

CASE REPORT

Anaphylaxis probably induced by transfer of amoxicillin via oral sex

Nazaret Gómez Caballero,¹ Susana Almenara,² Antonia Tévar Terol,¹ José Francisco Horga de la Parte²

¹Department of Primary Care, Hospital General Universitari d'Alacant, Alicante, Spain

²Department of Clinical Pharmacology, Hospital General Universitari d'Alacant, Alicante, Spain

Correspondence to

Susana Almenara, susanaalmenara@gmail.com

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SUMMARY

We present a case of a possible amoxicillin-induced anaphylaxis in a sensitive woman triggered by an instance of oral sexual contact with a man who was taking amoxicillin-clavulanic acid treatment. To our knowledge, this is the first case reported of a suspicion of amoxicillin-induced anaphylaxis in a woman after a sexual contact with a man who was taking the drug, we hypothesised an oral drug transfer through semen.

Studies about amoxicillin concentrations achieved in semen after a drug intake are scarce. There are few cases reported of hypersensitivity reactions induced by drugs transported in semen but we have found some concern in sensitive patients about the possibility of transference of allergens via sexual intercourse. As clinicians, we consider that it is important to be aware of the existence of this possibility both in the diagnosis and in the prevention of anaphylactic reactions.

BACKGROUND

Anaphylaxis is defined by the Committee of the World Allergy Organization as a severe, life-threatening generalised or systemic hypersensitivity reaction.¹

The incidence of anaphylaxis in most recent studies is about 50 episodes per 100 000 person-years with a mortality of 0.12%–0.16%.² Foods are the most frequent causative agents in children while in adults these are drugs, particularly beta-lactam antibiotics and non-steroidal anti-inflammatory drugs.^{2,3} Anaphylactic reactions to penicillins occur in 0.004%–0.015% of treatment courses.⁴ Different studies in the UK, Australia, the USA and Spain have shown that the incidence of anaphylaxis is increasing over time, especially in paediatric population and in relation to food.^{3,5–7}

An uncommon cause of anaphylaxis in women is seminal plasma allergy (SPA). In SPA, symptoms occur during or after sexual intercourse and most of these reactions are the result of an IgE-mediated response to a specific protein in seminal plasma.⁸ Coital allergic reactions can also be induced in allergic women by the transfer of allergens (drugs or food) present at low concentrations in the seminal plasma of their partners.⁹

In case of anaphylaxis, it is essential to make a correct and early diagnosis in order to initiate adequate treatment and to avoid fatalities. Anaphylaxis can be underdiagnosed in a 66% of patients

assisted at an emergency department.¹⁰ The aetiologic diagnosis and provision of educational measures are important as a safeguard against future events.

Here, we present a case of a suspicion of drug anaphylaxis by seminal transfer of amoxicillin during sexual intercourse with oral ejaculation.

CASE PRESENTATION

A 31-year-old woman appeared at the emergency room with abundant vomiting, dyspnea and full-body urticaria. She had not taken any medication, unusual food or sustained sun exposure and did not present any insect bites. Her blood pressure was 110/74 mm Hg, her pulse rate 80 bpm, her temperature 36°C and she had an oxygen saturation of 98%. Lung auscultation revealed normal vesicular murmur and diffuse expiratory wheezing. Symptoms started after a sexual encounter with no barrier methods used including vaginal and oral sex with oral ejaculation.

Her partner, a 32-year-old man was on treatment with ibuprofen 600 mg and amoxicillin-clavulanic acid (Augmentine) 500/125 mg every 8 hours because an otitis media. When symptoms started he was in the fifth day of treatment. He took both medications approximately 4 hours before the sexual contact.

The patient never presented similar manifestations in previous sexual relationships and her only relevant medical history was penicillin allergy that was diagnosed in childhood by a compatible skin reaction after taking amoxicillin.

The clinical event was consistent with a moderate anaphylactic reaction and consequently epinephrine, methylprednisolone and nebulised salbutamol were administered.

INVESTIGATIONS

In order to study, the reaction she was given an appointment at allergology consultation but she did not attend, nor did any test subsequently.

OUTCOME AND FOLLOW-UP

Dyspnea gradually improved until it completely resolved after 6 hours of treatment administration. A blood test and an ECG were performed showing no relevant alterations. A week later, she was fully recovered.

DISCUSSION

Anaphylaxis is easily suspected when there are clear manifestations such as urticaria, oedema or dyspnea



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and there is indication of recent contact with a known allergen, but the clinical spectrum of anaphylaxis may be more complex, featuring symptoms that can potentially be confused with other conditions as asthma attack, anxiety or vasovagal syncope and considering that, in many cases, finding the causative agent is not possible.

In adults, the most frequent cause of anaphylaxis are drugs, with symptoms usually appearing 30 min after taking the drug.³ Here, to establish causation, the history of penicillin allergy and the time elapsed between sexual intercourse and the development of symptoms, are important. The patient declared penicillin allergy and hence we suspect that the causative agent of anaphylaxis was the amoxicillin taken by her partner and transferred through semen during sexual intercourse that included oral and vaginal sex without the use of a condom and with oral ejaculation. According to the Naranjo algorithm,¹¹ amoxicillin was considered a possible causal agent with a score of 6, while ibuprofen and clavulanic acid (possibly transported by semen too) obtained a score of 5. The difference between these scores is due to the re-exposure criterion that is only met with amoxicillin. SPA is uncommon and the patient never presented hypersensitivity reactions during or after previous contacts with semen.

There are few studies on drug concentration in the ejaculate and most of them are focused on the penetration of antibiotics into prostatic tissue in order to identify those agents clinically effective against prostatic infections.¹² In this sense, it is important to note that the contribution of the prostate to semen in healthy human males is approximately 30% while some 60% originates from the seminal vesicles, and the remaining 10% comes from the epididymis, ampullae, bulbourethral and urethral glands.¹³

The lipid solubility of drugs is an important factor to their passing into semen. The degree of protein binding, the size and shape of the molecule are also important and another influential factor is the dissociation-constant degree.¹² Semen pH is alkaline (8.2 ± 0.3) while plasma pH is between 7.35 and 7.45, meaning that weak acids will concentrate in semen.¹⁴ Amoxicillin is a weak acid and has lipid solubility so theoretically it will concentrate amply in semen.

We did not find pharmacokinetics studies about semen concentrations achieved during treatment with amoxicillin in humans but there are some studies of amoxicillin concentrations in human prostate that show poor penetration, probably due to the acidic pH of prostatic fluid (approximately 6.6 in healthy humans).^{12, 15} In a pharmacokinetic study, the prostate/serum ratio of amoxicillin at 3, 4, 6, 8 and 10 hours after amoxicillin-clavulanic 875/125 mg oral dose were 0.15, 0.28, 0.63, 0.64 and 1.80.¹⁶ Presumably, the concentration of amoxicillin in ejaculate fluid will be higher than that reached in the prostate since contribution of the prostate to seminal fluid is only 30%. The contribution of the seminal vesicles and other glands as well as the possibility of urethral remnants eliminated during urination must also be taken into account.¹³

In any case, allergic anaphylaxis is considered an idiosyncratic reaction and, if present in semen in any concentration, may trigger the response.

We have found few reports of allergic reactions related to drug transfer via sexual intercourse. There are reports of women with local symptoms or urticaria after sexual intercourse in relation to thioridazine, vinblastine and penicillin.^{17–19} We have found also four cases reported of drug-fixed eruptions in the genitals of men, in the context of intercourse and contact with bodily fluids containing the drug antigen.^{20, 21} Also reported are cases

of allergic reactions to amoxicillin and bacampicillin transferred through kissing, but this kind of transferring is more frequent to affect in case of personal history of food allergy.²²

To our knowledge, this is the first reported case of a possible amoxicillin induced anaphylaxis in a woman after an oral sexual contact with a man who was taking the drug.

We have detected some concern about this issue in consultations carried out by sensitive patients in internet forums. This concern on the part of patients is accompanied by a lack of scientific information around this question. We think that as clinicians it is important to be aware of this phenomenon so was to inform and prevent potentially serious reactions in sensitised patients. We also recommend condom use during treatment with drugs that can induce hypersensitivity responses in partners.

This adverse reaction was reported to the Spanish Pharmacovigilance System (notification number: 10-601436).

Learning points

- ▶ Anaphylaxis is a common medical emergency.
- ▶ A correct and early diagnosis is fundamental in order to initiate adequate treatment and avoid fatalities.
- ▶ To be aware of a possible sexual transfer of an allergen can be useful in diagnosis, treatment and prevention.
- ▶ To inform patients about the possibility of allergen transfer from sexual partners could be a good preventive measure.

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