

1 **Drug-induced intradermal test-related fatal anaphylaxis**

2 **– appeal to comply with available guidelines**

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22 **Key words:** anaphylaxis, intradermal test, skin prick test, drug hypersensitivity

23 **Key message:** Skin testing with drugs is associated with a risk of severe anaphylaxis and precautions
24 have to be considered

25 Word count: 466 words

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27 There has been a report on a fatal anaphylactic reaction after skin testing with ceftriaxone in
28 Allergy Net, which necessitates to emphasize some general principles concerning skin tests
29 with drugs (1). A 59-year-old man with chest and abdominal trauma was admitted to the
30 emergency department. The patient's wife reported a previous allergic reaction to ceftriaxone
31 1 month before. An intradermal skin test with an undetermined concentrated ceftriaxone
32 solution was performed. Five minutes after the injection, the patient experienced severe
33 anaphylaxis with consecutive respiratory failure and died after delayed application of
34 adrenaline.

35 Skin testing is associated with well-known risk of severe anaphylactic reactions (2).
36 Betalactam antibiotics are one of the most important elicitors of severe or fatal reactions to
37 skin testing (2). Thus, when diagnosing patients with suspected betalactam hypersensitivity,
38 physicians have to 1) know about the risk involved and 2) take appropriate precautions. In
39 order to harmonize diagnostic procedures, the European Network on Drug Allergy, which is
40 the basis of the Drug Hypersensitivity Interest Group of the EAACI, has proposed guidelines
41 on how to perform skin testing in general (3), and on how to test patients with suspected
42 betalactam hypersensitivity specifically (4). Unfortunately, these guidelines were not
43 followed in the described case. It thus appears necessary to highlight important aspects
44 detailed in these guidelines. First, the exact type and severity of the allergic reaction in the
45 history should have been determined. Second, it remains unclear, why the treatment was not
46 done with an unrelated antibiotic of a different non-betalactam class and why the test
47 procedure was not postponed. It is always an excess risk to test a patient outside the routine
48 setting, where one is prepared and knowledgeable about possible side effects. Third, before
49 performing an intradermal test, a skin prick test should be done as recommended (3,4). Only
50 if this is negative after 15–20 min, an intradermal test can be performed for higher sensitivity.
51 Fourth, when testing patients with higher risk (e.g. severe previous reaction, unstable
52 condition), a careful risk-benefit analysis as well as initial testing with higher dilutions and

53 slow titration until regular test concentrations (for ceftriaxone: 2mg/ml) have been
54 recommended (3, 4). It remains unknown, which concentration has been initially used in the
55 described patient. Finally, emergency treatment has to be readily available and the staff has to
56 be experienced with the treatment of such reactions, which appears questionable in the
57 described case considering adrenaline was given 15 minutes later. If experience with skin
58 testing and emergency treatment can not be guaranteed, the patient should have been sent for
59 testing to a different referral center later. The described case had medicolegal consequences;
60 the judge considered the physician negligent in the test procedures and in emergency
61 treatment. This may have been avoided by a better knowledge of and by complying with
62 available guidelines.

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