Letters in Response to Previously Published Articles

Immunotherapy or not? The mystery deepens

Sir,

This is with reference to the study by Saoji *et al*. on immunotherapy of warts with purified protein derivative (PPD).[1] Although it is a carefully executed study; in our view, the use of the term "immunotherapy" is an inappropriate description for the method employed by the authors. We understand that they achieved good clearance rates using the methods described in the report but injecting PPD into multiple lesions defies the true meaning of immunotherapy.

In the section methods, they write "2.5 tuberculin units (TU) of PPD was injected into each lesion.[1] In case of multiple lesions, a maximum of 10 representative lesions covering all the sites and a maximum of 25 TU of PPD was injected during each session." Immunotherapy is defined as treatment designed to produce immunity to a disease or enhance the resistance of the immune system to an active disease process. It involves injecting a specific dose of antigen at specific intervals in order to sensitize the immune system. Vaccination is also a type of immunotherapy and all vaccines are administered as a single dose, not as multiple doses throughout the body. Booster doses are given for many vaccines but that is not to be considered as multiple doses. By that principle, immunotherapy for warts should not be given into all or multiple lesions, but only one lesion.

We are not suggesting that injecting tuberculin or any other form of immunotherapy into multiple warts in the same patient is wrong. The authors have shown that it works well but this practice may lead to confusion for clinicians and future researchers attempting this modality of treatment. It may create doubt as to how many warts to inject and how much to inject in each patient. Therefore, the exact and effective dose of the antigen will not be recognized and proper treatment guidelines cannot be formulated. Moreover, it has been shown in multiple studies that immunotherapy works well even if we inject the agent in only one lesion.[2-5] The authors of this letter have conducted a similar study in which a specific amount of PPD (0.1 ml) was injected in the same target wart with up to 100% results.[5] Therefore, we suggest that following this protocol will maintain uniformity and may avoid confusion for future studies as well as clinical practice.

Immunotherapy is a new treatment modality for warts and many studies are reporting its beneficial effect. However, recent British guidelines state that there is no robust evidence to support the use of intralesional immunotherapy.[6] This recommendation stems from the fact that randomized controlled trials are lacking. Most studies do not have a control group and simply mention cure rates without comparison to either control or another traditional modality of treatment. Nofal and Nofal included saline as control in their comparative study for evaluating the efficacy of intralesional measles, mumps and rubella vaccine[2] Interestingly, complete or partial response was also seen in the saline group (27.5% and 15%, respectively). The response in the saline group could be related to some amount of tissue autoinoculation occurring during intralesional injection. The study protocol dictated injection into the single largest wart for all patients. But if we increase the number of warts to be injected, this would increase the chance of autoinoculation of wart tissue and thereby increase the clearance rates of either group. Therefore, while it may be useful for boosting response rates, this is not true immunotherapy but simply manipulation of the lesion.

There is another important precaution to be taken while administering tuberculin which may have been ignored. The authors mention that history of tuberculosis was not considered as an exclusion criterion. But, according to the tuberculin package insert, PPD should be administered with caution, or not at all, in persons with documented active tuberculosis or documented treatment in the past because of the severity of reactions (e.g., vesiculation, ulceration or necrosis) that may occur at the test site.[7] This may be of additional concern in a country like India where tuberculosis is endemic and frequent. Moreover, if we

inject multiple lesions, the chances of a severe local reaction may increase further.

In conclusion, this study does not concretely define the amount of PPD required and the number of lesions to be injected. In addition, there is uncertainty about how to decide the amount of PPD required in relation to the extent of the disease, whether to inject the same dosage in subsequent sittings and what to do if numbers of lesions reduce. More studies are needed to resolve these ambiguities.

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Conflicts of interest
There are no conflicts of interest.

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