575

Factors associated with Acquired Anti IFN- γ autoantibody in Patients with Nontuberculous Mycobacterial Infection

Pakpoom Phoompoung[1], Nasikarn Ankasekwinai[1], Suporn Foongladda[1], Pinklow Umrod[1], Manop Pithukpakorn[1], Bhoom Suktitipat[1], Surakhameth Mahasirimongkol[2], Sasisopin Kiertiburanakul[3], Yupin Suputtamongkol[1]

[1]Faculty of Medicine, Siriraj Hospital. [2]Department of Medical Science, Ministry of Public Health. [3]Faculty of Medicine, Ramathibodi Hospital. Bangkok, Thailand

2 Prannok Rd, Bangkoknoi, Bangkok, Thailand, 10700
Email: benefat@hotmail.com Tel: 6682-419-7783

Background

- Disseminated nontuberculous mycobacterial (NTM) diseases in non-HIV infected patients is now well recognized in association with an acquired autoantibody to Interferon-gamma (anti-IFN γ autoantibody)[1].
- Risk factors of this syndrome are unknown.

Method

- Unmatched case-control study among patients with NTM disease.
- Anti-IFN γ autoantibody was assayed by enzyme-linked immunosorbent assay.
- Cases were patients with NTM disease and detectable anti-IFN γ autoantibody.
- Controls were randomly selected from those with NTM disease but undetectable anti-IFN γ autoantibody.
- Data collection included demographic data, clinical presentations, laboratory results and suspected risk factors such as HLA analysis.
- Univariate and multivariate analyses were performed to identify factors associated with this syndrome.

Result

- 70 cases and 72 controls.
- Baseline characteristics are shown in **Table 1**.
- *Mycobacterial abscessus* was the most common NTM pathogen found in both groups.
- Disseminated NTM disease was significantly more common in cases (92.9%) than in controls (13.9%, p < 0.001).
- Details of NTM species and site of isolation are shown in **Table 2**.
- Among cases, 44 patients (62.9%) developed reactive skin lesions associated with active NTM diseases; sweet syndrome (37.1%), acute generalized exanthematous pustulosis (20%) and erythema nodosum (14.3%).
- Reactive arthritis was also detected in 6 patients among cases (8.6%).
- Anemia, leukocytosis, eosinophilia and thrombocytosis were more common among cases than among controls.
- ESR and CRP were significantly higher in cases. Higher globulin and lower albumin levels in cases were observed.
- Independent factors associated with anti-IFN γ autoantibody were shown in **Table 3.**

Table1: Baseline characteristics

Variable	Case	Control	p-value
Male, n (%)	40 (57.1)	39 (54.2)	0.721
Mean (SD) age, yrs	50 (11)	58 (19)	0.002
Birthplace, n (%)			< 0.001
- Central	21 (30)	53 (73.6)	
- Northeast	18 (25.7)	3 (4.2)	
- North	16 (22.9)	1 (1.4)	
- West	10 (14.3)	6 (8.3)	
- Other	5 (7.1)	9 (12.5)	
Comorbidities, n (%)			
- Yes	4 (5.7)	25 (34.7)	< 0.001
Previous OIs, n (%)			
- Yes	33 (47.1)	11 (15.3)	< 0.001
HLA studies			
no tested, no+ve (%ve)			
- DRB1*15/16:02	61,49 (80.3)	54,11 (20.3)	< 0.001
- DQB1*05:01/02	61,59 (96.7)	53,17 (32.1)	< 0.001

Table2: Nontuberculous mycobacterial disease

Variable, n (%)	Case	Control	p-value
Type of NTM			
- Rapid grower	57 (81.4)	44 (61.1)	0.008
Species of NTM			
- *M. abscessus*	51 (72.9)	30 (41.7)	< 0.001
- MAC	8 (11.4)	15 (20.8)	
- *M. fortuitum*	7 (10)	12 (16.7)	
- *M. kansasii*	1 (1.4)	6 (8.3)	
- *M. simiae*	1 (1.4)	2 (2.8)	
- *M. haemophilum*	1 (1.4)	1 (1.4)	
- Others	0 (0)	3 (4.2)	

Table 3: Associated factors

Factors	Crude OR	Adjusted OR	95%CI	p-value
Age	0.97	0.97	0.94-1.01	0.164
Comorbidities	0.11	0.11	0.03-0.48	0.003
Birthplace in central region	0.15	0.24	0.08-0.73	0.012
Previous OIs	4.95	5.94	1.50-23.59	0.011
HLA DRB1*15/16:02 DQB1*05:01/02	29.5	21.69	5.06-92.92	< 0.001

Conclusion

- Patients with NTM disease associated with anti-IFN γ autoantibody were almost always previously healthy and non-HIV infected.
- Nearly all of them presented with disseminated NTM diseases, in association with reactive skin lesions.
- Factors associated with this syndrome were lack of comorbidities, birthplace in non-central region of Thailand, previous OIs and specific HLA

Acknowledgement

Funding by National Science and Technology Development Agency (NSTDA), Thailand.

Reference

1. Browne SK, Burbelo PD, Chetchotisakd P, Suputtamongkol Y, Kiertiburanakul S, Shaw PA, et al. Adult-onset immunodeficiency in Thailand and Taiwan. N Engl J Med. 2012;367(8):725-34.
2. Pithukpakorn M, Roothumnong E, Angkasekwinai N, Suktitipat B, Assawamakin A, Luangwedchakarn V, et al. HLA-DRB1 and HLA-DQB1 are Associated with Adult-Onset Immunodeficiency with Acquired Anti-Interferon-Gamma Autoantibodies. PLoS One. 2015;10(5):e0128481.