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Role of Weil Felix Test for Rickettsial Infections

Dr. Deepali Danave , Dr SN Kothadia
(Dept of Microbiology, Dr Vaishampayan Memorial Govt. Medical College, Solapur, Maharashtra, India)

Abstract: *Rickettsial diseases are being under reported from India but they are significant contributors of pyrexia. The present study deals with utilization of Weil Felix test (WF) as screening test for diagnosis of rickettsial diseases in patients of fever and rash. Latex agglutination test PROGEN from Tulip Diagnostics (P) Ltd. was used for screening 156 samples out of which 27 samples (17.30%) were positive. Maximum positivity was shown towards OX-2 antigen (88.88%) followed by OX-19 (66.66%) and least towards OX-K (11.11%). Weil Felix test though being non specific is user friendly, non-tedious and cannot be discarded altogether from laboratory set-up.*

Key words : *Pyrexia, rickettsial infections, Weil Felix test.*

I. Introduction

Most fevers in acutely ill patients with rash often present a diagnostic challenge for physicians. Rickettsial infections constitute an important etiology when fever presents in concert with distinctive appearance of an eruption. In general terms laboratory confirmation of rickettsial infection maybe obtained by isolating and biotyping the rickettsia from the patient or by demonstrating an antibody response during the disease or in special circumstances by demonstrating and identifying the organisms in the lesions. The difficulties and dangers of working with live pathogenic rickettsias preclude isolation of the organism as a diagnostic measure in most clinical laboratories. [1] Hence cultivation of rickettsia in cell culture is technically feasible but seldom undertaken. For most clinical microbiology laboratories the diagnosis of suspected clinical cases of rickettsial infections will be restricted to testing of blood samples for antibody. Serologic assays for the diagnosis of rickettsial infections include the "gold standard" indirect immunofluorescence assay (IFA), indirect immunoperoxidase assay, latex agglutination, enzyme immunoassay (EIA), Proteus vulgaris OX-19 and OX-2, Proteus mirabilis OX-K strain agglutination, line blot, Western immunoblotting and rapid flow assays. Other serologic tests include indirect haemagglutination (IHA), microagglutination and complement fixation(CF).[2]

Historically the most common diagnostic test for rickettsial infections has been the Weil Felix test (WF).This heterophile agglutination test was developed from chance observation of Weil & Felix that sera from patients with typhus agglutinated strains of Proteus vulgaris. The basis of the test is the sharing of an alkali stable carbohydrate antigen by certain strains of Proteus viz. Proteus vulgaris OX-19 and OX-2, Proteus mirabilis OX-K.[3] The test is usually done as tube agglutination though rapid slide agglutination methods have been employed for screening.

We undertook this study for evaluation of Weil Felix test (WF) as a rapid screening technique in the diagnosis of rickettsial infections.

II. Materials And Methods

The study was conducted in our institute during the period Nov. 2008- March 2009. Blood samples were obtained from patients presenting to our hospital. Possible cases (>3 years) were chosen clinically on the basis of diverse symptoms and signs as fever (>5days), headache, myalgia, macular rash, hepatomegaly, increased respiratory rate and physicians requisition for WF test. Single blood sample was collected from each patient amounting to total 156 samples. Sera were separated out and tested by latex agglutination test. Antigen used for Weil Felix test was 'PROGEN' obtained from Tulip Diagnostics (P) Ltd. Goa. Three antigens were present viz. Progen OX19, ProgenOX2, ProgenOXK. Each serum sample was tested with all the three antigens by rapid slide screening test according to manufacturer's protocol. Agglutination obtained within one minute was considered a positive reaction indicating the presence of the corresponding antibody in the patients sera.
Analysis of results was done as per table no. 1

Table no. 1- Analysis of results

Disease	Agglutination pattern with		
	OX19	OX2	OXK
Epidemic typhus	+++	+	-
Endemic typhus	+++	+ /-	-
Tickborne spotted fever	++	++	-
Scrub typhus	-	-	+++

III. Results

A total of 156 serum samples were tested by the WF test of which 27 samples (17.30%) were positive while 129 samples (82.69.%) were negative – Table 2. Of the positive 27 samples, male cases were nine (33.33%) while female cases were double in number i.e. eighteen (66.66%) -Table 3. Maximum antigen reactivity was seen towards OX-2 (88.88%) followed by OX-19 (66.66%) and OX K (11.11%) – Table-4. Antigen wise six samples were reactive to OX2, three to OX-K but none to OX19 individually. When reactivity was seen towards two or more antigens in the same serum sample only one combination of antigens demonstrated it i.e. OX19+OX2. Eighteen serum samples (66.66%) were positive for this combination – Table 5. Thus 24 positive samples (88.88%) were indicative of typhus fever / spotted fever group and three positive samples (11.11%) of scrub typhus.

Table 2 -Total cases with their reactivity

Positive	Negative	Total
27(17.30%)	129(82.69%)	156

Table 3- Sex -wise distribution of total cases

	Positive	Negative	Total
Males	9	68	77
Females	18	61	79
Total	27	129	156

Table 4-Antigen wise distribution of positive cases

	OX19	OX2	OXK
Males	13	9	0
Females	5	15	3
Total	18	24	3

Table 5- One or more antigen positivity in same sample

Antigen	Positive test
0 X 19	0
0 X 2	6
0 X K	3
0 X 19 +0 X 2	18
0 X 19 + 0 X K	0
0 X 2 + 0 X K	0
0 X 19 + 0 X 2 + 0 X K	0

IV. Discussion

Increasingly it is realized that rickettsial diseases are underdiagnosed and that they contribute substantially to the acute febrile burden and preventive illness in many populations.[4] Study conducted by Parul Sinha et al in Jaipur regarding recent outbreak of scrub typhus in North - Western part of India has attested to this fact. [5] Our isolates were indicative of typhus fever / spotted fever group (88.88%) and scrub typhus (11.11%).

In most clinical microbiology laboratories, assays for antibodies to rickettsiae are the only tests performed. In recent years the micro immunofluorescene assay (IFA)has become the reference test. The procedure appears to be the most sensitive and specific method for the diagnosis of rickettsial infections. [6] But the micro-IFA requires skilled technicians and expensive equipment. Also shared antigens of OmpA, OmpB and group specific lipo-polysaccharide impede establishment of species-specific diagnosis by serologic methods.[2] Cumbersome expensive cross absorption of sera prior to IFA or Western immunoblotting is more effective in establishing a species specific diagnosis.[2]

Latex agglutination tests which are now commercially available are in more general use. The CF test although specific is cumbersome and lacks sensitivity. The IHA requires micro- titre equipment. Only a portion of these assays are available as commercial kits or as assays performed in reference laboratories for some but not all rickettsial infections. Serologic tests as IHA, micro-agglutination and CF are no longer in general use. [2]

Interpretation of these test results require careful evaluation of the performance of valid controls, the quality and quantity of each antigen preparation and the potential for the occurrence of infection by an untested even as yet unrecognized agent.[2] Specific diagnosis is no longer limited to the geographical origin of the case as in the past. Unfortunately many laboratories are not equipped with the instruments and reagents to perform these assays. These laboratories depend on the Weil Felix test which requires no elaborate equipment as a screening procedure. The assays that have been most widely used for diagnosis of rickettsial diseases are agglutination of the OX-19 and OX-2 strains of Proteus vulgaris for ricketssioses and the OX-K strain of Proteus mirabilis for O. tsutsugamushi infections. [2]

The well-known cross-reaction between certain Proteus strains and Rickettsia species give characteristic agglutination patterns with sera of patients infected with different rickettsial agents.

Casteneda reported that Proteus strain OX19 possessed an acid stable and moderately alkali stable polysaccharide antigen responsible for the cross-reaction with rickettsia spp.[7] Schramek et al described the presence of a biologically active lipopolysaccharide (LPS) fraction in the typhus group rickettsiae and Anacker et al demonstrated the patterns of LPS in R. ricketsii by SDS-PAGE.[8,9]

In a preliminary report Amano et al suggested that the cross reactivity between the Japanese spotted fever rickettsia and Weil Felix test antigens was probably due to the common antigenicity of their LPS.[10]

Amano et al also concluded that LPS from SFG rickettsiae contains the amino sugar quinovosamine that maybe responsible for the cross reactivity between SFG rickettsiae and Proteus strain OX2.[11] Vinogradov et al reported that the O-specific polysaccharide of LPS in P.vulgaris 5/43 belonging to 0X19 (0 variants) contained glucose, N-acetyl glucosamine and N-acetyl quinovosamine.[12]

But because the antigen is non-rickettsial the WF test results are non specific. Yet WF test is simple, technically uncomplicated rapid screening procedure for sero - diagnosis of rickettsial infections. It maybe especially useful in small laboratories in areas where typhus is endemic and where sophisticated equipment is not available.

Our study focused primarily on the utility of WF test as a qualitative screening test and not the quantitative demonstration of titre or rise in titre. Hechemy et al demonstrated 70% agreement between WF test and micro IF results especially with a rise in WF titre.[13]

In developing countries there are situations where the choice is between the Proteus agglutination tests and none at all for the detection of important public health problems such as outbreaks of louse borne typhus. In fact the evidence leading to the discovery of Japanese spotted fever and Flinders Island spotted fever included Proteus agglutinating antibodies. [2]

In set-ups with scarce diagnostic modality WF test could serve as a primary screening tool and with clinical co-relation help in better patient management. That could be the reason why it enjoys widespread applicability like Widal test though being non-specific. It would hence be premature to suggest that WF test be labelled as obsolete and discarded altogether from laboratory set- up.

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