

## **Is isolated angioedema in the perioperative setting an allergy symptom? – A retrospective single-centre study.**

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**Background:** Angioedema is a potentially life-threatening condition in the perioperative setting. Causes of angioedema are numerous and the pathophysiology not fully understood. Angioedema presenting with urticaria or other allergy symptoms may be IgE mediated, but the role of allergy in angioedema presenting as the only symptom is unknown.

The Danish Anaesthesia Allergy Centre (DAAC) is the national reference centre for investigation of perioperative allergy. Patients are investigated for all drugs and substances they were exposed to prior to the reaction using skin tests, specific IgE tests and provocation tests. A relevant clinical reaction is confirmed as allergy by a positive provocation test or two other positive test results.

The aim of this study was to examine whether allergy could be identified in patients referred to DAAC with angioedema as the only symptom of suspected perioperative allergy.

**Methods:** A retrospective review of the DAAC database included 421 patients (median age 56, 58% women) investigated for suspected perioperative allergy in the period 2004-2015. Symptoms i.e. other skin symptoms than angioedema, respiratory and circulatory symptoms were correlated to the result of allergy investigation in patients presenting with angioedema.

**Results:** In total 132 of 421 (31%) reacted with angioedema (70% women). Of these 115 (87%) had one or more additional symptoms suggestive of allergy e.g. skin (urticaria/unclassified rash/flushing), respiratory or circulatory symptoms. In this group allergy was confirmed in 44 (38%) and this was comparable to the proportion of confirmed allergy in the total cohort 158 of 421 (38%). The remaining 17 (13%) patients presented with isolated angioedema with no other allergy symptoms or additional itch only. Of these, only two had allergy confirmed on investigation: one had elevated tryptase at the time of reaction and the other was on antidepressants, which potentially inhibit allergic skin symptoms due to an antihistamine effect. In four of the 17 patients (24%) concomitant ACE inhibitor treatment could explain the reactions and none of these had allergy confirmed on investigation with exposures from the perioperative setting.

**Conclusion:** Angioedema presenting as the only symptom in the perioperative setting, with normal serum tryptase at the time of reaction in patients not on medication that inhibits skin symptoms, is unlikely to be due to allergy. ACE inhibitors can cause non-allergic angioedema, also in the perioperative setting.