^3/μL, C-reactive protein (CRP): 170 mg/L, procalcitonin: 0.17 μg/L, lactate dehydrogenase (LDH): 341 U/L, fibrinogen: 647 mg/dL, erythrocyte sedimentation rate (ESR): 104 mm/hour, D-dimer: 938 μg/L, ferritin: 222 μg/L. Due to lack of hemato-

Figure 1. A: Unilateral, multiple, painful, sized 30 × 30 mm lymph nodes in the right cervical area.
B: Unilateral, multiple, painful, fluctuant lymph nodes in the right cervical area after drainage.
C: Cervical abscess after treatment (blue arrow).
formation enlarged 50 × 50 mm, involving lymphadenomegaly as well as surrounding tissues in the right half of the neck (Fig. 2). The abscess was drained (Fig. 1B) and methicillin-susceptible S. aureus (MSSA) growth in bacterial culture. Acute phase reactants declined immediately after drainage. However, the patient developed abscess again in the same area 3 days after the first drainage, and acute phase reactants increased (Fig. 3). Otolaryngologist performed drainage again. Acute phase reactants declined and the patient completely improved after the second drainage and he was discharged on the 21st day of hospitalization (Fig. 1C).

Written informed consent was obtained from the parents for the publication of their child’s pictures.

3. Discussion

We report a case of cervical abscess in an infant with COVID-19 who was first considered to have MIS-C due to the characteristic persistent fever and high inflammatory markers. To our knowledge, no cases of COVID-19 with cervical abscess caused by S. aureus in children or adolescents had been reported previously.

Co-infection is possible among COVID-19 patients and has also been reported in patients with severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), but there is limited knowledge on co-infections among children with COVID-19. In adults, the prevalence of COVID-19-associated co- and secondary infection ranged from 0.6% to 45.0% in previous studies [6–10]. Co-pathogens included bacteria, such as Streptococcus pneumoniae, Mycoplasma pneumoniae, S. aureus, Klebsiella pneumoniae; and viruses such as influenza virus, coronavirus, rhinovirus, enterovirus, parainfluenza virus [11]. In the case series by Zheng et al. [12], bacterial co-infection was reported in 16% and viral co-infection in 8% of the children. A meta-analysis by Lansbury et al. [13] evaluated co-infections in COVID-19 patients and demonstrated that the most common bacterial pathogen was M. pneumoniae (42%) followed by Pseudomonas aeruginosa, Haemophilus influenzae, K pneumoniae, Enterobacter species, Acinetobacter baumannii, Chlamydia species, Enterococcus faecium, methicillin-resistant S. aureus (MRSA), and Serratia marcescens.

A total of 20 children with COVID-19 were included in another study, bacterial co-infection rate was found to be 20% [14]. Since April 2020, Kawasaki-like disease associated with COVID-19 has been reported in children. Preliminary diagnosis included MIS-C and co-infection with a bacterial pathogen on the presentation of our case. Therefore, we administered IVIG 2g/kg. Despite IVIG therapy, fever persisted and the findings of bacterial lymphadenitis appeared. On the fifth day of admission, the patient developed a cervical abscess and we consulted the patient with an otolaryngologist who suggested draining of the abscess. However, drainage could be performed on the 5th day due to the concern of aerosol-generating procedure and risk of COVID-19.

Empirical intravenous antibiotics should be initiated in patients with suppurative lymphadenitis or neck abscess. Additionally, they also should be evaluated for possible incision and drainage. If MRSA is uncommon in the geographic area, oxacillin or nafcillin 150 mg/kg per day or cefazolin 75–100 mg/kg per day can be used. Antibiotic therapy for cervical lymphadenitis is usually administered for 10 days and continued for at least 5 days after the acute signs and symptoms resolve [15]. In our case, S. aureus was isolated in the bacterial culture of the abscess. Blood culture was negative.

Leukocytosis, elevated ESR, and CRP are common laboratory findings in neck infections [16]. Our case had leukocytosis, high ESR, and high CRP. While lymphopenia was a common finding in COVID-19 patients, leukocytosis was considered due to bacterial co-infection in our patient. In a recent study by Xia et al. [17], a high level of procalcitonin was common among pediatric patients infected with COVID-19. It is unknown whether the elevated...
procalcitonin level is due to an inflammatory response or a bacterial co-infection. In our case, a high procalcitonin level was considered as an indicator of bacterial infection.

The incidence of MIS-C in children was 2 per 100,000 [18]. In a recent multicenter study evaluating children with MIS-C, the prevalence of MIS-C reported as 7% in children infected with SARS-CoV-2 younger than 1-year of age and previous studies reported the frequency of cervical lymphadenopathy in MIS-C patients as 10–25% [18–20]. In our case, it was reasonable to diagnose MIS-C because prolonged fever was present in addition to the laboratory findings and there were no inflammatory findings on lymphadenopathy at the beginning.

Similar to Kawasaki disease, IVIG treatment is recommended for MIS-C. A high dose of IVIG was also administered to our patient for...
the suspicion of MIS-C. On the fifth day of admission, inflammation manifestations appeared and fever persisted despite IVIG treatment, the diagnosis of bacterial co-infection came to the forefront. It should be kept in mind that in patients having MIS-C features, cervical lymphadenopathy may also be related to other factors such as infectious agents, therefore these patients should always be carefully examined physically, and performed imaging studies for possible concomitant pathologies and diagnosis of different diseases, paying attention to contact precautions.

4. Conclusion

To the best of our knowledge, this is the first case of co-infection of SARS-CoV-2 and MSSA in a child. During the pandemic, pediatricians faced MIS-C which can cause multisystem involvement and severe illness requiring pediatric intensive care unit admission. We challenged this case due to cervical lymphadenitis, prolonged fever, and several findings that were compatible with MIS-C. Bacterial co-infection should be kept in mind in children infected with SARS-CoV-2 and showing MIS-C findings.

Author contributions

S.Y.A and Z.S.B conceived the paper and wrote the first draft of the manuscript. G.G.O, N.M.B, N.Z.K, F.F.O. contributed data and performed data analyses, and participated in critical review and editing of the manuscript. All the authors were involved in the care of the patient. All authors read and approved the final manuscript.

Declaration of competing interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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References

[1] WHO coronavirus disease (COVID-19) dashboard. Available at: https://covid19.who.int/. [Accessed 29 October 2020].
[2] Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. Pediatrics 2020;145(6):e2020007.
[3] European Centre for Disease Prevention and Control Rapid Risk Assessment. Paediatric inflammatory multisystem syndrome and SARS CoV 2 infection in children. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/covid-19-risk-assessment-paediatric-inflammatory-multisystem-syndrome-15-May-2020.pdf. [Accessed 27 October 2020].
[4] Centers for Disease Control and Prevention Health Alert Network (HAN). Multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease 2019 (COVID-19). Available at: https://emergency.cdc.gov/han/2020/han05432.asp. [Accessed 25 October 2020].
[5] World Health Organization. Multisystem inflammatory syndrome in children and adolescents with COVID-19. Scientific Brief; 2020. Available at: https://www.who.int/publications-detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19. [Accessed 27 October 2020].
[6] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497e506.
[7] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507e13.
[8] Wang M, Wu Q, Xu W, et al. Clinical diagnosis of 8274 samples with 2019-novel coronavirus in Wuhan. medRxiv 2020 Feb 12. https://doi.org/10.1101/2020.02.12.20022327. preprint.
[9] Ding Q, Lu P, Fan Y, Xia Y, Liu M. The clinical characteristics of pneumonia patients coinfected with 2019 novel coronavirus and influenza virus in Wuhan, China. J Med Virol 2020 Mar 20;92(9):1549–55.
[10] Xing Q, Li G, Xing Y, Chen T, Li W, et al. Precautions are needed for COVID-19 patients with coinfection of common respiratory pathogens. medRxiv 2020 Mar 5. https://doi.org/10.1101/2020.02.29.20027698.
[11] Lai CC, Wang CY, Hsueh PR. Co-infections among patients with COVID-19: the need for combination therapy with non-anti-SARS-CoV-2 agents? J Microbiol Immunol Infect 2020;53(4):505–12. https://doi.org/10.1016/j.jmii.2020.05.013.
[12] Zheng F, Liao C, Fan QH, Chen HB, Zhao XG, Xie ZG, et al. Clinical characteristics of children with coronavirus disease 2019 in Hubei, China. Curr Med Sci 2020 Apr;40(2):275–80.
[13] Lansbury L, Lim B, Baskaran V, Lim WS. Co-infections in people with COVID-19: a systematic review and meta-analysis. J Infect 2020 Aug;81(2):266–75.
[14] Xia W, Shao J, Guo Y, Peng X, Li Z, Hu D. Clinical and CT features in pediatric patients with COVID-19 infection: different points from adults. Pediatr Pulmonol 2020 May;55(5):1169–74.
[15] Gosche JR, Vick L. Acute, subacute, and chronic cervical lymphadenitis in children. Semin Pediatr Surg 2006 May;15(2):99–106. https://doi.org/10.1053/j.sempedsurg.2006.02.007. PMID: 16616313; PMCID: PMC7111159.
[16] Cengiz AB, Kara A, Kazra G, Seymeer G, Ceyhan M, Ozan M. Acute neck infections in children. Turk J Pediatr 2004;46:153–8.
[17] Xia W, Shao J, Guo Y, Peng X, Li Z, Hu D. Clinical and CT features in pediatric patients with COVID-19 infection: different points from adults. Pediatr Pulmonol 2020;55:1169–74.
[18] Dufort EM, Koumans EH, Chow EJ, Rosenthal EM, MUSE A, Rowlands J, et al. New York state and centers for disease control and prevention multisystem inflammatory syndrome in children investigation team. Multisystem inflammatory syndrome in children in New York state. N Engl J Med 2020 Jul 23;383(4):347–58.
[19] Yasuhara J, Watanabe K, Takagi H, Sumitomo N, Kunio T. COVID-19 and multisystem inflammatory syndrome in children: a systematic review and meta-analysis. Pediatr Pulmonol 2021 Jan 11. https://doi.org/10.1002/ppul.25245.
[20] Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, et al. Overcoming COVID-19 investigators; CDC COVID-19 response team. Multisystem inflammatory syndrome in U.S. Children and adolescents. N Engl J Med 2020 Jul 23;383(4):334–46.