High incidence of giant cell arteritis during the COVID-19 pandemic: no causal relationship but possible involvement of stress

Sirs,

Giant cell arteritis (GCA) is the most common vasculitis in older adults. The mechanism causing the disease is not known, but infectious triggers have been suggested (1). The coronavirus 2 (SARS-CoV-2) disease 2019 (COVID-19) pandemic began in China at the end of 2019 and then spread rapidly worldwide. COVID-19 has various clinical presentations, from asymptomatic forms to acute respiratory distress syndrome and multi-organ failure. The vascular tropism of SARS-CoV-2 may result in endothelial activation with thrombosis (2) and viral-induced systemic vasculitis (3). We observed an increase in the incidence of GCA in our hospital in 2020, which suggested SARS-CoV-2 pandemic to be a trigger. We thus explored a possible direct relationship between SARS-CoV2 infection and GCA occurrence.

From 2010 through December 2020, we prospectively enrolled all patients diagnosed with GCA using the American College of Rheumatology criteria in the Internal Medicine department of a tertiary-care teaching hospital. The main GCA features of patients diagnosed in 2020 were compared with those of patients diagnosed during the previous decade. To track the regional SARS-CoV-2 pandemic, we collected the number of daily hospitalisations related to the virus during 2020 in our hospital's main catchment area, the Haute-Vienne Department, from the French public health website, which records daily hospitalisation declarations from each health centre in the department. Serum samples were analysed using two FDA-approved tests for the qualitative detection of IgG antibodies to SARS-CoV-2 in human serum and plasma using a chemiluminescence microparticle immunoassay (CMIA). The Alinity SARS-CoV-2 IgG (Abbott, Chicago, USA) assay detects IgG antibodies to the SARS-CoV-2 nucleocapsid protein and Liaison SARS-CoV-2 S1/S2 IgG (DiaSorin, Saluggia, Italy) detects IgG antibodies to the SARS-CoV-2 spike (S1/S2). Total RNA was extracted from biopsies in paraffin with a Maxwell® 16 LEV RNA FFPE Purification kit (Promega, Madison, USA). PCR was performed with the SARS-COV-2 R-GENE® kit (bioMérieux, Marcy-l'Étoile, France) allowing qualitative detection of SARS-CoV-2. In accordance with French law, the study was approved by the local ethics committee. Informed consent was obtained from all assessed patients.

During 2020, we diagnosed GCA in 28 patients. Figure 1 shows the incidence of new patients hospitalised for COVID-19 in Haute-Vienne and monthly new cases of

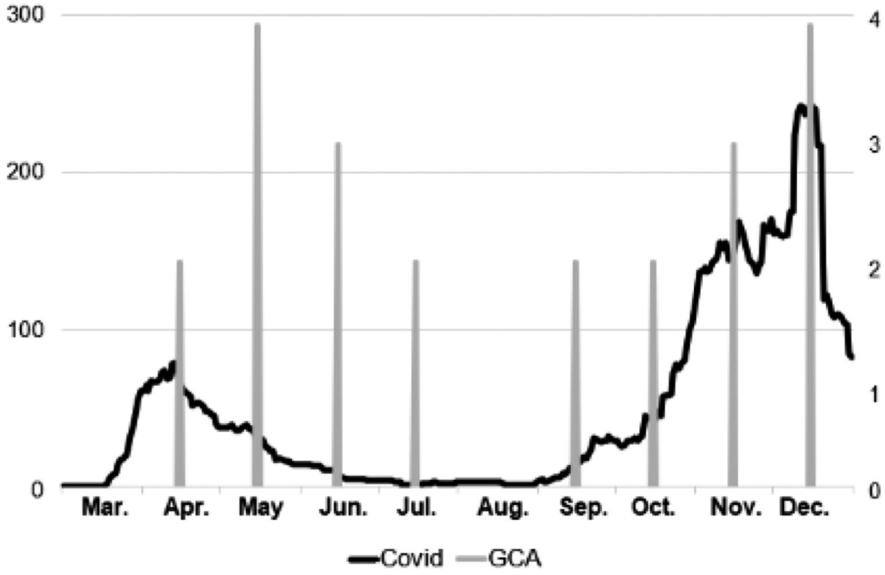

Fig. 1. Evolution of daily patients hospitalised for COVID-19 in Haute-Vienne, France (right *y*-axis) compared with new monthly cases of giant cell arteritis (GCA) (left *y*-axis) in 2020.

Table I. Comparison of characteristics of patients diagnosed with GCA in 2020 with those of patients diagnosed in 2010 to 2019.

Characteristic	2020 (n=28)	2010–2019 (n=205)	*p*-value
Demographic characteristics			
Age	72.3 [7.5]	74.7 [8.5]	0.1666
Female	20 (71.4)	140 (68.3)	0.8270
Disease history			
Diagnosis delay, days	93.6 [97.9]	85.3 [96.4]	0.3910
Acute form	16 (59.3)	92 (45.5)	0.1800
Reported trigger	1 (3.7)	44 (21.6)	**0.0350**
Constitutional symptoms			
General symptoms	24 (88.9)	136 (68.0)	**0.0252**
Fever	11 (40.7)	54 (26.6)	0.1253
Aortitis	10/25 (40.0)	41/106 (38.7)	0.9030
Rheumatological symptoms			
Polymyalgia rheumatica	8 (29.6)	64 (31.2)	0.8667
Peripheral arthritis	2 (7.4)	21 (10.2)	0.9999
Cranial symptoms			
Headaches	23 (85.2)	159 (77.6)	0.4613
Temporal artery abnormalities	17 (63.0)	123 (60.0)	0.7673
Scalp tenderness	16 (59.3)	90 (44.1)	0.1379
Occipital pain	19 (70.4)	93 (45.6)	**0.0155**
Neuro-ophthalmic symptoms			
Fugax visual symptoms	9 (33.3)	52 (25.6)	0.3934
Permanent amaurosis fugax	4 (14.8)	37 (18.0)	0.8841
Bilateral amaurosis fugax	0	11 (5.4)	0.4693
Stroke	3 (10.7)	8 (3.9)	0.1325
Buccal, throat and ear symptoms			
Number of pharyngeal symptoms	3.3 [2.5]	2.1 [1.9]	**0.0112**
Jaw claudication	7 (25.9)	64 (31.2)	0.5748
Painful mouth opening	12 (44.4)	48 (23.6)	**0.0208**
Maxillary pain	16 (59.3)	83 (41.3)	0.0770
Throat pain	9 (33.3)	44 (22.3)	0.2073
Dysphagia	6 (22.2)	25 (12.7)	0.1786
Dry cough	12 (44.4)	51 (26.2)	**0.0482**
Hoarse	8 (29.6)	26 (13.5)	**0.0307**
Otalgia	8 (29.6)	45 (23.4)	0.4818
Laboratory			
Erythrocyte sedimentation rate, mm	71.2 [30.2]	81.9 [30.1]	0.0981
C-reactive protein, mg/L	81.8 [65.9]	90.4 [71.2]	0.5858
Histology			
Positive temporal artery biopsy	18 (75.0)	122 (63.9)	0.2811

The values are reported as the absolute number (percentage) or mean [standard deviation].

GCA during 2020. Of the 28 patients, 22 were diagnosed beginning in March, when the Covid-19 pandemic started in Haute-Vienne. As Table I shows, we observed more constitutional and ear-nose-throat (ENT) symptoms, but no excess visual loss or other permanent ischaemic complications in the patients diagnosed in 2020 compared with those diagnosed over the previous decade. Of the 28 patients, 17 had serological tests with both assays and 25 a PCR study of a temporal artery biopsy for SARS-CoV-2. All serological and PCR tests were negative.

The COVID-19 pandemic has disrupted hospital care worldwide. We observed an increase in incident GCA cases in our department in 2020, as reported elsewhere (4, 5). We did not observe longer mean delays in GCA diagnosis and treatment, particularly in terms of access to hospital services, eye clinic consultations, vascular imaging, or temporal artery biopsy, contrary to reports from severely affected regions, such as Lombardy, Italy (6). Similarly, we did not see any increase in GCA-related ischaemic complications, particularly permanent loss of vision, in the 2020 group compared to the cohort 2010-2019. This observation is at odds with the report by Monti *et al*. (6), but consistent with reports from regions less impacted by the pandemic (4). The COVID-19 pandemic occurred in Haute-Vienne after it began in northern Italy and eastern France, which allowed us to organise regional care services. The increase in numbers of cases during 2020, with more cases observed during the COVID-19 pandemic peaks, suggests a role for the pandemic on GCA onset. The negative results of this study reasonably rule out the possibility of a direct relationship between SARS-CoV-2 infection and GCA occurrence. The role of stress, which has been previously emphasised in systemic diseases (7-9), is plausible, although we cannot push the hypothesis of chance aside. Finally, COVID-19 and GCA share some clinical and laboratory overlap that could be misleading (10). We found an increased frequency of ENT symptoms in GCA patients diagnosed in 2020 compared to patients diagnosed in the previous decade. During the pandemic, GCA onset involving prominent ENT symptoms might carry a risk of misdiagnosing GCA as SARS-CoV-2 infection, incorrectly leading to the patient's isolation with all the attendant ischaemic risks. Family physicians should be advised of the existence of symptom overlap between GCA and SARS-CoV-2 infection. Our observations call for well-designed prospective studies of stress in these patients during subsequent COVID-19 waves and on the potential impact of widespread COVID vaccination on GCA epidemiology.

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