

DELAYED RESPONSE TO INTRADERMAL TEST BY BENZATHINE PENICILLIN

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Summary

A delayed, - Tuberculin type-response to intradermal (ID) test with benzathine penicillin is described in a 50 year old female. She did not develop any sign of drug reaction on receiving intramuscular injection of that drug. None of the 65 patients who were studied in detail for the ID test response to various penicillins showed such a delayed response.

Introduction

With the ever-increasing use of drugs in the treatment of diseases, more and more adverse reactions are noted each year and they manifest often as cutaneous reactions. The penicillins, like all other drugs, have the capacity to provoke a variety of reactions, the incidence of which varies from 1 to 10%¹. The role of humoral antibodies in penicillin allergy is well understood². The delayed (48 hr.) type response to intradermal test with penicillin was first described in 1944³. Redmuud and Levin found that the delayed hypersensitivity to penicillin was identical to that produced by tuberculin⁴. Among all those tests to detect hypersensitivity to penicillin,^{5,6,7,8} the intradermal test is widely used due to its simplicity. A positive reaction to the test is indicated by the development of wheal and erythema⁹ usually within half an hour. In addition to its antigenic property, penicillin has irritative property also¹⁰ which is responsible for the pain and

sterile inflammatory reaction at the site of injection¹¹. A patient who showed delayed hypersensitivity response to I.D. benzathine penicillin is presented in this article.

Case report

A 50 year old housewife who had been suffering from filarial elephantiasis and infective eczema of both of her legs for 6 years, was admitted to the Dermatology ward at Medical College Hospital, Trivandrum in May 1980. Excepting for mild pallor, clinical examination showed no abnormality.

An intradermal test with benzathine penicillin (Benzathine Penicillin G - *Hindusthan Antibiotics*) did not show any wheal and flare response after half an hour at the test site on forearm. Patient was given 2.4 mega units of benzathine penicillin deep I.M. into her buttocks. She had no itching or other symptoms after the injection. On the third day of receiving the injection patient developed a painless and non tender circumscribed indurated swelling at the test site. The swelling gradually increased in size and measured 3 cm. on the 5th day and subsided

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Received for publication on 22-12-1980

completely by the 9th day leaving no sequelae. The development of an indurated swelling on the third day without evidence of earlier wheal and flare response at the test site was unusual and attracted our attention. The possibility of accidental injection of the test material into the subcutis was thought of. After 3 weeks, before giving another injection of benzathine penicillin, patient was again tested intradermally with 0.1 ml of 1/10,000 solution of this drug. Great care was taken to introduce the drug into the dermis itself and not into the subcutis. To our surprise the patient again showed a delayed-tuberculin-type response only (Fig. 1) without showing any early wheal and erythema response to the test dose. Again a series of I.D. tests were performed with benzathine penicillin, benzyl penicillin and procaine penicillin. It was found that only benzathine penicillin was capable of producing this type of delayed hypersensitivity reaction. Sixty five patients who had received I.D. tests with different preparations of penicillins were closely observed to study the pattern of reaction at the test sites. It was found that 5 (7.7%) had early flare and wheal response to test dose while none developed delayed - tuberculin - type reaction (Table 1). A patch test done with solution of benzathine penicillin gave negative result. Histological study of an I.D. test-induced nodule revealed dense collection of mononuclear cells in the deep dermis and subcutis. There was no evidence of vasculitis or necrosis of the fat in the subcutis.

Investigations

Blood: Hb - 10 Gm%; Total count 8400 cells/cmm.

Differential count P₅₀L₄₀E₁₀M₀, E.S.R. 30mm/1st hr (Westergren).

V. D. R. L. Non reactive. *Urine:* Normal.

X-ray: Chest PA view - Normal.

Discussion

Immunological reactions to penicillins are not uncommon. The role of humoral antibodies in various types of reactions like anaphylaxis, serum sickness, arthus reaction etc. following penicillin administration are well studied^{1,2}. A wheal and erythema at the site of I.D. test with penicillin is usually considered as hypersensitivity to that drug⁹. This response develops within $\frac{1}{2}$ hr. and subsides in a few hours. Though false results may occur, the I.D. test is generally considered essential before injection of penicillin. Without showing any evidence for early wheal and erythema response at the test site, our patient developed a delayed tuberculin-type response to benzathine penicillin. We have not come across such a response to any

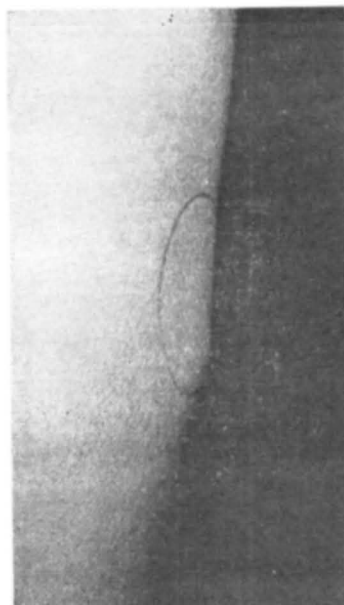


Fig: 1

Note delayed (72 hr.) response to I.D. test on forearm with benzathine penicillin.

type of penicillin in the past. In our patient, only benzathine penicillin could produce this type of response. Usually penicillins cross react antigenically^{11,13}. But our patient did not show such a delayed hypersensitivity to procaine penicillin and benzyl penicillin. None of the 65 patients who were studied in detail for the I.D. test response to various penicillins developed a delayed response, though 5 of them had immediate wheal and erythema at the test site. We do not agree with Redmund and Levin's⁴ statement that the incidence of delayed hypersensitivity is ten times higher than the actual sensitivity to penicillin. The significance of this delayed response is not well understood. In a considerable number of patients it is not associated with drug reaction. This simply indicates that the patient has been exposed to that drug and has developed an immunological but not necessarily a clinical reaction to it¹⁴. But De Weck¹⁵ is of opinion that most of the exanthematic drug eruptions are due to delayed hypersensitivity. Peck et al¹⁶ considered this type of response to I.D. test as the most important test for penicillin sensitivity. Our patient did not develop any sign of drug eruption. Benzathine penicillin by its irritative property, if injected into the subcutis may result in necrosis of the fat and subsequent development of a sterile abscess. But in our case, great care was taken to introduce the drug into the dermis itself. Further, histology did not reveal any acute inflammatory cells or necrosis of the fat. The collection of mononuclear cells in the deeper dermis and subcutis further strengthens the diagnosis of "cell mediated immune response" at the test site. Our patient gave a negative result to the patch test with benzathine penicillin. The role of patch test in diagnosis of delayed hypersensitivity in allergic contact eczema and fixed drug eruption are important. But its

value in the diagnosis of hypersensitivity to drugs given systemically is very limited⁹.

TABLE 1

Intradermal test response to various penicillins

No. of patients	Penicillin Preparation	Response	
		Early	Delayed
25	Benzathine penicillin	3	0
25	Procaine penicillin	2	0
15	Benzyl penicillin	0	0
Total 65		5	0

Acknowledgement

I am grateful to Dr. C. Gangadharan, Professor, Department of Dermatology and Superintendent, Medical College Hospital, Trivandrum for his kind permission to utilise hospital records.

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A symposium on Rural Dermatology is being held in Manila in May, 1982.

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