

## ANAPHYLACTIC REACTION TO MANTOUX TEST

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Anaphylactic reaction (type I hypersensitivity) following Mantoux test with purified protein derivative was observed in a 17-year-old girl who had no evidence of tuberculosis in her. Repeated injections of the test antigen produced more and more severe hypersensitivity reactions.

**Key words :** Mantoux test, Tuberculin, Anaphylaxis, Tine test.

Tuberculin test detects delayed hypersensitivity to tuberculo-protein. The old tuberculin has now been replaced by purified protein derivative (PPD) which is introduced into the skin either intradermally (Mantoux test), or by multiple puncture method (Tine test). A positive test indicates that the individual has been infected with tubercle bacilli in the past, but it does not always indicate present active disease. Even though various circulating humoral antibodies form against different antigens of *Mycobacterium tuberculosis* in an invaded host, there is no immediate reaction following the intradermal injection of this tuberculo-protein.<sup>1</sup> The local reaction which develops 6-8 hours after the test has been correlated with the level of circulating antimycobacterial antibodies that form complexes with the antigen leading to the dermal reaction of the Arthus type.<sup>2</sup> An indurated papule of more than 10 mm diameter develops after 48 to 72 hours at the test site, in an individual who has delayed hypersensitivity against this bacterium. This reaction is mediated by sensitised T lymphocytes. The intensity of the skin reaction in the hypersensitive individual bears no relationship to the level of antibodies that may be demonstrated by complement fixation test, precipitation test, haemagglutination test or by other tests.

Atypical local reactions after tuberculin test have been observed in the past. Arany in 1953 reported six instances of large areas of intense

erythema and a small area of infiltration 24 hours after the test which completely faded at 48 hours.<sup>3</sup> Anaphylaxis and death following old tuberculin Tine test was first reported in 1975.<sup>4</sup> This was in a 19-year-old male who collapsed 2 minutes after the test and was pronounced dead 30 minutes after collapsing. Post mortem study did not show any anatomic or toxicologic cause of sudden death in this patient. It was presumed to be due to anaphylactic reaction by the test material, though Peirach and Burchall<sup>5</sup> did not agree with this presumptive diagnosis. Other complications that have been reported following tuberculin test are uveitis and retinal periarteritis,<sup>6</sup> induction of Koebner's phenomenon in psoriasis<sup>7</sup> and recurrent ulcerative tuberculids with arthritis.<sup>8</sup> We are reporting an instance of severe anaphylaxis (Type I hypersensitivity) following Mantoux test with PPD, in a young girl.

### Case Report

A 17-year-old girl had multiple painful, shallow ulcers with bluish margin on the front of both her legs since 2 months. There was no personal or family history of tuberculosis. She had BCG vaccination at the age of 5 years. Systemic examination did not reveal any abnormality.

Routine laboratory tests on blood, urine and stools did not show any abnormality. X rays of the chest and legs were normal. Smear taken from the edge of the ulcers did not show any acid fast bacilli. Biopsy of the lesion was non-specific. A Mantoux test with PPD 1 unit/0.1ml

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was first performed on the right forearm and the site was observed for 3 days. But there was no significant change. On the 9th day however, she developed severe itching at the test site and developed a wheal which increased to a size of 10 cm in diameter with pseudopod-like extensions. There was no induration and it subsided completely in 3 days. After 2 weeks, the patient was retested with PPD in the same dose, with special care not to contaminate the syringe with any other drug. Within 5 minutes, the patient developed an itchy wheal which attained a size of 12 cm diameter within an hour. It subsided completely within 24 hours without development of an indurated papule. The possibility of Type I hypersensitivity was suspected and the patient was again tested with one unit of PPD (Mantoux test) on the left forearm. Within 30 seconds, at the test site she developed a wheal along with generalised erythema, piloerection, urticaria, hypotension (BP, 80/60) and giddiness. There was a slight difficulty in breathing also. She was immediately resuscitated with intramuscular injections of adrenaline, betamethasone and pheniramine maleate. Piloerection and urticaria subsided and the BP rose to normal. There was no induration at the test site even on the fourth day. Later, multiple pin-prick test performed with solutions of Tween 80 and chinosol did not show any local or systemic manifestations of hypersensitivity. The leg ulcers healed completely with a course of cotrimoxazole.

### Comments

Tuberculin antigen generally induces a delayed hypersensitivity reaction which is mediated by T lymphocytes and manifests as an indurated papule of more than 10 mm diameter within 48 to 72 hours. Skillful administration and careful reading are essential in Mantoux test. Induration is the important feature of the lesion at the test site, but the intensity of this reaction bears no relationship to the level of antibodies in the serum. Serum containing

such antibodies does not confer protection, nor does it have any lytic or bactericidal effect on tubercle bacilli.<sup>9</sup>

Our patient developed an unusual response to the test on the ninth day only after the first Mantoux test. It seems that the protein used for this test has acted both as a sensitising and an inducing agent for immediate type of hypersensitivity, though it is believed that tuberculin does not sensitise an individual.<sup>10</sup> Subsequent Mantoux tests in our patient showed a more immediate type of response. The last test produced not only a local immediate reaction but signs of generalised manifestations of anaphylaxis which included giddiness, hypotension, generalised pruritus, urticaria and piloerection. Though several patients were tested with PPD in this hospital, none was observed to develop this type of allergic response, though these patients are generally not followed up for more than 3 days after the test. Further, repeated Mantoux tests are performed only rarely in them. The diluent used in the test antigen is a sterile phosphate buffer solution isotonic with blood (PH 7.38) to which are added chinosol and Tween 80.<sup>11</sup> Skin tests done in our patient with solutions of Tween 80 and chinosol did not show any local or systemic manifestations of hypersensitivity. A positive Mantoux test after BCG persists only for 3 to 7 years.<sup>12</sup> So a negative reaction to this test in our patient, who had received BCG vaccination 10 years ago is not surprising.

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