

Supplementary Table S1. Naranjo Adverse Drug Reaction Probability Scale Assessment

Question	Answer	Score	Answer in this Case
1. Are there previous conclusive reports on this reaction?	Yes	0	No previous reports describing naltrexone-induced olfactory hypersensitivity were found in the literature.
2. Did the adverse event appear after the suspected drug was administered?	Yes	+2	Yes. The reaction emerged within 24 hours after starting oral naltrexone (50 mg/day).
3. Did the adverse reaction improve when the drug was discontinued?	Yes	+1	Yes. The hypersensitivity and dyspnea resolved after discontinuing naltrexone.
4. Did the adverse reaction reappear when the drug was readministered?	Do not know	0	Rechallenge not performed due to ethical concerns and patient refusal.
5. Are there alternative causes (other than the drug) that could have caused the reaction?	No	+1	Unlikely. No concurrent medications or substance use were present at onset.
6. Did the reaction reappear when a placebo was given?	Do not know	0	Not applicable.
7. Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	No	0	No measurement was performed.
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	Do not know	0	Not applicable (single fixed dose).
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	Yes	+1	Yes. The patient had an episode of acute respiratory distress after intravenous morphine administration in the past.
10. Was the adverse event confirmed by any objective evidence?	No	0	Only clinical observation and chronological relationship were available (no physiological testing).
Total Score		5	Probable association according to Naranjo scale classification.

Interpretation

According to the Naranjo algorithm, a total score of **5** indicates a *probable* relationship between naltrexone administration and the observed acute olfactory hypersensitivity with respiratory distress.

The **Naranjo Adverse Drug Reaction Probability Scale** is a standardized questionnaire used to assess the likelihood that an adverse event is related to a specific drug. It consists of ten structured questions, each assigned a weighted score based on the response. The questions evaluate aspects such as temporal association, dechallenge and rechallenge effects, presence of alternative causes, dose–response relationships, prior exposure, and objective verification.

A positive temporal relationship between the drug and the onset of symptoms, improvement after discontinuation, and recurrence upon re-exposure increase the total score, while evidence of alternative explanations or lack of consistency decrease it. Scores are summed to yield a total between –4 and +13. A total score of **9 or higher** indicates a *definite* adverse drug reaction, **5 to 8** suggests a *probable* relationship, **1 to 4** denotes a *possible* link, and **0 or less** is considered *doubtful*. This scale provides a systematic and reproducible approach for causality assessment in clinical pharmacology and case reports.