Giant cell arteritis and COVID-19: similarities and discriminators, a systematic literature review

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Short running head: GCA and COVID-19

Abstract

Objectives

To identify shared and distinct features of giant cell arteritis (GCA) and Coronavirus disease 2019 (COVID-19) to reduce diagnostic error that could cause delays in correct treatment.

Methods

Two systematic literature reviews determined the frequency of clinical features of GCA and COVID-19 in published reports. Frequencies in each disease were summarised using median and range.

Results

Headache was common in GCA but was also observed in COVID-19 (66% for GCA, 10% for COVID-19). Jaw claudication or visual loss (43% and 26% in GCA, respectively) were not reported in COVID-19. Both diseases featured fatigue (38% for GCA, 43% for COVID-19) and elevated inflammatory markers (CRP elevated in 100% of GCA, 66% of COVID-19), but platelet count was elevated in 47% of GCA but 4% of COVID-19. Cough and fever were commonly reported in COVID-19 and less frequently in GCA (cough, 63% for COVID-19 versus 12% for GCA; fever, 83% for COVID-19 versus 27% for GCA). Gastrointestinal upset was occasionally reported in COVID-19 (8%), rarely in GCA (4%). Lymphopenia was more common in COVID-19 than GCA (53% in COVID-19, 2% in GCA). Alteration of smell and taste been described in GCA but their frequency is unclear.

Conclusion

Overlapping features of GCA and COVID-19 include headache, fever, elevated CRP and cough. Jaw claudication, visual loss, platelet count and lymphocyte count may be more discriminatory. Physicians should be aware of the possibility of diagnostic confusion. We have designed a simple checklist to aid evidence-based evaluation of patients with suspected GCA.

Key words Giant cell arteritis, COVID-19, features

Giant cell arteritis (GCA) is the commonest form of systemic vasculitis and typically affects patients over the age of 50. GCA is still little known amongst the general public; the diagnosis is usually first suspected by a physician, most frequently in evaluating new-onset headache. Laboratory tests typically show an acute phase response. Rheumatologists play a key role in diagnostic confirmation. This is one of the most time-critical decisions in rheumatology: failure to treat may result in blindness, but misdiagnosis of GCA can lead to inappropriate immunosuppression and missed opportunity to treat the real underlying cause of the symptoms. The coronavirus disease 2019 (COVID-19) pandemic has presented new challenges in the evaluation of patients with suspected GCA, including the need to direct patients via either "hot" or "cold" pathways to minimise inadvertent transmission of SARS-CoV-2.

During much of the current pandemic, the incidence of COVID-19 in the community has been higher than that of GCA in many places. Early public health messaging emphasised fever, cough and shortness of breath as COVID-19 indicators; subsequently, alterations of taste/smell has been added. Anecdotally we saw patients referred for evaluation of GCA, who turned out to have COVID-19-related headache; and conversely, patients with persistent fever who were only suspected to have GCA after prolonged investigations for infection. Guidelines advise specialist evaluation of suspected GCA within 24 hours, and confirmation of diagnosis via vascular ultrasound or temporal artery biopsy; but during the COVID-19 pandemic, the close, sustained, personal contact with a healthcare practitioner during either of these procedures carries potential risk for both individuals. There is now an imperative for physicians to differentiate between GCA symptoms and COVID-19 symptoms and conduct a risk assessment before the ultrasound scan takes place. We reviewed the literature to gather the best available evidence on features that may discriminate between the two conditions.

Methods

We performed two systematic literature reviews. Searches were performed by two independent reviewers; discrepancies were resolved by wider consensus.

For the GCA literature review, a general search strategy for the diagnostic features of GCA had already been devised for a previous systematic review and meta-analysis (Supplemental

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Methods) and was updated to April 5th, 2020. We searched Pubmed, Embase and the Cochrane Database of Systematic Reviews to identify studies recruiting consecutive patients with suspected GCA. The preferred reference standard was temporal artery biopsy (TAB) or vascular imaging, but studies using a reference standard of clinical diagnosis were included if 75% or more of the patients clinically diagnosed with GCA had positive TAB or vascular imaging to confirm this diagnosis. For this review, we selected the four largest studies that reported the frequency of each symptom. However, for less-typical GCA features and laboratory tests with limited data available, we also performed a directed search in Pubmed to obtain data from other study types reporting these features in patients with GCA.

For the COVID-19 review, we identified all cohorts or case series published between January 1, 2020 and April 5th, 2020, that described patients diagnosed with COVID-19. We excluded retrospective case series of less than 50 patients, reports of patients that had all died, reports where all patients were in the intensive care unit, and reports where all patients had a particular comorbidity (eg cancer). Pubmed, Embase, and the Cochrane Database of Systematic Reviews were all searched. References from included studies as well as the NCBI database LitCovid (https://www.ncbi.nlm.nih.gov/research/coronavirus/) were searched to identify other potentially eligible studies. We did not review the frequency of hypoxaemia and tachypnoea as in the context of our review, these symptoms would have been likely to prompt further investigation and treatment for respiratory pathology.

For each selected publication, we extracted the reported frequencies of each symptom, sign or laboratory feature, and determined the median and range for the publications reviewed. Comparing the two diseases, we divided the features into those more typical of GCA, those more typical of COVID-19, and those observed in both. Risk of bias assessment was performed independently by two authors using the Institute for Health Economics quality appraisal checklist for case series studies (IHE, Edmonton, AB, 2014: http://www.ihe.ca/research-programs/rmd/cssqac/cssqac-about); see Supplementary Methods file. Any differences were adjudicated by a third author.

Results

A general search strategy for diagnostic features of GCA and additional directed search yielded 1666 unique hits (Supplemental Methods). Of these, 35 studies were included for analysis, of which 30 studies were selected from the general search strategy and the remaining 5 studies had been identified by the additional directed searches. No or limited published data on the frequency of lymphopenia or thrombocytopenia in GCA was found; therefore, two co-authors re-analysed raw data from a previously-published study[1].

From the COVID literature review, 253 studies were identified. After screening the title and abstract of each paper, 33 full texts were selected for review. Of these, 29 studies comprising 5623 patients were included in this analysis. One additional study, published after the updated search was concluded, was identified[2] and was included to provide information on the frequency of altered sense of smell or taste and, that had not been identified through the general search strategy; this study also included data regarding "vision impairment".

The main findings are presented in Table 1 and summarised in Figure 1. The overall risk of bias in the included studies was moderate: details are in the Supplementary Results. The main issue identified of the COVID-19 studies was that they were almost all restricted to hospitalised patients who were at various stages of disease. Since the commonest reason for hospitalisation is respiratory symptoms, respiratory symptoms may have been over-represented in the literature, and non-respiratory symptoms under-represented, compared to patients with COVID-19 presenting from the community. With regard to the GCA studies, the majority of studies were retrospective and involved collection of data from medical records, sometimes over many decades. In addition, the stated aim of many of the GCA studies was not to describe the features of the disease, but was focused towards a particular research question. The description of GCA features appeared to be largely intended to show that the "core" GCA features was similar to that in previously-published studies. The frequency of headache was always reported in the GCA studies, for example, but the frequency of cough was rarely reported. In the COVID-19 studies, the frequency of cough was reported in 27/29 studies and headache in 17/29 studies but some symptoms such as myalgia/arthralgia were less precisely defined than in the rheumatology literature.

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Discussion

In the over-50 age group GCA and COVID-19 may initially present with similar symptoms. As in previous literature, only around two-thirds of patients with GCA report headache; around one-quarter report fever. In the COVID-19 case series we identified, headache is reportedly present in between 2% and 34% and fever in 83%. Acute phase response is common in both conditions. Thrombocytosis might point more towards GCA, and lymphopenia towards COVID-19.

The possibility of reporting bias is important in interpreting these data: in large, single-disease cohorts, structured data collection tends to focus on features considered typical of the disease in question. Historically, dry cough has been under-recognised as a symptom of GCA; it was reported in only a minority of studies we identified (11, 32, 59-61, 65, 67). Patients presenting with new-onset GCA should be evaluated for cough, since this might be associated with involvement of the aorta and its proximal branches, a potential risk factor for relapse or aortic aneurysm in GCA; this hypothesis requires testing.

We were limited by not being able to stratify GCA by symptom duration. The average reported symptom duration in GCA is 9 weeks but this is highly variable; on average, symptom duration is somewhat longer in non-headache presentations, and shorter in those with isolated cranial symptoms(70). The average duration of COVID-19 symptom-onset to admission was typically 1-2 weeks in these studies(20, 22, 37, 58) but this might differ outside China.

Most of the COVID-19 data in our review comes from hospitalised cases in China. According to the WHO-China Joint Report, published 28 February 2020, even mild COVID-19 cases were compulsorily removed either to Fangcang shelter hospitals or acute hospitals designated for COVID-19. Patients over 65 or with comorbidity such as hypertension were not eligible for care in Fangcang hospitals and instead were admitted to acute hospitals. The average age of patients in the studies we identified was 53.6 years. At that time anosmia was not universally recognised as a COVID-19 symptom and so appears in few publications

from this period. This illustrates that it cannot be assumed that a symptom not reported in a disease is always absent. We surmise however that it is likely that the most prominent features of any disease will be the ones reported: therefore, our findings are likely to remain clinically relevant. For features less typical of GCA, if larger studies did not report the frequency of these features, a compromise was reached by including additional small studies, one of which also included polymyalgia rheumatica (PMR)(66).

This review raises new research questions that are testable by prospectively collecting data during the current pandemic. Firstly, in patients presenting with headache due to COVID-19, what is the frequency of "GCA-like" features such as scalp tenderness, temporal artery tenderness, difficulty chewing, transient visual loss, weight loss, dysphagia or trismus in patients? Secondly, in patients presenting with GCA, what is the frequency of "COVID-like" features such as dry cough, sore throat, dyspnoea, confusion, anosmia or alteration in sense of taste, lymphopenia, thrombocytopenia, elevation in lactate dehydrogenase or elevation in creatine kinase? Thirdly, given that most of the data on COVID-19 symptoms patterns identified in this review comes from China, is there variation in the clinical presentation of COVID-19 according to ethnicity or culture? Fourthly, how does the clinical picture of GCA patients presenting with a short symptom duration (days to weeks) differ from those presenting with a long symptom duration (months to years)? Lastly, is cough at presentation of GCA associated with an increased relapse risk?

It has always been true that most new-onset headaches will not be due to GCA, and many will be due to minor viral infections; however the novel situation at the time of writing is that currently, many new-onset headaches might be due to COVID-19. Based on the evidence we identified in our literature search, we have designed a simple clinical checklist (Figure 2) that might aid clinicians in assessing patients with suspected GCA during the COVID-19 pandemic, as well as generating data that may answer some of the research questions identified here.

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Figure 1. Features of giant cell arteritis and COVID-19 based on reported frequencies.

This Venn diagram represents features that are more commonly reported in GCA, COVID-19 and features that may be seen in both conditions (overlapping section). Headache and elevated inflammatory markers (in the dotted box), often considered the cardinal features of GCA, may be observed in both GCA and COVID-19.

Abbreviations: ESR = erythrocyte sedimentation rate, CRP = C-reactive protein, Hb = haemoglobin, WBC = white blood cell count, LDH = lactate dehydrogenase, CK = creatine kinase, GI upset = gastrointestinal upset (diarrhoea or vomiting).

Figure 2. A checklist to support evidence-based history and examination in evaluation of patients with suspected giant cell arteritis.

This checklist was constructed in an Excel spreadsheet, informed by the findings of the literature review presented here. The checklist is primarily intended to aid clinicians who are conducting a telephone consultation with a patient referred with suspected giant cell arteritis, prior to their face-to-face appointment during the COVID-19 pandemic. There is also space for relevant physical examination findings and laboratory test results to be added, if provided by the referrer. This checklist has been piloted in Leeds, where it has been further customised to allow automated generation of relevant alerts (via conditional formatting) and risk scores (based on local audit data and the published literature) to support clinical decision-making.

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References

1. van Sleen Y, Graver JC, Abdulahad WH, van der Geest KSM, Boots AMH, Sandovici M, et al. Leukocyte dynamics reveal a persistent myeloid dominance in giant cell arteritis and polymyalgia rheumatica. Front Immunol 2019;10:1981.

2. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol 2020.

3. González-López JJ, González-Moraleja J, Burdaspal-Moratilla A, Rebolleda G, Núñez-Gómez-Álvarez MT, Muñoz-Negrete FJ. Factors associated to temporal artery biopsy result in suspects of giant cell arteritis: A retrospective, multicenter, case-control study. Acta Ophthalmol 2013;91:763-8.

4. Hayreh SS, Podhajsky PA, Raman R, Zimmerman B. Giant cell arteritis: Validity and reliability of various diagnostic criteria. Am J Ophthalmol 1997;123:285-96.

5. Ing EB, Miller NR, Nguyen A, Su W, Bursztyn L, Poole M, et al. Neural network and logistic regression diagnostic prediction models for giant cell arteritis: Development and validation. Clin Ophthalmol 2019;13:421-30.

6. Younge BR, Cook BE, Jr., Bartley GB, Hodge DO, Hunder GG. Initiation of glucocorticoid therapy: Before or after temporal artery biopsy? Mayo Clin Proc 2004;79:483-91.

7. Marí B, Monteagudo M, Bustamante E, Pérez J, Casanovas A, Jordana R, et al. Analysis of temporal artery biopsies in an 18-year period at a community hospital. Eur J Intern Med 2009;20:533-6.

8. Gabriel SE, O'Fallon WM, Achkar AA, Lie JT, Hunder GG. The use of clinical characteristics to predict the results of temporal artery biopsy among patients with suspected giant cell arteritis. J Rheumatol 1995;22:93-6.

9. Hall S, Persellin S, Lie JT, O'Brien PC, Kurland LT, Hunder GG. The therapeutic impact of temporal artery biopsy. Lancet 1983;2:1217-20.

10. Nir-Paz R, Gross A, Chajek-Shaul T. Reduction of jaw opening (trismus) in giant cell arteritis. Ann Rheum Dis 2002;61:832-3.

11. Liozon E, Jauberteau MO, Ly K, Loustaud V, Soria P, Vidal E. Reduction of jaw opening in giant cell arteritis. Ann Rheum Dis 2003;62:287-8.

12. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: Retrospective study. BMJ 2020;368:m1091.

13. Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (sars-cov-2) outside of Wuhan, China: Retrospective case series. BMJ 2020;368:m606.

14. Yan Y, Yang Y, Wang F, Ren H, Zhang S, Shi X, et al. Clinical characteristics and outcomes of patients with severe covid-19 with diabetes. BMJ Open Diabetes Res Care 2020;8.

15. Wang Z, Yang B, Li Q, Wen L, Zhang R. Clinical features of 69 cases with coronavirus disease 2019 in Wuhan, China. Clin Infect Dis 2020.

16. Wu J, Liu J, Zhao X, Liu C, Wang W, Wang D, et al. Clinical characteristics of imported cases of covid-19 in Jiangsu province: A multicenter descriptive study. Clin Infect Dis 2020.

17.   Tian S, Hu N, Lou J, Chen K, Kang X, Xiang Z, et al. Characteristics of covid-19 infection in Beijing. J Infect 2020;80:401-6.

18.   Xu YH, Dong JH, An WM, Lv XY, Yin XP, Zhang JZ, et al. Clinical and computed tomographic imaging features of novel coronavirus pneumonia caused by SARS-CoV-2. J Infect 2020;80:394-400.

19.   Zhu W, Xie K, Lu H, Xu L, Zhou S, Fang S. Initial clinical features of suspected coronavirus disease 2019 in two emergency departments outside of Hubei, China. J Med Virol 2020.

20.   Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020.

21.   Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of cardiac injury with mortality in hospitalized patients with covid-19 in Wuhan, China. JAMA Cardiol 2020.

22.   Yang W, Cao Q, Qin L, Wang X, Cheng Z, Pan A, et al. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (covid-19):A multi-center study in Wenzhou city, Zhejiang, China. J Infect 2020;80:388-93.

23.   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;395:507-13.

24.   Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. New Engl J Med 2020.

25.   Qian GQ, Yang NB, Ding F, Ma AHY, Wang ZY, Shen YF, et al. Epidemiologic and clinical characteristics of 91 hospitalized patients with covid-19 in Zhejiang, China: A retrospective, multi-centre case series. QJM 2020.

26.   Han R, Huang L, Jiang H, Dong J, Peng H, Zhang D. Early clinical and ct manifestations of coronavirus disease 2019 (covid-19) pneumonia. AJR 2020:1-6.

27.   Mo P, Xing Y, Xiao Y, Deng L, Zhao Q, Wang H, et al. Clinical characteristics of refractory covid-19 pneumonia in Wuhan, China. Clin Infect Dis 2020.

28.   Toren A, Weis E, Patel V, Monteith B, Gilberg S, Jordan D. Clinical predictors of positive temporal artery biopsy. Can J Opthalmol 2016;51:476-81.

29.   Myklebust G, Gran JT. A prospective study of 287 patients with polymyalgia rheumatica and temporal arteritis: Clinical and laboratory manifestations at onset of disease and at the time of diagnosis. Br J Rheumatol 1996;35:1161-8.

30.   Baldursson O, Steinsson K, Björnsson J, Lie JT. Giant cell arteritis in Iceland. An epidemiologic and histopathologic analysis. Arthritis Rheum 1994;37:1007-12.

31.   Kermani TA, Schmidt J, Crowson CS, Ytterberg SR, Hunder GG, Matteson EL, et al. Utility of erythrocyte sedimentation rate and C-reactive protein for the diagnosis of giant cell arteritis. Semin Arthritis Rheum 2012;41:866-71.

32.   Hu Z, Yang Q, Zeng S, Li J, Wu X, Cao L, et al. Giant cell arteritis in China: A prospective investigation. Angiology 2002;53:457-63.

33.   Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, china. Allergy 2020.

34.   Cao J, Tu WJ, Cheng W, Yu L, Liu YK, Hu X, et al. Clinical features and short-term outcomes of 102 patients with corona virus disease 2019 in Wuhan, china. Clin Infect Dis 2020.

35.   Liu KC, Xu P, Lv WF, Qiu XH, Yao JL, Gu JF, et al. CT manifestations of coronavirus disease-2019: A retrospective analysis of 73 cases by disease severity. Eur J Radiol 2020;126:108941.

36.   Chen J, Qi T, Liu L, Ling Y, Qian Z, Li T, et al. Clinical progression of patients with covid-19 in Shanghai, china. J Infect 2020;80:e1-e6.

37.   Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with covid-19 in Wuhan, china: A retrospective cohort study. Lancet 2020;395:1054-62.

38.   Rodríguez-Pla A, Rosselló-Urgell J, Bosch-Gil JA, Huguet-Redecilla P, Vilardell-Tarres M. Proposal to decrease the number of negative temporal artery biopsies. Scand J Rheumatol 2007;36:111-8.

39.   Vilaseca J, González A, Cid MC, Lopez-Vivancos J, Ortega A. Clinical usefulness of temporal artery biopsy. Ann Rheum Dis 1987;46:282-5.

40.   Stuart RA. Temporary artery biopsy in suspected temporal arteritis: A five year survey. N Z Med J 1989;102:431-3.

41.   Fernandez-Herlihy L. Temporal arteritis: Clinical aids to diagnosis. J Rheumatol 1988;15:1797-801.

42.   Sundholm JKM, Pettersson T, Paetau A, Albäck A, Sarkola T. Diagnostic performance and utility of very high-resolution ultrasonography in diagnosing giant cell arteritis of the temporal artery. Rheumatol Adv Pract 2019;3:rkz018.

43.   Hop H, Mulder DJ, Sandovici M, Glaudemans A, van Roon AM, Slart R, et al. Diagnostic value of axillary artery ultrasound in patients with suspected giant cell arteritis. Rheumatology 2020.

44.   Gonzalez-Gay MA, Vazquez-Rodriguez TR, Gomez-Acebo I, Pego-Reigosa R, Lopez-Diaz MJ, Vazquez-Triñanes MC, et al. Strokes at time of disease diagnosis in a series of 287 patients with biopsy-proven giant cell arteritis. Medicine 2009;88:227-35.

45.   Gonzalez-Gay MA, Lopez-Diaz MJ, Barros S, Garcia-Porrua C, Sanchez-Andrade A, Paz-Carreira J, et al. Giant cell arteritis: Laboratory tests at the time of diagnosis in a series of 240 patients. Medicine 2005;84:277-90.

46.   Bley TA, Weiben O, Uhl M, Vaith P, Schmidt D, Warnatz K, et al. Assessment of the cranial involvement pattern of giant cell arteritis with 3T magnetic resonance imaging. Arthritis Rheum 2005;52:2470-7.

47.   Liu K, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei province. Chin Med J 2020;133:1025-31.

48.   Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, china. JAMA Intern Med 2020.

49.   Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al. Kidney disease is associated with in-hospital death of patients with covid-19. Kidney Int 2020;97:829-38.

50.   Foroozan R, Danesh-Meyer H, Savino PJ, Gamble G, Mekari-Sabbagh ON, Sergott RC. Thrombocytosis in patients with biopsy-proven giant cell arteritis. Ophthalmology 2002;109:1267-71.

51.   Brittain GP, McIlwaine GG, Bell JA, Gibson JM. Plasma viscosity or erythrocyte sedimentation rate in the diagnosis of giant cell arteritis? Br J Ophthalmol 1991;75:656-9.

52.   Walvick MD, Walvick MP. Giant cell arteritis: Laboratory predictors of a positive temporal artery biopsy. Ophthalmology 2011;118:1201-4.

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53. Oh LJ, Wong E, Andrici J, McCluskey P, Smith JEH, Gill AJ. Full blood count as an ancillary test to support the diagnosis of giant cell arteritis. Internal Med J 2018;48:408-13.

54. El-Dairi MA, Chang L, Proia AD, Cummings TJ, Stinnett SS, Bhatti MT. Diagnostic algorithm for patients with suspected giant cell arteritis. J Neuroophthalmol 2015;35:246-53.

55. Grossman C, Barshack I, Koren-Morag N, Ben-Zvi I, Bornstein G. Baseline clinical predictors of an ultimate giant cell arteritis diagnosis in patients referred to temporal artery biopsy. Clin Rheumatol 2016;35:1817-22.

56. Nesher G, Nesher R, Mates M, Sonnenblick M, Breuer GS. Giant cell arteritis: Intensity of the initial systemic inflammatory response and the course of the disease. Clin Exp Rheumatol 2008;26:S30-4.

57. Martinez-Lado L, Calviño-Díaz C, Piñeiro A, Dierssen T, Vazquez-Rodriguez TR, Miranda-Filloy JA, et al. Relapses and recurrences in giant cell arteritis: A population-based study of patients with biopsy-proven disease from northwestern Spain. Medicine 2011;90:186-93.

58. Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, et al. A trial of lopinavir-ritonavir in adults hospitalized with severe covid-19. New Engl J Med 2020.

59. Ješe R, Rotar Ž, Tomšič M, Hočevar A. The role of colour doppler ultrasonography of facial and occipital arteries in patients with giant cell arteritis: A prospective study. Eur J Radiol 2017;95:9-12.

60. Nuenninghoff DM, Hunder GG, Christianson TJ, McClelland RL, Matteson EL. Incidence and predictors of large-artery complication (aortic aneurysm, aortic dissection, and/or large-artery stenosis) in patients with giant cell arteritis: A population-based study over 50 years. Arthritis Rheum 2003;48:3522-31.

61. Becourt-Verlomme C, Barouky R, Alexandre C, Gonthier R, Laurent H, Vital Durand D, et al. Inaugural symptoms of Horton's disease in a series of 260 patients. La Revue de Medecine Interne 2001;22:631-7.

62. Zhao W, Zhong Z, Xie X, Yu Q, Liu J. Relation between chest CT findings and clinical conditions of coronavirus disease (covid-19) pneumonia: A multicenter study. AJR 2020;214:1072-7.

63. Wang K, Kang S, Tian R, Zhang X, Zhang X, Wang Y. Imaging manifestations and diagnostic value of chest CT of coronavirus disease 2019 (covid-19) in the Xiaogan area. Clin Radiol 2020;75:341-7.

64. Xie H, Zhao J, Lian N, Lin S, Xie Q, Zhuo H. Clinical characteristics of non-ICU hospitalized patients with coronavirus disease 2019 and liver injury: A retrospective study. Liver Int 2020.

65. Oiwa H, Ichimura K, Hosokawa Y, Araki K, Funaki M, Kawashima M, et al. Diagnostic performance of a temporal artery biopsy for the diagnosis of giant cell arteritis in Japan-a single-center retrospective cohort study. Intern Med 2019;58:2451-8.

66. Berlit P. Clinical and laboratory findings with giant cell arteritis. J Neurol Sci 1992;111:1-12.

67. Gur H, Rapman E, Ehrenfeld M, Sidi Y. Clinical manifestations of temporal arteritis: A report from israel. J Rheumatol 1996;23:1927-31.

68. Mao L, Wang, M., Chen, S., He, Q., Chang, J., Hong, C., Zhou, Y., Wang, D., Li, Y., Jin, H., Hu, B. Neurological manifestations of hospitalized patients with covid-19 in Wuhan, China: A retrospective case series study. medRxiv 2020.

69.	Vaira LA, Salzano G, Deiana G, De Riu G. Anosmia and ageusia: Common findings in covid-19 patients. Laryngoscope 2020.

70.	Prior JA, Ranjbar H, Belcher J, Mackie SL, Helliwell T, Liddle J, et al. Diagnostic delay for giant cell arteritis - a systematic review and meta-analysis. BMC Med 2017;15:120.

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Table 1. Frequency of symptoms, physical signs, and laboratory abnormalities in giant cell arteritis (GCA) and COVID-19.

	Disease feature	Frequency in GCA median (range)	Number of patients, references	Frequency in COVID-19: median (range)	Number of patients, references
Demographics	Male (%)	31%		54%	
	Age: mean (sd)	74.9 (2.2)		53.6 (7.3)	
	Ethnicity	91% white (range, 55-100%)		Predominantly Asian	
Features more commonly reported in GCA than COVID-19	Jaw claudication	43% (38% to 48%)	1025 patients (3-6)	Not reported	-
	Abnormal temporal artery	43% (20% to 69%)	798 patients (4, 5, 7, 8)	Not reported	-
	Visual loss	26% (13% to 27%)	965 patients (3, 5, 6, 9)	1.4%	214 patients (2)
	Trismus, or difficulty opening the mouth	15% (10% to 21%)	278 patients (10, 11)	Not reported	-
Features that may be common to both diseases	Headache	66% (56% to 67%)	1025 patients (3-6)	9.8% (2.2% to 34%)	3378 patients (12-27)
	Scalp tenderness	26% (9% to 48%)	588 patients (4, 6, 9, 28)	Not reported	-
	Fatigue	38% (9% to 79%)	360 patients (29-32)	43.0% (13.2% to 75.3%)	3574 patients (12, 14, 15, 17, 18, 20, 21, 24-27, 33-37)
	Malaise	50% (38% to 71%)	260 patients (4, 28, 38, 39)	26.5% (23% to 30%)	149 patients (15, 16)
	Arthralgia	24% (0% to 40%)	151 patients (28, 39-41)	16.0% (14.9% to 61%)	1304 patients (18, 24, 27)
	Myalgia	36%	296 patients	15.0% (3.4% to 35.3%)	1681 patients

		(29% to 52%)	(3, 4, 28, 38)		(12, 15, 16, 18, 20-23, 25, 26, 34, 37)
	Sweats	34% (26% to 64%)	91 patients (29, 42, 43)	12.95% (11.8% to 14.1%)	251 patients (20, 22)
	Loss of appetite	40% (18% to 57%)	511 patients (6, 28, 38, 41)	24.6% (10.0% to 35.2%)	869 patients (12, 14, 15, 20, 25, 33)
	Weight loss	39% (24% to 54%)	563 patients (3, 6, 28, 38)	Not reported	-
	Dysphagia	7% (5% to 10%)	504 patients (11, 44)	Not reported	-
	Elevated CRP	100% (88% to 100%)	211 patients (7, 29, 45, 46)	66% (33% to 99%)	3332 patients (12, 15, 16, 18, 19, 22-26, 33, 34, 47-49)
	Elevated ESR	92% (79% to 100%)	356 patients (29, 45, 50, 51)	81.6% (50% to 93.8%)	1431 patients (15, 16, 19, 23, 36, 48, 49)
	Anaemia	67% (13% to 76%)	602 patients (4, 6, 7, 38)	36.1% (15% to 51%)	461 patients (16, 23, 25, 37)
	High platelet count	47% (20% to 57%)	436 patients (50, 52-54)	3.65% (0% to 54%)	419 patients (16, 22, 23, 25)
	Leukocytosis	31% (15% to 36%)	415 patients (29, 55-57)	9.15% (0% to 33%)	2981 patients (12, 13, 15, 16, 18, 19, 22-26, 33, 37, 47, 48, 58)
Features more	Cough	12%	621 patients	63.3% (34.6% to 82.2%)	4628 patients

commonly reported in COVID-19 than GCA		(8% to 26%)	(11, 59-61)		(12-27, 33-37, 47, 48, 62-64)
	Sputum production	Not reported	-	29% (4.4% to 56%)	3037 patients (12, 13, 15, 18, 19, 21, 22, 24, 25, 35, 37, 47, 48, 63, 64)
	Dyspnoea	6%	16 patients (65)	26.1% (1% to 59.6%)	3870 patients (12, 14-17, 20-25, 27, 36, 47, 48, 62-64)
	Fever	27% (17% to 33%)	422 patients (3, 4, 8, 28)	83% (32.5% to 98%)	5623 patients (12-27, 33-37, 47-49, 58, 62, 64)
	Sore throat	Not reported	-	8.5% (2.9% - 14.1%)	2808 patients (12-16, 18, 21-24, 26, 34, 36, 62, 63)
	Confusion	Not reported	-	9%	99 patients (23)
	GI upset (diarrhoea and/or vomiting)	4%	49 patients (66)	8% (1% to 39.6%)	4092 patients (12-16, 18-27, 33, 34, 36, 37, 47, 62-64)
	Altered sense of taste	10%	39 patients (29)	6%	214 patients (2)
	Altered sense of smell	4%	49 patients (66)	5%	214 patients (2)
	Lymphopenia	2%	42 patients (1)	53.2% (28% to 83.2%)	3332 patients (12, 13, 15, 16, 18, 19, 22-26, 33, 34, 36, 37, 47, 48, 58)

Thrombocytopenia	0% (0%-0%)	53 patients (1, 42)	12.7% (4.6% to 36.2%)	2018 patients (16, 22-25, 37, 48, 58)
High LDH	15%	39 patients (67)	41.5% (21.2% to 76%)	2423 patients (12, 13, 15, 16, 22-24, 37, 48, 58)
High CK	Not reported	-	13.2% (6.7% to 28.9%)	2019 patients (13, 16, 22-24, 33, 37, 58)

Comparison of the frequency of disease features reported in the GCA literature, compared to those in COVID-19 literature. Differences in the reporting of some of these features in the different diseases necessitated some subjective decisions in the presentation of the data, as follows. The frequency of scalp tenderness is unknown in COVID-19; but even during the pre-COVID era, scalp tenderness was common in patients referred with GCA who are not ultimately diagnosed with this disease (according to the classic meta-analysis of Smetana and Shmerling in 2002, scalp tenderness is present in around 1 in 4 of patients with suspected GCA who are not ultimately diagnosed with this disease). Therefore we made the conservative decision to present scalp tenderness here as a feature that may be common to both diseases. The "fatigue" category presented here does not include eight COVID-19 studies reporting "fatigue or myalgia", since it was not possible to separate the two symptoms from data presented in those publications.

Giant cell arteritis

- Jaw claudication
- Abnormal temporal artery
- Visual loss
- $\uparrow$platelets

- Headache
- $\uparrow$ESR / $\uparrow$CRP
- Scalp tenderness
- Fatigue / malaise
- Arthralgia / myalgia
- Sweats
- Anorexia / weight loss
- $\downarrow$Hb
- $\uparrow$WBC

COVID-19

- Cough
- Sputum
- Dyspnoea
- Fever
- Sore throat
- Confusion
- GI upset
- Alteration of smell / taste
- $\downarrow$lymphocytes
- $\downarrow$platelets
- $\uparrow$LDH /$\uparrow$CK
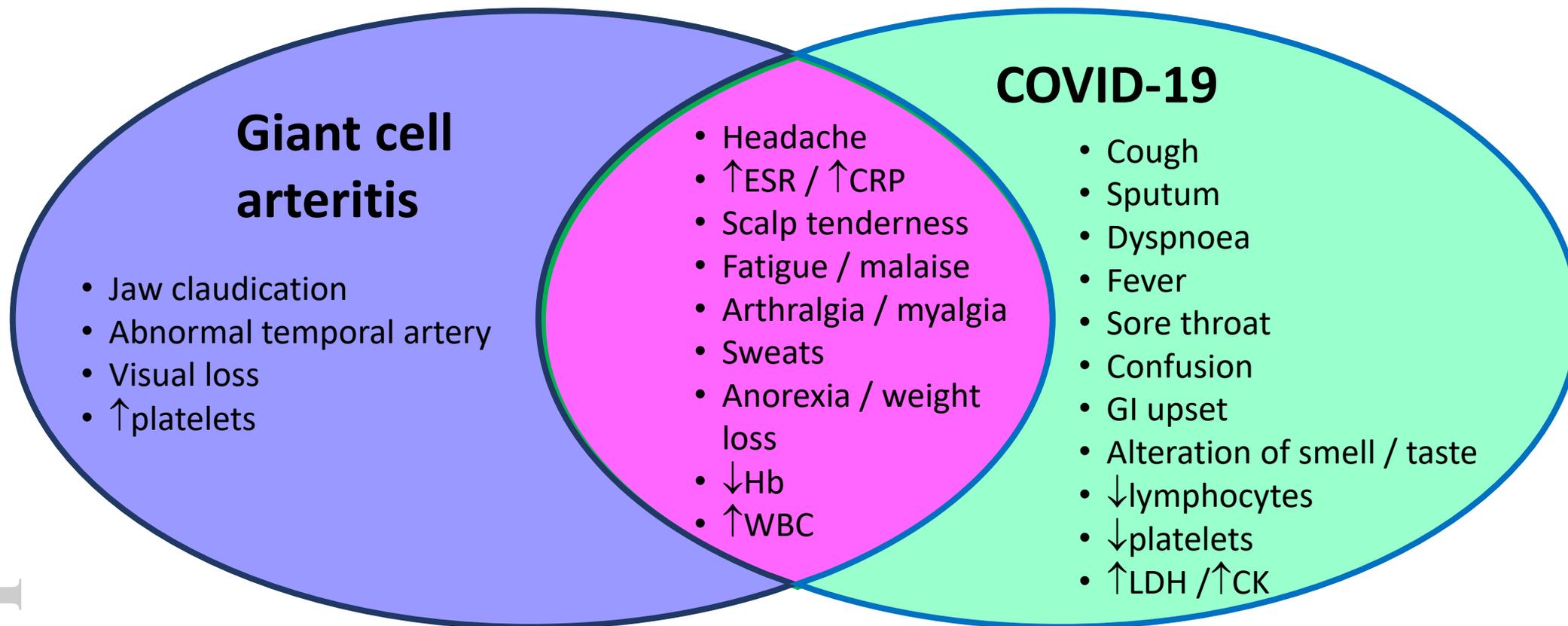
Patient NHS no:

Fill yellow boxes: 1 = yes, 0 = no

Male	*Age:*		*Symptom duration:*		*COVID19 risk:*	
Female		50-60		12-24 weeks		Work
		61-65		6-12 weeks		Home
		66+		<6 weeks		Hobbies

		GCA		**GCA/COVID**		**COVID**
head		Jaw claudication		Headache		Sore throat
		Hard to open mouth		Neck pain		Hoarse voice
		Tongue claudication		Scalp tenderness		Loss smell/taste
				Stroke		Confusion
				TIA		Dizziness
eye		Transient visual loss				Red eye
		Diplopia				Watery eye
		Visual fatigue				Chemosis
body		Shoulders stiff+achy		Back pain		Chilblains finger/toe
		Hips stiff+achy		Myalgia		
				Gen. arthralgia		
abdomen		Weight loss		Loss of appetite		Vomiting
						Diarrhoea
						Abdominal pain
chest		Arm claudication		Tingling hands/feet		Cough
						Sputum
						Shortness of breath
						Chest pain
						Palpitations
						Haemopytsis
temperature				Sweats		Rash
				Fatigue		Fever/chills
				Malaise		Rigors
exam vital signs		Thickened TA		Tender TA		High temp
		Nodular TA				High HR
		Pulseless TA				High RR
		Scalp necrosis				Low BP
		Bruit				
		Cranial nerve palsy				
		AION				
		CRAO				
		Visual field loss				
bloods		High platelets		CRP 6 to 10		Low lymphocytes
		High monocytes		CRP 11 to <25		Low eosinophils
				CRP 25+		Low platelets
				Elevated ESR		High D-dimer
				Elevated PV		High LDH
				Low Hb		High CK
						Acute kidney injury

Clinical probability of GCA (>50%/20-50%/<20%)