Short Communication

Differentiation between viral exanthema and allergic exanthema by IFN-γ and IL-4 assay

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Macular and maculo-papular skin reactions are frequent events in viral infections as well as in allergies (1,2,3). Their histology and clinical morphology is often similar and clinical diagnosis of rash is often difficult and misdiagnosis is not rare, specially in failure to detect virus specific antibodies of the IgM class (4,5,6,7,8). Measles, rubella and parvovirus B19 are the most important childhood exanthematic disease, but some other viruses (enteroviruses, HHV-6, EBV ,etc) can cause exanthema(9) that diagnosis of each of them separately, requires spending lots of time and money. On the other hand, allergies are another important cause of exanthema and differentiation between viral exanthema and allergic exanthema can be difficult sometimes (10).

Studies on viral specific T cell lines have shown that these cells are frequently associated with elevated IFN-γ levels at the early phase of disease (8,11,12,13). More over allergic specific T cells represent a significant source of IL-4 (8,14,15).

In this study, we applied this hypothesis to demonstrate whether we can use IFN-γ and IL-4 serum levels to differentiate between viral exanthema and allergic exanthema and if we can, how many of our negative measles, rubella and parvovirus B19 cases are associated with viral infections and how many of them are associated with allergies. Patients sera were taken from measles suspected cases (all patients presenting with rash, high fever, and at least one of the following symptoms: Cough, Coryza or Conjunctivitis) (16) by health care workers from the epidemiological surveillance in Iran**.** Sera were collected from 27 provinces of Iran in 2005 and sent to Department of Virology/School of Public Health and Institute of Health Research of Tehran University. With Each Samples, there was a questionnaire that included information such as age, sex, province and vaccination status. This sera were tested in terms of measles, rubella and B19 by ELISA and then A total of 88 negative measles, rubella and B19 cases were analyzed for serum IFN-γ and IL-4 by by a commercially available ELISA kits (were bought from Austrian Bender med system company). Among 88 cases for analyzing in terms of IFN-γ and IL-4 , in 30 cases only IFN-γ, in 25 cases only IL-4 , in 3 cases both IFN-γ and IL-4 and in 30 cases none of they were positive. IFN-γ and IL-4 level in 22 normal sera were tested by producing company and in the most cases were lower than 8 pg/ml. in all of our positive cases ,this cytokine levels were upper than 8 pg/ml. however among our positive IFN-γ cases ,in only 10 sera ,IFN-γ level was upper than 20 pg/ml and also in only 17 cases of our IL-4 positive cases, IL-4 level was upper than 20 pg/ml. assuming that IFN-γ positive cases (34%) are due to viruses and IL-4 positive cases (28%) are due allergies, the cause of exanthema in 38% of cases was still unknown (Fig. 1).

It can be concluded that about 30 cases of negative measles, rubella and B19 cases in which the serum IFN-γ level was higher than normal range are associated to viruses and about 25 cases of them in which IL-4 level was higher than normal range are associated to allergies. However, in 30cases none of these cytokine increased , which can be due to different factors such as the interval between rash occurrence and sampling time(other studies has shown that levels of these cytokine will decreased as time passes) (8,11,12), freeze – thawed of sera and type of kits. In addition, in 3 cases both of these cytokine levels were higher than normal

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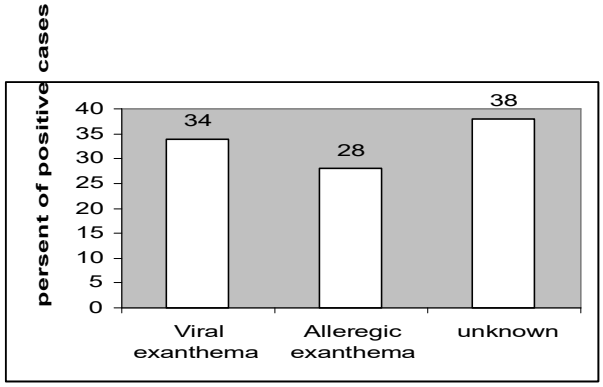

Fig. 1: Incidence of exanthema in the study population

range that can be due to factors as simultaneous occurrence of viral infections and allergies or allergy caused by the viruses (e.g. RSV). Consider resulting of this study, we can't say that using these two cytokines is effective for definite differentiating between viral and allergic exanthema and applying this hypothesis is related to careful studies and controlling all stages of the process, which includes sampling, maintaining the samples, performing the tests and analyzing the results in the future. However, clearly, using of serum cytokines is useful in differentiating viral exanthema from allergic exanthema in spite of the similar clinical picture.

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