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O1050 Frequent misdiagnoses in patients with neutralising anti-interferon-gamma autoantibodies

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Background: Although neutralizing anti-interferon-gamma autoantibodies (anti-IFNγ Abs) have been increasingly reported in otherwise healthy adults with disseminated nontuberculous mycobacterial (NTM) infections, early diagnosis remains difficult given the protean manifestations of this disorder and absence of standard laboratory assay. In this study, we sought to investigate the prevalence and causes of initial misdiagnoses and subsequent inappropriate treatment in these patients.

Materials/methods: We prospectively enrolled patients who had disseminated nontuberculous NTM infections in the absence of recognized immunocompromised conditions from six hospitals located in northen, middle and southern Taiwan. ELISA and flow cytometry were used to determine the presence of biologically-active anti-IFNγ Abs in their plasma. Demographics and detailed past medical history including initial presentations and empiric treatment during disease onset were recorded.

Results: Among 40 patients tested positive for neutralizing anti-IFNγ Abs, 60% were male and the median age at disease onset was 55 years (range: 28-82 years). The most common organs involved were lymph node (67.5%), bone (62.5%), lung (55%), skin and soft tissue (25%). Slow-growing NTM (primarily *Mycobacterium avium* complex and *Mycobacterium Kansasii*) were isolated from 65% of patients, while 47.5% of patients were infected by rapid-growing NTM. Malignancy was suspected in half of these patients prior to the identification of neutralizing anti-IFNγ Abs due to multiple lymphadenopathy or multi-organ involvement. Among them, the most common radiographic diagnoses were lung cancer with bone metastases followed by lymphoma. The histopathological findings of a biopsied lymph node were initially misinterpreted as angioimmunoblastic T-cell lymphoma by an experienced pathologist. Fifty-five percent of patients were mistaken for disseminated TB infection due to unexplained fever with multi-organ involvement and/or isolation of acid-fast bacilli from cultures or biopsied specimens, resulting in the prescription of unnecessary anti-TB therapy in 35% of patients. The median time from disease onset to the recognition of the presence of anti-IFNγ Abs was 1 year.

Conclusions: Over 50% of patients with neutralizing anti-IFNγ autoantibodies were initially misdiagnosed as malignancy or TB at disease onset leading to delayed or inappropriate treatment. Oncologists, pulmonologists, pathologists, radiologists and infectious diseases specialists are often consulted and need to be aware of this emerging disorder.