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AB0411 RISK OF REACTIVATION OF HEPATITIS B VIRUS IN RHEUMATOID ARTHRITIS PATIENTS WHO RECEIVED LONG-TERM LOW DOSE CORTICOSTEROID THERAPY

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Background: It is well known that the use of corticosteroids results in increased viral replication and elevated ALT in patients with hepatitis B virus. The use of high dose corticosteroids for more than 4 weeks usually results in hepatitis worsening after cessation of steroids. However, few studies have investigated the effect of low dose corticosteroids on hepatitis B virus (HBV) reactivation.

Objectives: The aim of this study is to investigate the reactivity of HBV in rheumatoid arthritis (RA) patients treated with long term low dose corticosteroids and its risk factor.

Methods: Patients with HBsAg positive who were diagnosed with RA and who received prednisolone of less than 10 mg/day over four weeks and immunosuppressive agent were selected at four university hospitals in South Korea between June 1996 and March 2017. Medical records and laboratory data were retrospectively analysed and multivariate analysis was performed.

Results: One hundred forty five patients were included in the study and 26 (17.9%) patients were reactivated with HBV. Mean age at diagnosis of RA was 50.7 years and 41 (28.3%) patients were male. Baseline characteristics including sex, age and laboratory findings at diagnosis of rheumatoid arthritis were not significantly different in patients with HBV reactivation compared to those without HBV reactivation. The average daily dose of prednisolone was 3.65±2.77 mg and the mean duration of prednisolone was 5.11±5.05 years and the average cumulative dose of prednisolone was 5821.6±7021.3 mg. Eleven (42.3%) of 26 HBV reactivated patients were reactivated within one year after prednisolone administration and the period from the start of prednisolone administration to the reactivation was 4.08±5.77 years on average. The duration of prednisolone administration, mean daily dose of prednisolone, and cumulative prednisolone dose and administration of methotrexate, tacrolimus, tumour necrosis factor inhibitor and hydroxychloroquine did not significantly affect HBV reactivation in both univariate and multivariate analyses. However, the administration of leflunomide showed a significant difference in the reactivation of HBV (adjusted odd ratio 3.76; p=0.04)

Conclusions: The hepatitis B virus can be exacerbated by spontaneous viral reactivation, so it is difficult to conclude that hepatitis is caused by the administration of steroids. In this study, the administration of low-dose steroids did not affect the reactivation of HBV. However, leflunomide increased the risk of HBV reactivation when the effects of other disease modifying antirheumatic drug (DMARD) were corrected. Therefore, a prospective study is needed to evaluate the effect of DMARDs on HBV reactivation in the long-term administration of low-dose corticosteroids in RA patients.

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AB0412 DYNAMICS OF QUANTITATIVE BODY COMPOSITION INDICES BY THE METHOD OF DUAL-ENERGY X-RAY ABSORPTIOMETRY (DRA) IN PATIENTS WITH EARLY RA DEPENDING ON THE ACHIEVED ACTIVITY OF THE DISEASE

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Background: Adipose tissue an active endocrine organ. In pts with RA the redistribution of body fat mass. Using BMI and WC do not allow to distinguish between

fat and lean (muscle) mass. Performing dual-energy X-ray absorptiometry allows to specify the quantitative composition of the body(mass of adipose tissue and muscle) in pts with early RA.

Objectives: to compare the indicators of the quantitative composition of the body in groups of RApts with different disease activity before and after the appointment of therapy.

Methods: included 37pts with early RA(ACR/EULAR2010), 57 [46.5, 62] yrs, duration of disease 6 [5.5,15.5]mths, IgMRF seropositive antiCCP, with high RA activity(DAS285.5 [5.1,6], SDAI 32.4 [22.4, 42], CDAI 29 [19.7, 39.5]). After inclusion in the study, all pts started receiving MTX 10 [10-15 mg/week], after 12 weeks, with ineffective MTX, ADA 40 mg/² weeks was prescribed. The quantitative composition of the body was determined initially and after 6mths by means of DXA using the apparatus HOLOGIC,analysing the following parameters:the total, of fat and lean mass.

Results: By the 24th week of therapy, 13 (35%)pts with earlyRA received combined therapy(ADA, MTX), 24 (65%) pts with RA monotherapy MTX. Depending on the activity of RA(DAS28)by the 24th week of therapy, pts are divided into 2groups: I(n=18) pts with remission/low activity, II(n=19)with moderate/high RA activity (table 1). Initially, the groups differed in fat mass:this index was higher in the group of pts with moderate/high activity persisting, compared with the group of pts with remission/low activity of RA:30.2 kg versus 19.4 kg. In the I group of pts before the treatment and after 6mths of therapy,a statistically significant decrease in muscle mass was observed:from 45.2 kg to 41.6 kg. A decrease in the mass of adipose tissue after 24 weeks of therapy was noted in the IIgroup of pts with RA: from 30.2 kg to 28.2 kg. The difference in the indices between the groups by the 6 month of therapy was noted for the mass of adipose tissue. This composition of the body score was also higher in pts with moderate and high RA activity, compared to the group of pts with remission/low RA activity: 28.2 kg versus 18.9 kg (p<0.05 in all cases).

Abstract AB0412 – Table 1

	Group I(n=18)Remission/low activity			GroupII(n=19)Medium/high activity		
	0	24 weeks	Δ, %	0	24 weeks	Δ, %
Fat mass, kg	19,4	18,9	-3	30,2	28,2	-7
	[15,8;25,9]**	[16,4;24,3]***		[20,7;37,6]	[22,7;40,2]*	
Lean mass, kg	45,2	41,6	-8	42,9	44,2	+3
	[38,9;54,4]	[38,6;48,4]*		[38,9;54]	[40,1;55,4]	
Total weight, kg	70	64,9	-7	72,8	74,7	+3
	[58;80,8]	[59,5;81]		[60,;102]	[64;97,9]	
BMI, kg/m ²	23,4 [21,5;27,5]	23,8	+1	26,8	26,0	-2
		[20,2;26,5]		[22,8;34,6]	[23,3;34,3]	

*p<0,05 reliability of differences in factors before treatment and after 6mth(Wilcoxon);

**p<0.05 differences in baseline values in Groups I and II(Mann-Whitney test);

***p<0.05 difference in the indices between the groups by the 6mth of therapy; Δ,% the difference between the indices between the groups by the 6mth of therapy.

Conclusions: pts with RA who achieved Igroup after 6 mths of therapy initially had a smaller volume of adipose tissue, compared with pts with moderate and high RA activity. Despite the achievement of remission after 6mths of therapy,a loss of lean mass(probably the development of rheumatoid cachexia) continued in some pts, but these data need confirmation in studies with a large number of pts and a longer period of follow-up.

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AB0413 NODULAR POLYARTERITIS AS AN UNFORESEEABLE ADVERSE REACTION IN RA PATIENT TREATED WITH TOFACITINIB

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Background: Tofacitinib basic prescribing information and guidelines for medical use do not provide any description of such adverse drug reaction (ADR) as vasculitis, in particular polyarteritis nodosa. We present a clinical case of vasculitis emerging during tofacitinib therapy.

Objectives: demonstration of an unexpected reaction to tofacitinib

Demonstration of an unexpected reaction to tofacitinib

Methods: A 59 y.o. RA female patient was hospitalised in December 2016 due to eruption of indurated nodules on her hips and legs producing sharp pain, ulceration of nodules on the legs, painful hip and ankle joints, and morning stiffness lasting for about one hour.

Results: Seropositive RA was diagnosed in this patient in April 2004 with subsequent DMARD with methotrexate (MT) at 7,5 mg/week. The remission achieved

lasted until November 2005. Gradual dose escalation up to 20 mg/week was required during 2006 in view of RA exacerbations, nevertheless, clinical and lab RA activity persisted. Therefore tofacitinib (Jakvinius) was administered in November 2015 at 10 mg/day, with rapid achievement of minimum RA activity (DAS28=3.0). By the end of May 2016 clinical manifestations of vasculitis emerged, and in June 2016 tofacitinib was discontinued due to increasing lab activity of the disease. Clinical examination: patient's condition is moderately grave. The thinned skin looks dry, showing multiple regenerating ulcers on the anterior leg surface and sharply painful ulcerated indurations on the right inner thigh producing serosanguinous fluid. The RA activity is equal to DAS28=5.72, Hb 125 g/L, WBC $6.0 \times 10^9/L$, platelets $40 \times 10^9/L$, ESR 22 mm/h, CRP 42 mg/L, RF 413 IU/ml, antibody to cyclic citrullinated peptide (ACPA) is 195 U/ml, TNF – 13.9 pg/ml. Wrist and distal foot radiographs show moderate extended osteoporosis, narrowing of some joint spaces, rare bone and articular surface erosions, subluxation of some joints. Histopathology of skin and subcutaneous fat biopsy samples is presented on figure 1a,1b. Histopathology data suggests the presence of cutaneous and subcutaneous fat productive and destructive vasculitis and acute, predominantly lobular, panniculitis; such structural changes are usually present in cutaneous polyarteritis nodosa and other systemic vasculitis. The casual relationship between this ADR and tofacitinib therapy was assessed as probable using Naranjo scale.

Abstract AB0413 – Figure 1

Conclusions: development of vasculitis (polyarteritis nodosa) in RA patient can be caused by tofacitinib.

Disclosure of Interest: None declared

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AB0414 RELATIONSHIP BETWEEN SERUM OXYTOCIN LEVELS AND DEPRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Oxytocin (OXT), also referred to as a happy hormone, has been associated with various psychiatric disorders, including depression. However, the relationship between depression and rheumatoid arthritis (RA) has not yet been clarified.

Objectives: The objective of this study was to investigate the relationship between serum oxytocin levels and disease activity, depressive state, activity of daily life (ADL), and quality of life (QOL) in RA.

Methods: This study included 119 RA patients. We measured the following variables: baseline characteristics including age, sex, disease duration, smoking history, body mass index, prednisolone dose, and methotrexate (MTX) dose, serum levels of rheumatoid factor, matrix metalloproteinase-3, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level. The disease activity of RA was assessed using the Simplified Disease Activity Index (SDAI); depression was assessed using the Hamilton Depression Rating Scale (HAM-D); ADL were assessed using the Health Assessment Questionnaire; and QOL was assessed using the 36-Item Short Form Health Survey (SF-36). Serum OXT levels were determined by enzyme-linked immunosorbent assay. The subjects were divided into two groups according to the higher or lower of the serum OXT levels, and a retrospective study was performed.

Results: The serum OXT levels were correlated with the disease duration ($r=0.443$, $p=0.000$). Weak correlations of MTX dose ($r=0.208$, $p=0.030$), swollen

joint count (SJC) ($r=-0.306$, $p=0.001$), ESR ($r=-0.245$, $p=0.010$), CRP ($r=-0.283$, $p=0.003$) and the mental component summary (MCS) score ($r=-0.196$, $p=0.041$) of SF-36. The binominal logistic analyses findings were as follows: younger age ($p=0.0209$, odd ratio: 0.96, 95% CI: 0.94–0.99) and longer disease duration ($p=0.0053$, odd ratio: 1.08, 95% CI: 1.02–1.13). Other items did not correlate to the serum OXT levels included with the HAM-D score.

Conclusions: The serum oxytocin levels were correlated with longer disease duration and younger age.

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Rheumatoid arthritis – biological DMARDs

AB0415

DISEASE FLARES AMONG EARLY RHEUMATOID ARTHRITIS PATIENTS TREATED WITH CONTINUED METHOTREXATE EITHER ALONE OR IN COMBINATION WITH ADALIMUMAB

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Background: Some rheumatoid arthritis (RA) patients (pts) may experience flares in their disease even after reaching stable low disease activity (sLDA), but the consequences of even temporary elevations in disease activity are poorly understood.

Objectives: The purpose of this analysis was to explore the rates of flares after reaching sLDA in pts treated to target with either methotrexate (MTX) monotherapy or adalimumab combination therapy (ADA+MTX).

Methods: This post hoc analysis included pts from the randomised, double-blind, double-period OPTIMA¹ trial achieving sLDA [DAS28(CRP) <3.2 at weeks (wks) 22 and 26] at the end of period 1 (P1). In P1, pts were randomised to receive ADA +MTX or placebo (PBO) +MTX for 26 wks. Pts on ADA +MTX achieving sLDA were randomised to receive PBO +MTX (ADA Withdrawal) or continue on ADA +MTX (ADA Continuation) for an additional 52 wks in period 2 (P2). Pts who achieved sLDA on PBO +MTX in P1 continued their treatment in P2 (MTX Continuation). Pts achieving sLDA in each treatment group were categorised based on whether they experienced a flare [change in DAS28(CRP) ≥ 0.6 at consecutive visits and DAS28(CRP) ≥ 3.2]; the proportion of pts experiencing flares and time to flare were assessed. For each group, mean change from wk 26 to wk 78 in disease activity [DAS28(CRP)], functional (HAQ-DI) and structural (mTSS) measures were analysed.

Results: In pts achieving sLDA at the end of P1, flare rates in P2 differed based on initial treatment assignment (ADA Continuation: 11.7% [11/94]; MTX Continuation: 22.4% [22/98]). Interestingly, flare rates in pts randomised to withdraw ADA in P2 (ADA Withdrawal: 25% [22/88]) were numerically similar to the MTX Continuation group. The mean time to flare was 193, 191, and 177 days in the ADA Withdrawal, ADA Continuation, and MTX Continuation groups, respectively. During P2, the mean DAS28(CRP) scores were predictably higher in pts who flared compared with those who did not across treatment groups. In pts experiencing flares in P2, disease activity and functional measures worsened from wk 26 to wk 78 as compared with pts without flares (table 1). Of the individual DAS28(CRP) components, pt global assessment of disease activity (PtGA) showed the greatest worsening. There were small differences in radiographic progression between pts experiencing flares compared with pts without flares.