



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Case report

Acquired Angioedema Acute Attack After Administration of the Moderna COVID-19 (mRNA-1273) Vaccine

Alessandro Graziani^{a,*}, Caterina Savrie^b, Maria Giulia Sama^c

^a Medicina Interna Area Sub Intensiva Ospedale Santa Maria delle Croci, Viale Randi, 48121 Ravenna, Italy

^b Medicina Interna Azienda Ospedaliera Universitaria Ferrara, Italy

^c Medicina Interna Ospedale Santa Maria Delle Croci, Italy

Angioedema is an acute swelling of the deeper layers of the soft tissues or mucosa, caused by increased, localised permeability of the blood vessels.

There are two different conditions of angioedema, namely hereditary and acquired. Hereditary angioedema (HAE) is a rare form of severe angioedema caused by genetic mutations in the complement C1 inhibitor (C1-INH) gene, often leading to a decrease in C1-INH. Clinically, HAE is a disorder characterised by recurrent episodes of severe swelling (angioedema). The worst affected areas of the body are the limbs, face and intestinal tract, whilst airways are affected less frequently.¹ Acute attacks can be triggered by infections, emotional stress or trauma, but sometimes no trigger is identified. Acquired angioedema (AAE) typically affects patients over 40 with no family history of angioedema and onsets due to increased consumption (Type 1) or inactivation (Type 2) of C1-INH.

Low serum levels of C1q concentrations differentiate AAE from HAE.² An 86-year-old man presented at the Emergency Department following the onset of progressive edemas of the face, lips, neck and uvula after administration of the 4th dose of SARS-CoV-2 vaccine COVID-19 Moderna mRNA-1273 72 h prior. Previous SARS-CoV-2 vaccinations had been Pfizer-BioNTech. No urticaria was observed and the remainder of the physical examination was unremarkable. In the last eight weeks before the admission, he referred repeated episodes of acute swelling of the upper limbs in the absence of obvious triggers and lasted 3–5 days. At the admission, parenteral corticosteroids, antihistamines and epinephrine aerosol therapy were administered due to the clinical worsening and rapid development of respiratory failure in the patient, but to no benefit. He underwent a fibro bronchoscopy that showed edemas of the oropharynx and glottis and was subsequently sedated, and urgent orotracheal intubation performed. During the second day of hospitalisation, a surgical tracheostomy was performed owing to the persistence of significant laryngeal soft tissue oedema, evident on CT scans (Fig. 1). Blood tests showed C4 and C1 esterase inhibitor deficiencies (C4 0.02 g/l [0.1–0.4 g/l]; C1 29% [70–130%]), normal



Fig. 1. CT scan revealed a significant laryngeal soft tissue oedema.

tryptase and histamine. The haematological disease panel showed signs of Monoclonal Gammopathy of Undetermined Significance (MGUS), and the only therapeutic indications were clinical, and laboratory follow up. The patient was treated with tranexamic acid (1500 mg/day). In the case described, we believe that AAE was secondary to a haematological disease. It is most likely that the vaccine triggered an acute event in a patient who already had clinical manifestations of AAE.³ Watts MM et al. documented three cases of angioedema after an mRNA Pfizer-BioNTech vaccination that did not require tracheal intubation and improved after medical treatment (steroids, antihistamines). Angioedema onset times varied from 26 to 60 h after administration of the vaccine.⁴ To the best of our knowledge, this is the first report describing the occurrence of AAE after administration of the Moderna vaccination. Physicians examining patients who are to undergo SARS Cov-2 vaccinations should also take into account these less common symptoms and refer patients for further investigation in order to make a correct diagnosis.

* Corresponding author.
E-mail address: alessandro.graziani@auslromagna.it (A. Graziani).

References

1. Aberer W. Hereditary angioedema: an orphan but an original disease? *J Allergy Clin Immunol.* 2021;148:994–5, <http://dx.doi.org/10.1016/j.jaci.2021.07.026> [Epub 05.08.21; PMID: 34364956].
2. Cicardi M, Zanichelli A. Acquired angioedema. *Allergy Asthma Clin Immunol.* 2010;6:14.
3. Gobert D, Paule R, Ponard D, Levy P, Frémeaux-Bacchi V, Bouillet L, et al. A nation-wide study of acquired C1-inhibitor deficiency in France: characteristics and treatment responses in 92 patients. *Medicine (Baltimore).* 2016;95:e4363.
4. Watts MM, Maurer LE, Grammer LC, Saltoun CA, Stevens WW. Delayed angioedema after administration of the severe acute respiratory syndrome coronavirus 2 messenger RNA vaccine. *Ann Allergy Asthma Immunol.* 2022;128:215–6.