中文題目：Reverse Batwing 徵兆與新冠肺炎

英文題目：Reverse Batwing sign in a patient with COVID-19 pneumonia

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**Introduction:**

Since the first diagnosis in China's Hubei province in December 2019, Coronavirus disease 2019 (COVID-19) has now become a global pandemic. COVID-19 is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1]. Frequently, abnormalities on chest radiographs in COVID-19 patients consist of unilateral or bilateral, patchy or diffuse reticular–nodular opacities and consolidation, with basal and peripheral distribution[2,3,14]. We report a rare case of reverse batwing sign in a COVID-19 patient.

**Case presentation:**

A 79-year-old male presented to the emergency department with complaints of progressive shortness of breath, intermittent fever, sore throat, productive cough, and rhinorrhea for ten days. He had a past medical history of coronary artery disease, type 2 diabetes mellitus, and hypertension. The patient did not smoke tobacco, chew betel nut, or drink alcohol. He ever received 3 doses of COVID-19 vaccine. He had started taking Molnupiravir on the first day of COVID-19 symptom onset and completed the full 5-day treatment course.

Upon arrival, the patient's body temperature was 39.5 degrees Celsius, the pulse 98 beats per minute, the respiratory rate 16 breaths per minute, blood pressure 155/71 millimeters of mercury, and oxygen saturation 92% while the patient was breathing ambient air.

Laboratory investigations showed lymphocytopenia (146/ul) and 0% eosinophils. Levels of HS C.R.P (29.500 mg/dl), PCT (1.47 ng/ml), lactate dehydrogenase (329 IU/l), ferritin (591.0 ng/ml), myoglobin (381.0 ng/ml), erythrocyte sedimentation rate (89 mm/hr), and D-dimer (2393.60 ng/ml) were all elevated.

Chest radiograph revealed bilateral, peripheral opacities, sparing perihilar regions,

consisting with the reverse batwing sign (Figure 1A).

The nasopharyngeal swab was tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reverse transcription polymerase-chain reaction (RT-PCR) via cobas® Liat® system. It showed positive result, with a cycle threshold (CT) value of 23.

Remdesivir (6/28-7/2) and Dexamethasone (6/28-7/7) were prescribed for severe grade COVID-19, whereas Piperacillin-tazobactam (6/28-7/6) and Levofloxacin (6/29-7/13) were administered due to difficulty in distinguishing COVID-19 from bacterial pneumonia.

Two days after admission (day 12 after symptom onset), the patient developed respiratory failure, which required intubation and mechanical ventilation. The arterial blood gas analysis showed pH 7.425, PO2 108.3 mmHg, PCO2 32.5 mmHg, and HCO3 21.5 mmol/L, under non-rebreathing mask with oxygen flow rate of 12 L/min. The patient was treated with Tocilizumab (6/30) for critical COVID-19. Enoxaparin (7/4-7/10) was given for thromboprophylaxis due to elevated D-dimer level (5853.69 ng/ml on day 15).

From 6/30 to 7/10, the patient participated in a COVID-19 clinical trial, which compared the efficacy of PG2 Injection 500 mg addition to the standard treatment compared to the standard treatment only.

Despite antibiotic and antiviral treatment, persistent bilateral lung consolidation was found on the chest x-ray on day 23 (Figure 1B). Hence, the patient underwent chest computed tomography scan, revealing subpleural and peribronchiolar predominance of perilobular ground-glass opacities (GGO) and consolidations, with reversed halo sign and arcade-like sign. Organizing pneumonia was the leading diagnosis. Corticosteroid at the initial dose of 0.625 micrograms prednisolone per kilogram was administered. On day 30, the pulmonary opacification on chest radiography subsided after corticosteroid treatment (Figure 1C).

Extubation was performed on day 24 after symptom onset. On day 31, he was

discharged. Pulmonary-function test was conducted on day 34 and showed no ventilatory defect. The pulmonary opacification resolved on day 55 (Figure 1D).

## Discussion:

Reverse bat wing sign, also known as photographic negative of pulmonary edema, is characterized by peripheral opacities of the lungs, with ill-defined margins and without lobar or segmental distribution, sparing the perihilar region. It was first described by Gaensler and Carrington in 1977 as the typical radiographic pattern of chronic eosinophilic pneumonia (CEP) [7].

It is a relatively unusual appearance with narrow differential diagnosis, which include CEP, organizing pneumonia (formerly bronchiolitis obliterans with organizing pneumonia), adenocarcinoma of the lung (entities previously classified as bronchoalveolar carcinoma), pulmonary vasculitides, pulmonary contusion, pulmonary hemorrhage with/without infarction, and recurrent aspiration[8,9].

Globally, as of August 2022, there have been almost 600 million confirmed cases of COVID-19 reported to the World Health Organization (WHO) [10]. However, reverse batwing sign in COVID-19 pneumonia has been reported in only three publications[4-6].

Manna et al. reported that chest radiography findings in COVID-19 patients typically peaked 10–12 days after symptom onset. Frequently, abnormalities on chest radiographs in COVID-19 patients consist of unilateral or bilateral, patchy or diffuse reticular–nodular opacities and consolidation, with basal and peripheral distribution[2,3,14]. The typical appearances of COVID-19 pneumonia on chest CT are peripheral, posterior as well as diffuse or basal lung predominance of GGO with or without consolidation[15]. GGO with crazy paving pattern and findings of organizing pneumonia are also described frequently[15]. King et al. reported that radiologic findings of organizing pneumonia resolved within three months after diagnosis[3,11]. Similar to their descriptions, our patient's radiographic findings showed reverse bat wing sign on day 10 after symptom onset and resolved on day 55.

The patient had no hemoptysis, choking, contusion of the chest wall, asthma or atopic disorders. The blood eosinophilia count was 0/ul. Blood tests for connective-

tissue disease (antinuclear antibody, rheumatoid factor, anti-ENA (SSA), anti-ENA (SSB)) were unremarkable. However, anti-cyclic citrullinated peptide, antitopoisomerase (anti-Scl-70) antibody, anticentromere antibody, anti-double-stranded DNA antibody, and anti-Jo-1 were not tested. Computed tomography of the chest showed no evidence of pulmonary embolism.

Although the definitive etiology of the reverse bat wing sign in this patient cannot be determined due to lack of histopathological confirmation and bronchoalveolar lavage analysis, organizing pneumonia secondary to SARS-CoV-2 infection was the most likely diagnosis based on history, clinical presentation, blood test, and treatment response.

Organizing pneumonia might benefit from high dose corticosteroid therapy[12]. The chest radiography in this patient showed marked improvement after Methylprednisolone (7/13-7/17) administration.

Cordier reported that pulmonary-function tests often showed a restrictive ventilatory defect and reduced diffusing capacity for carbon monoxide in patients with organizing pneumonia. The lungs were non-compliant at diagnosis and returned to normal in patients who had a response to treatment[13]. Our patient received his first pulmonary-function test on day 34 after symptom onset during outpatient follow up, and it showed a normal ventilatory function. Since the patient did not perform pulmonary-function test prior to treatment, it cannot be confirmed whether the patient had ventilatory defect or reduced diffusing capacity of carbon monoxide during his clinical course.

To the best of our knowledge, there have been only three reported cases of reverse batwing sign in COVID-19 patients[4-6]. Reverse bat wing sign is characterized by peripheral opacities of the lungs, with perihilar region sparing[7].

We would like to report this rare finding because the reverse bat wing sign in Covid-19 patients has only been reported three times globally and once in Taiwan. Further studies are needed to evaluate the prevalence of reverse bat wing sign in COVID-19 patients, as it may be underreported.

## Conclusion:

Since the COVID-19 pandemic, organizing pneumonia secondary to COVID-19 should be included in the differential diagnosis of reverse batwing sign. Raising awareness for organizing pneumonia secondary to COVID-19 is important as treatment with steroid might be beneficial.

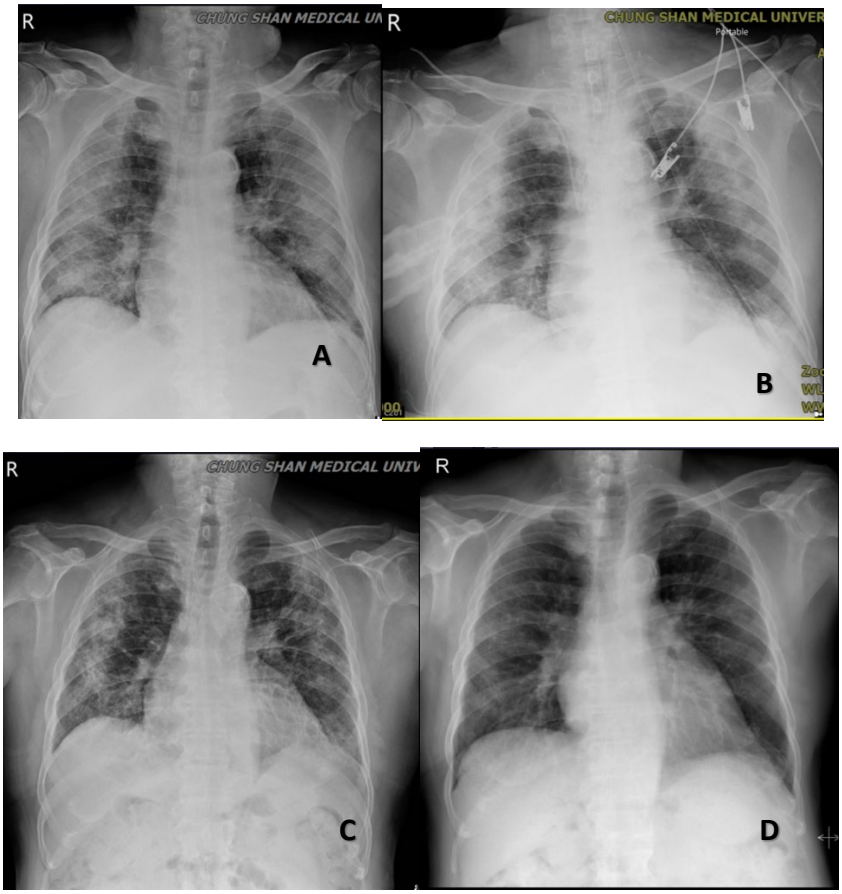


Figure 1. Chest radiography in a patient with COVID-19 on day 10 after symptom onset revealed reverse batwing sign (A); persistent bilateral lung consolidation on day 23 despite antibiotic and antiviral treatment (B); improvement on day 30 after steroid treatment (C); and resolution of opacities on day 55 (D).

References:


1. Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. *Acta Biomed*. 2020;91(1):157-160. Published 2020 Mar 19. doi:10.23750/abm.v91i1.9397
2. Cozzi D, Albanesi M, Cavigli E, et al. Chest X-ray in new Coronavirus Disease 2019 (COVID-19) infection: findings and correlation with clinical outcome. *Radiol Med*. 2020;125(8):730-737. doi:10.1007/s11547-020-01232-9
3. Manna S, Wruble J, Maron SZ, et al. COVID-19: A Multimodality Review of Radiologic Techniques, Clinical Utility, and Imaging Features. *Radiol Cardiothorac Imaging*. 2020;2(3):e200210. Published 2020 Jun 1. doi:10.1148/ryct.2020200210
4. Ghosh S, Nandolia KK, Tale S, Mrudula K, Soibam PM, Vinay G. Reverse Batwing sign in COVID-19 pneumonia. *QJM*. 2020;113(11):836. doi:10.1093/qjmed/hcaa223
5. Chang CJ, Pan SW, Chen YM. Chest Film Demonstrating Reverse Batwing Pulmonary Opacities in a Patient with COVID-19 Pneumonia. *Tuberc Respir Dis (Seoul)*. 2022;85(1):96-97. doi:10.4046/trd.2021.0148
6. Arora N, Kumar H M. 'The photographic negative of pulmonary oedema' in COVID-19 pneumonia. *Postgrad Med J*. 2021;97(1148):401. doi:10.1136/postgradmedj-2020-139265
7. Gaensler EA, Carrington CB. Peripheral opacities in chronic eosinophilic pneumonia: the photographic negative of pulmonary edema. *AJR Am J Roentgenol*. 1977;128(1):1-13. doi:10.2214/ajr.128.1.1
8. Kazerooni EA, Gross BH. Cardiopulmonary imaging. (2004) ISBN:0781736552
9. Chaddha U, Lee C. Subacute Respiratory Illness with Peripheral Pulmonary Opacities. *Ann Am Thorac Soc*. 2018;15(1):107-109. doi:10.1513/AnnalsATS.201708-659CC
10. WHO coronavirus (COVID-19) dashboard [Internet]. Geneva: World Health Organization; 2021 [cited 2021 Oct 10]. Available from: https://covid19.who.int
11. King TE Jr, Lee JS. Cryptogenic Organizing Pneumonia. *N Engl J Med*. 2022;386(11):1058-1069. doi:10.1056/NEJMra2116777
12. de Oliveira Filho CM, Vieceli T, de Fraga Bassotto C, da Rosa Barbato JP, Garcia TS, Scheffel RS. Organizing pneumonia: A late phase complication of

COVID-19 responding dramatically to corticosteroids. *Braz J Infect Dis*. 2021;25(1):101541. doi:10.1016/j.bjid.2021.101541

13. Cordier JF. Cryptogenic organising pneumonia. *Eur Respir J*. 2006;28(2):422-446. doi:10.1183/09031936.06.00013505
14. Wong HYF, Lam HYS, Fong AH, Leung ST, Chin TW, Lo CSY, Lui MM, Lee JCY, Chiu KW, Chung TW, Lee EYP, Wan EYF, Hung IFN, Lam TPW, Kuo MD, Ng MY. Frequency and Distribution of Chest Radiographic Findings in Patients Positive for COVID-19. Radiology. 2020 Aug;296(2):E72-E78. doi: 10.1148/radiol.2020201160. Epub 2020 Mar 27. PMID: 32216717; PMCID: PMC7233401.
15. Simpson S, Kay FU, Abbara S, Bhalla S, Chung JH, Chung M, Henry TS, Kanne JP, Kligerman S, Ko JP, Litt H. Radiological Society of North America Expert Consensus Statement on Reporting Chest CT Findings Related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA - Secondary Publication. J Thorac Imaging. 2020 Jul;35(4):219-227. doi: 10.1097/RTI.0000000000000524. PMID: 32324653; PMCID: PMC7255403.