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CASE REPORT

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Oral Penicillin Desensitization in a Pregnant Patient with Syphilis and a History of Immediate Hypersensitivity: A Case Report

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ABSTRACT

Penicillin remains the only proven treatment for syphilis during pregnancy, as no alternative antimicrobial regimen has demonstrated comparable efficacy in preventing vertical transmission. A reported penicillin allergy may therefore represent a significant barrier to optimal management. We report the case of a pregnant woman at 25 weeks' gestation with syphilis and a remote history suggestive of an immediate hypersensitivity reaction to penicillin, characterized by syncope and loss of consciousness during childhood. Given the urgent need for penicillin therapy and the high-risk nature of the reported reaction, penicillin skin testing was not pursued. Instead, oral penicillin desensitization was performed under continuous cardiac and hemodynamic monitoring in an intensive care unit setting. A stepwise oral desensitization protocol was successfully completed without any objective or subjective signs of hypersensitivity. Following desensitization, standard weekly intramuscular benzathine penicillin therapy was administered without adverse reactions, and treatment was completed uneventfully. This case illustrates that oral penicillin desensitization, when performed with appropriate monitoring, can enable safe administration of first-line therapy in pregnant patients with high-risk penicillin allergy histories. Careful clinical judgment and individualized risk assessment remain essential in time-sensitive scenarios where alternative treatments are not acceptable.

Keywords: Penicillin allergy, drug desensitization, pregnancy, syphilis

INTRODUCTION

Syphilis diagnosed during pregnancy requires prompt and definitive treatment, as delays may lead to preventable adverse fetal outcomes. Despite advances in screening programs, maternal syphilis continues to be encountered in routine clinical practice, and treatment decisions often need to be made without delay (1).

Penicillin remains central to the management of this infection in pregnant patients. Benzathine penicillin G is the only antimicrobial agent with established efficacy for preventing vertical transmission, and no alternative regimen has demonstrated comparable fetal protection. For this reason, international recommendations consistently state that penicillin should be administered whenever syphilis is identified during pregnancy, even in the presence of a reported penicillin allergy (1). In clinical practice, however, a history of penicillin allergy may complicate management. Many such histories are remote, incompletely documented, or based on childhood events; yet they frequently influence treatment decisions (2). In pregnancy, where therapeutic alternatives are limited, this creates a narrow margin for clinical error.

Desensitization provides a practical pathway in situations where penicillin is clearly indicated but allergy concerns exist. By exposing the patient to gradually increasing doses, temporary tolerance can be achieved, allowing

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completion of therapy under close supervision (3). This tolerance is transient and dependent on uninterrupted exposure, a point that has been emphasized repeatedly in the literature (3,4). Oral desensitization protocols have been used for decades and continue to be applied in a variety of clinical settings, particularly when careful monitoring can be ensured (4,5). In selected high-risk cases, especially when the reported reaction suggests an immediate mechanism and treatment cannot be postponed, clinicians may reasonably proceed directly to desensitization rather than formal allergy testing (3,5). Such decisions are typically guided by clinical judgment, patient-specific risk factors, and the availability of appropriate monitoring.

We report here a pregnant patient with syphilis and a history compatible with an immediate reaction to penicillin who underwent successful oral penicillin desensitization under intensive care unit monitoring, followed by completion of weekly benzathine penicillin therapy without complications.

CASE PRESENTATION

A 27-year-old pregnant woman at 25 weeks' gestation (second trimester) was referred to the Allergy and Immunology service for evaluation and management of a reported penicillin allergy in the context of syphilis diagnosed at 25 weeks' gestation, for which penicillin is the only proven treatment during pregnancy. Her past medical history was unremarkable except for a childhood reaction attributed to penicillin. According to available medical records and patient report, at the age of 12 she had received intramuscular penicillin for acute pharyngitis and subsequently developed syncope accompanied by diaphoresis, transient loss of consciousness, and throat irritation. She had been evaluated at the emergency department at that time and was informed that the episode was consistent with a drug-related allergic reaction. No further diagnostic testing was performed, and lifelong penicillin avoidance was advised. No reliably documented subsequent exposures to penicillin or other β-lactam antibiotics were available. The specific penicillin formulation responsible for the index reaction could not be verified from the available history. Review of the electronic health records revealed no subsequent prescriptions or documented exposure to penicillin or other β-lactam antibiotics since the index event.

At the current presentation, she required urgent initiation of penicillin therapy for syphilis. Given the history suggestive of a high-risk immediate hypersensitivity reaction characterized by syncope and loss of consciousness, together with the pregnancy status, the time-sensitive need for definitive therapy, and the lack of acceptable alternatives, skin testing was not pursued. A direct desensitization approach was therefore planned. Baseline laboratory evaluation revealed a serum tryptase level within normal limits, measured outside the acute reaction period, suggesting the absence of underlying mast cell disease. Other routine laboratory findings were unremarkable. Written informed consent was obtained prior to desensitization after counseling regarding potential maternal and fetal risks, benefits, and alternatives.

Oral penicillin desensitization was performed in an intensive care unit setting to ensure maximal patient safety. The procedure was conducted under continuous cardiac and hemodynamic monitoring, with full resuscitation equipment and trained personnel immediately available throughout the process. A previously published stepwise oral penicillin desensitization protocol was applied, consisting of gradual dose escalation at predefined intervals until the target therapeutic dose was achieved (Table I).

Table I: Oral penicillin desensitization protocol used in the present case

Step	Penicillin concentration (U/mL)	Volume administered (mL)	Dose per step (U)	Cumulative dose (U)	Time interval (min)
1	1,000	0.1	100	100	15
2	1,000	0.2	200	300	15
3	1,000	0.4	400	700	15
4	1,000	0.8	800	1,500	15
5	1,000	1.6	1,600	3,100	15
6	1,000	3.2	3,200	6,300	15
7	1,000	6.4	6,400	12,700	15
8	10,000	1.2	12,000	24,700	15
9	10,000	2.4	24,000	48,700	15
10	10,000	4.8	48,000	96,700	15
11	80,000	1.0	80,000	176,700	15
12	80,000	2.0	160,000	336,700	15
13	80,000	4.0	320,000	656,700	15
14	80,000	8.0	640,000	1,296,700	15

The protocol was administered orally at 15-minute intervals under continuous cardiac and hemodynamic monitoring in an intensive care unit setting. Each dose was diluted in water prior to administration. No allergic reactions were observed during the procedure.

The patient was closely observed during each step for any subjective symptoms or objective signs of hypersensitivity. The desensitization protocol was completed successfully without interruption. No allergic reactions, including cutaneous, respiratory, cardiovascular, or gastrointestinal manifestations, were observed at any stage of the procedure. Vital signs remained stable throughout, and no rescue medications were required.

Following successful desensitization, standard intramuscular benzathine penicillin therapy was initiated on a weekly schedule in accordance with syphilis treatment guidelines. All subsequent doses were administered without adverse reactions, and penicillin therapy was completed uneventfully. The patient remained clinically stable, and no delayed hypersensitivity reactions were observed during follow-up.

DISCUSSION

Management of syphilis during pregnancy is time-sensitive, and treatment should not be delayed once the diagnosis is established. Benzathine penicillin G remains the only therapy with proven efficacy in preventing vertical transmission, making avoidance of penicillin an unacceptable option in pregnant patients with syphilis (1).

In the present case, the patient reported a childhood reaction to penicillin characterized by syncope and loss of consciousness. Although such histories do not always represent true IgE-mediated allergy, they are generally regarded as high risk in clinical practice. Under these circumstances, the role of penicillin skin testing becomes limited, particularly when diagnostic delays are unlikely to alter the need for penicillin therapy. Previous reports have described proceeding directly to desensitization in similar settings, especially during pregnancy (3,6). Oral penicillin desensitization was selected and performed under intensive care unit monitoring due to patient-specific risk factors rather than the route of administration itself. The protocol was completed without interruption or breakthrough reactions, supporting prior observations that oral desensitization can be safely applied when appropriate monitoring is available (5). Following desensitization, weekly intramuscular benzathine penicillin was administered without adverse reactions. As tolerance induced by desensitization is temporary and dependent on uninterrupted exposure, this outcome underscores the clinical effectiveness of the procedure in enabling completion of definitive therapy (4,5). Although limited by its single-patient nature, this case illustrates a pragmatic approach to a common yet challenging clinical scenario. A further limitation is the uncertainty regarding the exact culprit penicillin derivative. Additionally, the possibility of immunological forgetting — that is, a gradual decline in sensitization over the more than ten years that elapsed since the index reaction — cannot be excluded, and may have partly contributed to the uneventful course observed during desensitization.

Penicillin allergy is frequently overreported, and more than 90% of individuals labeled as penicillin-allergic are ultimately able to tolerate penicillin after formal evaluation (skin testing and oral challenge) (7). Mislabeling commonly reflects childhood events, non-IgE-mediated adverse effects, or incomplete documentation. In non-urgent settings, structured de-labeling strategies are encouraged; however, pregnancy with syphilis represents a uniquely time-sensitive context in which penicillin remains the only proven therapy to prevent vertical transmission. Accordingly, in this case we proceeded directly to desensitization, influenced not only by the reported high-risk features but also by the urgency of definitive treatment and the lack of acceptable alternatives.

In conclusion, this case highlights that oral penicillin desensitization, when performed under appropriate monitoring, can enable safe administration of first-line therapy in pregnant patients with high-risk penicillin allergy histories. Careful clinical judgment and individualized risk assessment remain central to management in such time-sensitive situations.

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Conflict of Interest

The authors declare no conflict of interest.

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The authors declare that no artificial intelligence (AI)-assisted technologies were used for data analysis or clinical decision-making in this study. The authors take full responsibility for the content and originality of the work.

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