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SAT0412 TUBERCULOSIS REACTIVATION DURING BIOLOGICAL THERAPY

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Background: With the increasing use and wide variety of biological therapies, there is a concomitant increase in concern for associated opportunistic infections, especially for *Mycobacterium tuberculosis*. ¹

Objectives: The aim of this study was to identify patients who have developed tuberculosis (TB) reactivation during treatment with a biological agent.

Methods: We included patients treated with biological agents in a tertiary Department of Rheumatology who had developed TB and were registered in the national registry for biological therapy. Demographic (urban or rural environment), clinical, therapeutic (biologic agent used) and comorbidities data were retrieved from the database.

Results: The database included 505 patients: 314 patients with rheumatoid arthritis (RA), 129 patients with ankylosing spondylitis (SA) and 62 patients with psoriatic arthritis (PsA).

Prior to the start of biological therapy, tuberculosis screening for latent infection was conducted in all patients. Eight patients (1.58%) were identified as being diagnosed with TB reactivation during biological therapy: 5 RA and 3 SA patients. Two had positive tuberculin test (TST) at baseline and required chemoprevention therapy prior to the initiation of the biological agent (respecting the preexisting guidelines).

Demographic data shows 62.5% patients from urban areas, 50% female and 50% male. Regarding comorbidities, one patient had biapical pachypleuritis (probably TB sequelae), antiphospholipid syndrome and pulmonary hypertension; one had chronic kidney failure and inflammatory bowel disease. The other six patients had minor comorbidities.

62.5% of patients were treated with oral corticosteroids combined with DMARDs. Four patients have been treated with infliximab, three with adalimumab and one with etanercept.

The average time to TB reactivation was 19.6 months (range 2 months to 52 months). Patients who had TB reactivation after two months of biologic therapy were treated with infliximab.

Four patients had developed pulmonary TB; one case was described as a miliary complicated with bacillary peritonitis (peritoneal biopsy). One patient had developed lymph node TB (lymph node biopsy) and one TB of the wrist (switch therapy was not chosen yet).

One particular case was of a patient that had developed TB meningitis with lymphadenitis and a compressible tuberculoma with spastic paraparesis. Switching of biological agent was chosen in 5 patients without another reactivation of tuberculosis. The biological agents chosen in 40% was rituximab, 20% was etanercept, 20% was adalimumab and 20% was infliximab.

Conclusions: Pulmonary and extrapulmonary TB reactivation equally occurred during anti TNF therapy. In some cases, reactivation of tuberculosis occurred even with chemoprevention.

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SAT0413

THE TREND OF INCIDENCE RATE, FREQUENCY, OUTCOMES AND HLA PHENOTYPE OF REACTIVE ARTHRITIS AND UVEITIS IN JAPANESE PATIENTS WITH BLADDER CANCER FOLLOWING INTRAVESICAL BCG THERAPY: A 20-YEAR, TWO-CENTRE RETROSPECTIVE STUDY

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Background: Intravesical instillation of Bacillus Calmette-Guerin (iBCG) is used as an effective immunotherapy of bladder cancer. However it may have, as adverse event, a reactive arthritis (ReA) and the frequencies are known as about 0.5% to 1% in Western countries.

Objectives: To evaluate the trend of incidence rate, frequency and HLA phenotype of reactive arthritis (ReA), uveitis and other adverse events in Japanese patients with bladder cancer following iBCG therapy.

Methods: The clinical findings of Japanese patients who received iBCG (n=555 [250 and 305 in Kochi Medical School Hospital and Kurashiki Medical Centre, respectively]) for bladder cancer from March 1997 to February 2017 were retrospectively assessed, with specific attention to patients with ReA and uveitis. HLA phenotypes of patients with ReA were also looked. Moreover, iBCG-induced ReA diagnosed from 1997 to 2007 were compared with that from 2007 to 2017. Finally, outcomes of ReA patients were also evaluated.

Results: Patients' mean age was 72±10 years and male/female ratio was 438/117. Fever, haematuria, and dysuria were presented in 91/555 (16.4%), 121/555 (21.8%), and 196/555 (35.3%), respectively of all enrolled patients. Of the 555 cases, ReA and uveitis were revealed in 11/555 (2.0%) and 4/555 (0.7%). The protocol of iBCG therapy was stable over the 20 years. Notably, HLA-B27, -B35, -B39 and -B51 positivity was more frequent in ReA patients (9.1%, 36.3%, 36.3% and 63.6%, respectively) (p<0.05) than in healthy subjects without ReA (0.3%, 8.3%, 4.0% and 9.1%, respectively). All 4 cases with uveitis had ReA, and showed positive HLA-B27 (25%), -B39 (50%) and -B51 (25%). Moreover, the overall incidence of iBCG-ReA was not different between from 1997 to 2007 and 2007 to 2017. Finally, all ReA patients did not progress to chronic type and spondyloarthritis (SpA) as outcomes.

Conclusions: The 2.0% iBCG-induced ReA frequency in Japanese patients exceeds that in Western countries, and its incidence has been stable and all ReA did not progress chronic type and SpA over the last 20 years. HLA phenotype, especially HLA-B51 and -B39 alleles in addition to -B27, may be a risk factor in iBCG-induced ReA in Japanese patients.

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SATURDAY, 16 JUNE 2018

SLE, Sjögren's and APS – clinical aspects (other than treatment)

SAT0414

DEVELOPMENT OF MALIGNANCY IN KOREAN SJÖGREN'S SYNDROME PATIENTS; WHOLE NATIONAL HEALTH INSURANCE DATA BASED ANALYSIS

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Background: Though ocular and oral dryness are the main symptoms of Sjögren's syndrome, extraglandular manifestations including lymphoma were also developed. However, prevalence of Sjögren's syndrome was too low, most studies about lymphoma and malignancy were done on a small-scale.

Objectives: For more large-scale research about development of malignancy in Sjögren's syndrome, we analysed this with whole Korean National Health Insurance data which include more than 95% of the population of the Republic of Korea.

Methods: We compared the incidence of malignancy in newly diagnosed Sjögren's syndrome patients from 2004 to 2015 with age-sex matched controls and calculated hazard ratio (HR) with multiple Cox's model.

Results: Among 198,872 Sjögren's syndrome patients, cancer developed in 9883 patients (5% of newly diagnosed Sjögren's syndrome patients) after diagnosed Sjögren's syndrome. The duration from diagnosis of Sjögren's syndrome to development of malignancy was 5.4 year and their mean age was 55.2 years old. Malignancy incidence was higher in men, increased with age from the forties. It was also higher in patients who smoking or smoked, drinking more than 3times a week, and having history of malignancy (HR; 1.588, 95% CI; 1.405~1.794). The

most common malignancy in patients with Sjogren's syndrome was thyroid cancer. The risk of overall malignancy was not higher than that of the control. However, the incidence of prostate cancer (HR; 1.339, 95% CI; 1.076~1.667), thyroid cancer (HR; 1.320, 95% CI; 1.093~1.594) and lymphoma (HR; 1.620, 95% CI; 1.066~2.462) were higher and hepatocellular carcinoma (HR; 0.591, 95% CI; 0.455~0.767) was lower than that of control. Lymphoma developed in 305 patients (3.1% of total malignancy); 10 cases of Hodgkin lymphoma, and 290 cases of non-Hodgkin lymphoma. Gender, age, smoking, drinking, body mass index, fasting blood glucose, and proteinuria were not significantly different from the control group in lymphoma development.

Conclusions: Sjogren's syndrome patients' overall malignancy risk was not higher than that of control group. However, risk of lymphoma, prostate cancer, and thyroid cancer was higher than control group.

Disclosure of Interest: None declared

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SAT0415 THE MRZ REACTION HELPS TO DISTINGUISH RHEUMATOLOGIC DISORDERS WITH CENTRAL NERVOUS INVOLVEMENT FROM MULTIPLE SCLEROSIS

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Background: Some rheumatologic disorders (RD) may initially manifest with central nervous system (CNS) affection, mimicking the clinical, magnetic resonance imaging, and cerebrospinal fluid (CSF) findings of multiple sclerosis (MS). Vice versa MS might be difficult to separate from some RD because of the presence of autoantibodies (e.g. ANA) in up to 50%. The MRZ reaction (MRZR), composed of the three respective antibody indices (AI) against measles, rubella, and varicella zoster virus, has been found positive frequently in MS patients. However, it is unclear whether the MRZR is helpful to distinguish rheumatologic disorders with CNS involvement (RDwCNS) from MS.

Objectives: To investigate the MRZ reaction as a diagnostic tool to distinguish patients with RDwCNS from patients with MS.

Methods: The MRZR was evaluated in 35 patients with RDwCNS and compared to 70 sex- and age- matched MS patients. An AI result ≥ 1.5 was indicative for intrathecal IgG production against the respective pathogen. Two previously established stringency levels, MRZR-1 (≥ 1 of 3 AIs positive) and MRZR-2 (≥ 2 of 3 AIs positive), were applied. CNS involvement of RDwCNS was defined as clinical manifestation with neurological symptoms and signs of inflammation in CSF analysis and/or cerebral/spinal magnetic resonance imaging (MRI). MRZR results were compared using the Fisher's exact test with $p < 0.05$ for statistical significance.

Abstract SAT0415 – Figure 1. Frequency of positive MRZ reaction (MRZR-1 and MRZR-2) in patients with RDwCNS compared to MS patients.

Results: Within the RDwCNS group, 31 patients suffered from systemic lupus erythematosus, four had a small vessel vasculitis. In both groups 77.1% were female, mean age ($\pm$ SD) was 43.2 years ($\pm$ 18.7) in RDwCNS and 47.5 years

($\pm$ 7.8) in MS ($p = n.s.$). All RDwCNS patients showed clinical symptoms indicative for CNS involvement and signs of inflammation in CSF analyses and/or MRI of the brain. In 52 MS patients autoantibody screening was performed. 42% were positive for ANA ($n=20$) or ANCA ($n=2$) in indirect immunofluorescence. Only 14.3% of RDwCNS patients had a positive MRZR-1 compared to 85.7% within the MS group ($p < 0.0001$). The more specific MRZR-2 was positive in 60% of the MS patients compared to only 8.5% of the RDwCNS patients ($p < 0.0001$). By using a higher threshold of >2.0 for a positive AI, the prevalence of positive MRZR-2 dropped to 5.7% ($n=2$) in the RDwCNS group compared to 54.3% ($n=38$) in the MS group ($p < 0.0001$). Oligoclonal bands were found in 94.3% of the MS and 28.6% of the RDwCNS patients ($p < 0.0001$).

Conclusions: Considering the high specificity of the MRZR-2 for MS confirmed in this study, this laboratory test may be a helpful diagnostic tool to distinguish RDwCNS from MS.

Disclosure of Interest: None declared

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SAT0416 LIFE-THREATENING PRIMARY SJÖGREN SYNDROME: CLINICAL CHARACTERISATION AND OUTCOMES IN 1535 PATIENTS (GEAS-SS REGISTRY)

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Objectives: To analyse the clinical features and outcomes of patients presenting with life-threatening systemic disease in a large cohort of Spanish patients with primary Sjogren syndrome (SjS).

Methods: The GEAS-SS multicenter registry was formed in 2005 with the aim of collecting a large series of Spanish patients with primary SS. By January 2018, the database included 1535 consecutive patients fulfilling the 2002/2016 criteria. Life-threatening systemic disease was defined as an activity level scored as "High" in at least one ESSDAI domain.

Results: 209 (14%) were classified as presenting with a life-threatening systemic disease: 194 presented one ESSDAI domain classified as high, 14 two domains and only one presented three high activity domains. The high-ESSDAI domains included lymphadenopathy in 78 (37%) cases, CNS in 28 (13%), PNS in 25 (12%), pulmonary in 25 (12%), renal in 22 (10%), cutaneous in 18 (9%), articular in 18 (9%), haematological in 7 (3%) and muscular in 4 (2%); the most frequent clinical presentations in each domain were, respectively, parotid lymphoma ($n=41$), focal neurological deficit ($n=20$), ganglionopathy ($n=11$), usual interstitial pneumonitis ($n=9$), renal failure ($n=11$), ulcerated cutaneous vasculitis ($n=9$), symmetric polyarthritis ($n=17$), severe thrombocytopenia ($n=3$) and severe myositis ($n=3$). With respect to therapeutic approach, 144 (69%) required glucocorticoids, 65 (31%) immunosuppressive agents and 42 (20%) biological therapies. During the follow-up, 36 (17%) patients died, mainly due to lymphoma ($n=16$), pulmonary fibrosis ($n=5$), end-stage renal failure ($n=4$), CNS progressive disease ($n=3$) and systemic vasculitis ($n=3$).

Conclusions: A 14% of patients with primary SjS develop a potentially life-threatening systemic disease (mainly lymphoma, but also severe internal organ involvements including nervous system, the lungs and the kidneys). This subset of patients requires intensive therapeutic management with a mortality rate of nearly 20% of cases.

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