CASE REPORT

Unpredicted clinical manifestation of COVID-19: a unique case report and review of literature

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Abstract

**Background:** Cervical lymphadenopathy in children is a common problem in daily clinical practice. Many cases of cervical lymphadenopathy after the COVID-19 vaccine were reported. However, there is yet no reporting a case of supraclavicular cervical lymphadenopathy due to COVID-19.

**Case presentation:** A 12-year-old girl presented with fever, cough, fatigue, anosmia, and ageusia. COVID-19 was confirmed by real-time PCR. The symptoms were resolved within 10 days. Seven days later, she complained of supraclavicular swelling. Physical examination revealed painless, multiple, and mobile supraclavicular lymph nodes. Ultrasound and fine-needle aspiration cytology were suspicious. Therefore, an excisional biopsy of the largest node was performed. The specimen was sent for histopathology and immunohistochemistry evaluation which confirmed the benign nature of the lymph node.

**Conclusion:** To our best knowledge, this is the first case of supraclavicular lymphadenopathy in a child with COVID-19. It is essential to put COVID-19 in the differential diagnosis of cervical lymphadenopathy.

**Keywords:** COVID-19, Supraclavicular lymph node, Cervical lymphadenopathy, Case report
(PCR) test of the nasopharyngeal swab. The test was positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Chest X-ray revealed a right-sided upper zone pneumonic patch. Supportive treatment in the form of antipyretic and tonic as well as antibiotics (azithromycin) was given as per the protocol of COVID-19 treatment approved by the Iraqi Ministry of Health.

The patient became well, and all presenting symptoms disappeared entirely during the 10-day follow-up.

One week later, a right supraclavicular lump appeared; it was painless and gradually increased in size (Fig. 1). Physical examination revealed a non-tender neck mass in the right supraclavicular region, oval in shape, $2 \times 1.5$ cm, freely mobile, with no scar, and no skin changes over the swelling or surrounding areas. There were no focal infective areas, masses, or other lymph node enlargement in the body. The patient took a 5-day antibiotic course but without benefit. Ultrasound examination revealed multiple cervical lymph nodes in the right supraclavicular area, the largest of $18 \times 10$ mm in diameter. These nodes showed abnormal fatty hilum, abnormal round index, and exaggerated hypo-echoic texture, as shown in Fig. 2. The possible differential diagnosis could be infectious mononucleosis, toxoplasmosis, cytomegalovirus infection, and less likely tuberculosis or lymphoma. No abnormalities were found on abdominal and axillary sonographic examination. Laboratory tests revealed all are normal apart from high IgM against SARS-CoV-2 and lymphocytosis. Fine needle aspiration cytology revealed a suspicion of abnormal cells. Excisional biopsy was subjected to histopathological examination and immunohistochemistry study. These examinations revealed reactive hyperplasia with no abnormal cells (Figs. 3 and 4). There was no lesion recurrence at the 2-month follow-up visit, and the patient made her normal daily living well. The possible cause of her neck swelling was COVID-19 owing to the patient’s clinical presentation, positive real-time PCR test of the nasopharyngeal swab, the result of the serological test of SARS-CoV-2, and no features on physical examination, and investigation supported other causes as listed in the differential diagnosis. The parents gave informed consent to publish the case.
Discussion

The head and neck contain around 2/3rd of the lymph nodes in the body. Besides, the inflammatory or malignant process in any area can reach the neck through the lymphatic system. Therefore, there is a huge list of causes of cervical lymphadenopathy (enlargement of a node > 1 cm in diameter) [7]. Cervical lymphadenopathy is common in the pediatric population, and most of the cases are benign. The first systematic review about the causes of cervical lymphadenopathy in children by Deosthali et al. [7] reported that 67.8% of the 2687 cases are due to nonspecific benign causes, followed by Epstein-Barr virus (8.86%), malignancy (4.69%), and granulomatous disease (4.06%). In the presenting case, the histopathology and immunohistochemistry evaluations revealed the reactive benign nature of the supraclavicular lymph node. The high possible cause of this cervical lymphadenopathy was COVID-19 because the patient was diagnosed as COVID-19 by real-time PCR of the nasopharyngeal swab and high IgM as well as an absence of indicators of other pathologies in the history, examination, and investigations. Accordingly, COVID-19 can lead to reactive cervical lymph node enlargement.

Involvement of the axillary and/or supraclavicular lymph nodes on the same side is a frequent adverse effect of the vaccines against COVID-19. This is due to local activation of the immune response [8–10]. Moreover, Distinguing et al. reported 3 cases of cervical lymphadenopathy in group 2 (upper jugular group) on magnetic resonance imaging (MRI) in patients with COVID-19. All those patients have complained of otorhinological symptoms (anosmia, aguesia, nasal obstruction, rhinorrhea, and sore throat). These symptoms are due to inflammation of the nose, nasopharynx, and oropharynx caused by SARS-CoV-2. As a result of this inflammation, a local immune reaction occurs, resulting in lymph node enlargement of the Waldeyer’s ring, neck, and parotid regions [6]. Interestingly, we presented the first case in the world of unilateral supraclavicular enlargement in a patient with COVID-19. Although the mechanism of supraclavicular lymphadenopathy is not yet known, it is necessary to put COVID-19 in the differential diagnosis of supraclavicular lymphadenopathy.

Identifying the possible ways of transmitting the SARS-CoV-2 has a major role in understanding the mechanism of the infection with its further treatment options. The specific coronavirus receptor (ACE-2 receptor) is distributed in all body tissues, including the lymph nodes [11]; therefore, it is possible to find the virus in the lymph node as in the presenting case, leading to inflammation and enlargement of the node. Another possible mechanism of getting enlargement of the supraclavicular lymph node is a local immune response in the lung.

According to the American College of Radiology (ACR) recommendations, chest X-rays and computerized tomography (CT) should not be used as a screening or first diagnostic tool for COVID-19 owing to the similarity of the radiological signs among various lung conditions. However, radiological investigation in the

Fig. 3 Showing a benign reactive lymph node, which has a mantle zone (red arrow) that is surrounding a pale germinal center (blue arrow). A H&E x 40 and B H&E x 100

Fig. 4 Showing positive immunohistochemical (IHC) expression of BCL-2 in the mantle zones and negative brownish discoloration of the nuclear and cytoplasmic stain. Besides, positive IHC expression of BCL-6 in the germinal centers of the lymph node with reactive hyperplasia, with a brownish discoloration of the nuclear stain.
pediatric population plays an essential role in the diagnosis and management of patients presenting with cervical lymphadenopathy. In our patient, the presence of COVID-19 vaccine side effects further supported the diagnosis of a benign condition.

Conclusion

Supravacular lymphadenopathy due to COVID-19 was not described in the literature. However, it might be a case of COVID-19 vaccine administered simultaneously with the primary disease. In our case, the child's clinical presentation and the histopathological analysis of the excisional biopsy of the lymph node revealed a benign finding, consistent with a reactive lymphoid hyperplasia.

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Authors’ contributions

RFA analyzed and interpreted the patient data regarding the clinical, laboratory, radiological, and pathological findings as well as writing the case presentation. ARM was a major contributor in writing the manuscript. The authors read and approved the final manuscript.

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Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was approved by the ethical committee of the University of Anbar. Written informed consent was obtained from the patient’s father for the publication of this case report and accompanying images.

Consent for publication

The patient’s father gave written informed consent for the publication of the data and materials contained within this study.

Competing interests

The authors declare that they have no competing interests.

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