Anti-Nuclear Antibody Expression in Severe Scrub Typhus Infection: Preliminary Observations

Sir,

Antinuclear antibody (ANA), although associated with autoimmune processes, is described in infections.[1] We assessed ANA positivity in severe scrub typhus infection and studied the relationship between ANA positivity and organ dysfunction and mortality.

Consecutive patients admitted to the ICU with severe scrub typhus infection and consenting to participate underwent an ANA test. The study was approved by the Institutional Review Board. Scrub typhus was diagnosed by a positive scrub IgM ELISA (≥16 units) in the presence of a characteristic eschar or the exclusion of other causes of febrile illness. ANA was detected by immunofluorescence using a commercially available assay at a serum dilution of 1:100. The reactions were scored independently by two technologists as negative (no fluorescence), weak positive or 1+ to 4+ based on the intensity of fluorescence.

Patients were treated with doxycycline (enteral) plus azithromycin (intravenous), as parenteral doxycycline is unavailable in our country. Those requiring organ support (ventilation, hemodynamic support, dialysis) were treated as per guidelines. Complications of ventilation and nosocomial infections were managed according to standard protocols. Demographic data, symptom duration, organ dysfunction, need for ventilation, ventilator-free days, length of hospital stay and hospital outcome were collected in pre-constructed data forms. Organ dysfunction was diagnosed if organ-specific SOFA score was ≥1.[2] Fisher's and t-test were used for analysis of dichotomous and continuous variables respectively using STATA® v11.

Over 9 months, 40 patients aged (Mean ± SD) 35.9 ± 14.0 years and APACHE-II score of 23.2 ± 8.4, presented with symptoms for 8.5 ± 3.8 days. Sixteen patients (40%) tested ANA positive; a speckled pattern in 9 and weak ANA positivity in 7. Patients tested negative for ANA had higher admission creatinine (P = 0.03), organ dysfunction (P = 0.06) and mortality (P = 0.06), compared with those who tested positive. Age, gender, dyspnea, altered mental status, fever duration, presence of eschar and APACHE-II score were not different between those tested ANA positive and negative [Table 1]. Ventilatory need and ventilator-

Table 1: Baseline characteristics and outcome data

Parameter	ANA negative (n = 24) (%)	ANA positive (n = 16) (%)	P value
Baseline characteristics			
Age (Mean±SD years)	38.2 (13.8)	32.3 (14.0)	0.10
Gender M:F	11: 13	5: 11	0.51
Duration of symptoms (Mean±SD days)	8.2 (3.4)	8.9 (4.3)	0.72
Dyspnea (n)	18 (75)	15 (62.5)	0.53
Duration of dyspnea (Mean±SD days)	2.94 (1.9)	2.93 (1.8)	0.49
Altered mental status	10 (41.7)	3 (18.8)	0.18
Eschar	11 (45.8)	7 (43.8)	1.00
APACHE II score (Mean±SD)	24.7 (9.2)	21 (6.6)	0.09
Admission creatinine (mg/dl)	2.17 (1.63)	1.33 (0.69)	0.03*
Outcome data			
Number ventilated	22 (91.7)	16 (100)	0.51
Ventilator free days (Mean±SD days)	13.3 (10.6)	17.1 (9.6)	0.13
Number of organ dysfunction	4.21 (1.41)	3.44 (1.60)	0.06‡
Mortality	8 (33.3)	1 (6.3)	0.06‡

ANA: Antinuclear antibody; SD: Standard deviation; M: F: Male: Female; N: Number of patients; APACHE: Acute physiology and chronic health evaluation; *P value significant; ‡borderline significance

free days were similar in ANA-positive and -negative patients.

ANA expression in scrub typhus is not surprising as this phenomenon is reported in other infections. Positivity may be explained in two ways. ANA positivity may be a non-specific response to the rickettsial infection as occurs with other infections. Alternatively, it may indicate a specific immunologic response to the (infective) vasculitis or occur as a marker of vasculitis demonstrated on histopathology in scrub typhus infection.[3]

The trend toward a negative association between ANA positivity and organ dysfunction and mortality is unexpected as ANA is generally a marker for worse prognosis.[4] Recent work suggests that ANA may have a dual role in promoting or inhibiting disease processes.[4] Interestingly, in septic shock, the presence of autoantibodies to high-mobility group-box 1 (HMGB-1), a type of ANA, is associated with increased survival, suggesting that the induction of autoantibodies by infection may be beneficial.[5] This implies that ANA may be involved in inducing immunological disturbances and also in attenuating them.[4] These observations warrant further investigation on the mechanism of ANA positivity in scrub typhus.

John Victor Peter, Mathew F. Griffith[1], John Antony Jude Prakash[2], Anugragh Chrispal[3], Kishore Pichamuthu, George M. Varghese[3]

Department of Critical Care, Medical Intensive Care Unit, Christian Medical College, Vellore, India, [1]Department of Medicine, University of Colorado School of Medicine, Aurora, CO USA, [2]Department of Microbiology, Christian Medical College, Vellore, India,[3]Department of Medicine, Christian Medical College, Vellore, India

Address for correspondence:
Dr. John Victor Peter,
E-mail: peterjohnvictor@yahoo.com.au

REFERENCES

1. Adebajo AO, Charles P, Maini RN, Hazleman BL. Autoantibodies in malaria, tuberculosis and hepatitis B in a west African population. Clin Exp Immunol 1993;92:73-6.
2. Moreno R, Vincent JL, Matos R, Mendonca A, Cantraine F, Thijs L, *et al.* The use of maximum SOFA score to quantify organ dysfunction/failure in intensive care. Results of a prospective, multicenter study. Working Group on Sepsis related problems of the ESICM. Intensive Care Med 1999;25:686-96.
3. Jeong YJ, Kim S, Wook YD, Lee JW, Kim KI, Lee SH. Scrub typhus: Clinical, pathologic, and imaging findings. Radiographics 2007;27:161-72.
4. Pisetsky DS. Antinuclear antibodies in rheumatic disease: A proposal for a function-based classification. Scand J Immunol 2012;76:223-8.
5. Barnay-Verdier S, Fattoum L, Borde C, Kaveri S, Gibot S, Marechal V. Emergence of autoantibodies to HMGB1 is associated with survival in patients with septic shock. Intensive Care Med 2011;37:957-62.

Access this article online

Quick Response Code:

Website: www.jgid.org

DOI: 10.4103/0974-777X.145260