

What comes after the lockdown? Clustering of ANCA-associated vasculitis: single-centre observation of a spatiotemporal pattern

Antineutrophil cytoplasm antibodies (ANCA)-associated vasculitides (AAV) are characterised by a heterogeneous clinical phenotype.¹ We report a cluster of 15 patients diagnosed with AAV either de novo (n=11) or with relapsing disease (n=4) during COVID-19 pandemic between February and August 2020. During this period, we observed two major phenomena: (1) an incidence-shift with a 'COVID-gap' of no diagnosed AAV cases during the lockdown period (March and April), followed by a 'postlockdown cluster' of 14 active patients (8 myeloperoxidase-ANCA, 6 proteinase 3-ANCA vasculitis) in the subsequent 4 months and (2) an increased incidence rate (figure 1 and online supplemental figure S3). Mean creatinine at baseline was 3.66 mg/dL. Inflammatory markers were significantly elevated in most patients, with a mean C reactive protein value of 9.93 mg/dL and an erythrocyte sedimentation rate of 83 mm per first hour. Despite detrimental effects on humoral immunity,² most patients received two doses of rituximab and methylprednisolone. No severe treatment complications occurred. SARS-CoV-2 PCR and serology were negative in tested patients. Further clinical and radiological characteristics are provided in online supplemental tables S1 and S2).

Comparable observations were recently reported from Italy, where a cluster of nine patients with AAV was detected in the second trimester of 2020. Kidney replacement therapy was necessary in seven of nine patients and one patient died.³ In contrast to these findings, disease courses in our cohort were comparably mild with a mean creatinine of 2.48 mg/dL at last follow-up and only one patient requiring intermittent kidney replacement therapy after spontaneous kidney bleeding from disseminated pseudoaneurysms.

The clustering of AAV in our centre may be attributable to a delayed presentation to our clinic. Containment measures may cause deferral of initial presentation after onset of symptoms by several means: (1) patients may be frightened of demanding healthcare services and (2) infrastructural cutbacks, such as restricted availability of public transports and an overall reduced access to healthcare institutions, further exacerbate this situation. Such delayed diagnoses may have significant impacts. For example, fast-track services facilitating immediate treatment have been

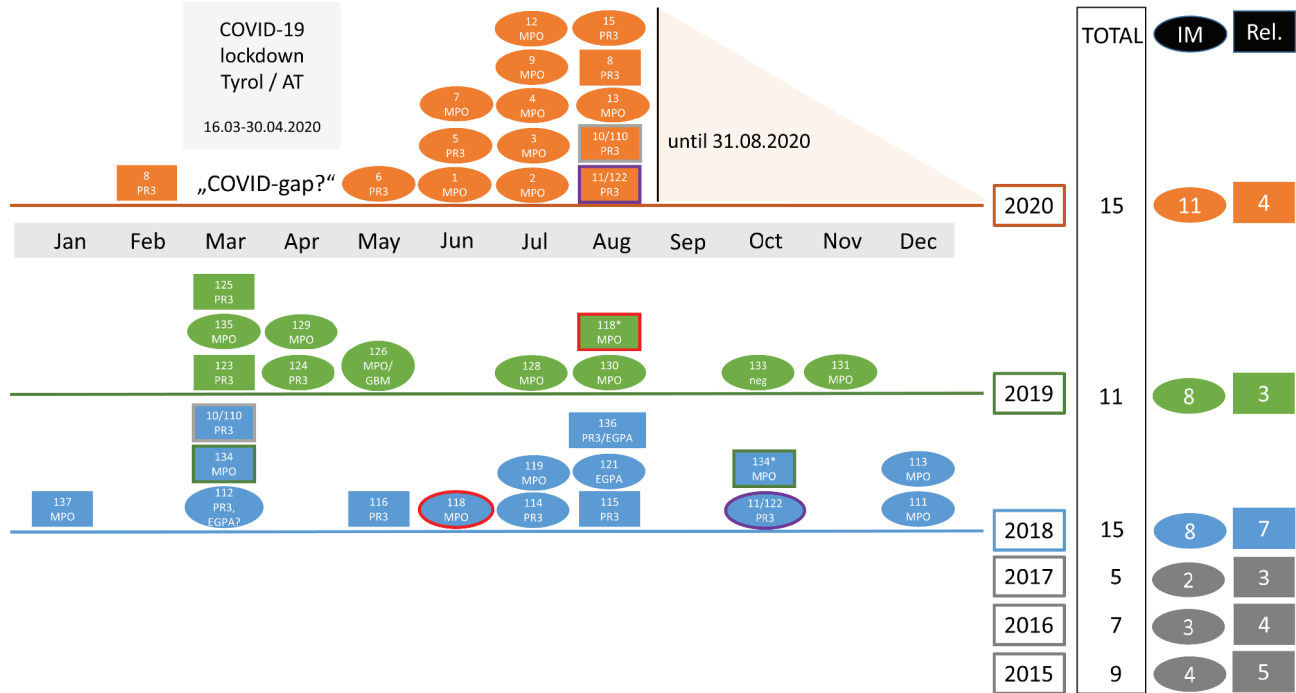




Figure 1 Timeline of incident ANCA-associated vasculitis cases in 2018, 2019 and 2020. Incident cases are posed on a timeline at the time of diagnosis of either initial manifestation (oval) or disease relapse (box). Duplicates are marked as such by a coloured frame. Numbers in boxes/ovals match with respective identity (ID) in online supplemental table S1. ANCA, antineutrophil cytoplasmic antibody; AT, Austria; IM, initial manifestation; MPO, myeloperoxidase; PR3, proteinase 3; Rel, relapse.

established for patients with giant cell arteritis who are at risk of blindness. A reduction of 75% in the request for such fast-track assessment, compared with the same time frame in 2019, was recently reported from a centre in Italy. Two cases of irreversible bilateral visual loss were attributed to a delayed diagnosis and deemed preventable.⁴

Our findings underline previous observations that the COVID-19 pandemic has significant impact on patients with diseases other than COVID-19.⁵ Although definite conclusions on clinical outcomes cannot be yet drawn, our observations indicate no detrimental effects of COVID-19 on clinical outcomes of non-infected patients with AAV. Nonetheless, prompt diagnoses and referrals currently affected by the ongoing global pandemic are crucial in the disease management. Compared with the previous years, we observed an over twofold increased incidence rate of AAV diagnoses (1.9 cases per month in 2020 vs 0.8 cases from 2015 to 2019) and almost threefold increased incidence rate of de novo AAV manifestations (1.2 de novo cases per month in 2020 vs 0.4 de novo cases from 2015 to 2019). This may not only be attributed to deferral of symptoms and delayed diagnoses, as patients showed significant overall improvement following initiation of immunosuppression. Though geographical clustering of AAV may be attributed to certain environmental factors,⁶ the impact of such factors on disease incidence remains elusive thus far. Finally, whether COVID-19 could be a trigger of regional clustering either directly (infection) or indirectly (effects of containment measures, eg, decreases in carbon dioxide emissions due to reduced air/ground travel or psychosocial consequences of a lockdown) is speculative and should be subjected to further investigation.

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