Low dose interleukin 10 and anti interleukin 1 in treatment of endometrial hyperplasia and rheumatoid arthritis

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Background:

Interleukin (IL)-10 and anti IL-1 could be useful in rheumatoid arthritis (RA) because of their ability to downregulate TH-1/TH-17 and TNF-alpha dependent inflammation.

Case report:

A 42 year old female patient complained of menorrhagia and dysmenorrhea since 6 months. Recent episode of menorrhagia lasted more than 15 days; and was controlled with oral Tab Pause-Xt. Her past menstrual history was inconsequential with nulligravida. She is suffering from RA since 5 years with joint disfigurement, severe pain and unresponsive to treatment such as methotrexate and DMARDs.

Her laboratory evaluations showed low haemoglobin and haematocrit. She had normal levels of oestrogen, progesterone but elevated levels of RA factor, highly sensitive C-reactive peptide (hsCRP) and erythrocyte sedimentation rate (ESR).

In Feb 2018, transvaginal ultrasound showed endometrial hyperplasia with 12.5 mm thickness; she was advised hysterectomy. Saliva sample was sent to Nutrional Genomix for gene testing of single-nucleotide polymorphism (SNPs - IL-1, IL-4, IL-6, IL-10, and IL-13). Reports showed that gene for IL-10 was downregulated and IL-1, IL-4 and IL-13 was upregulated.

Markers	Your Genotype	Composite Result	Effect
IL-1β (-31C > T)	CT	-+	Presence of risk allele i.e. Heterozygous positive is studied to be associated with slightly increased production of IL-1β, thus, at higher risk for inflammation.
IL-4 590C > T	CT	-+	Heterozygous positive individuals for the IL-4 polymorphism have been associated with higher circulating levels of IgE and thus, are at higher risk for developing eczema, atopy, or asthma.
IL-6 174 G > C	GG	--	The homozygous negative individual for this polymorphism of IL-6 is associated with normal plasma IL-6 levels and thus, is not associated with elevated plasma triglycerides, decreased HDL cholesterol or increased fasting serum glucose.
IL-10 627 C > A	AC	-+	Since you carry the risk allele for this polymorphism, it is studied to be associated with reduced secretion of IL-10 and therefore with greater tendency toward chronic inflammation including atherosclerosis, rheumatoid arthritis, inflammatory bowel disease, psoriasis, etc.
IL-13 R130Q G > A	AG	-+	Since Heterozygous positive individuals carry the risk allele for this polymorphism, which is associated with increased both serum total IgE and IgG antibody production thus, further increasing your risk of eczema, allergic rhinitis and asthma.

Treatment plan:

Based on the genomic profile her treatment comprised of oral 1 ml BID low dose of IL-10 and anti IL-1. Recombinant human IL-10 and anti IL-1 were purchased and was transformed into oral low dose form using sequential serial dilution and kinetic activation (SKA) method. SKA method employed by GUNA Lab (GUNA S.p.a., Milan, Italy) was used to amplify the therapeutic potential without adverse effects [1]. IL-4 and IL-13 are corelated with atopy and allergy, which was not relevant to this case.

Results:

In Jul 2018 endometrial thickness reduced to 7 mm and her menses restarted normally. ESR and hsCRP both corrected to normal range (see results in table below). RA factor reduced to half; from 342.1 to 123.8 IU/ml with symptomatic improvement in joint pain. Her rheumatic nodules have healed; crepitus is resolved and she is able to regain normal movements. The treatment is ongoing till RA factor turns normal. She does need to take oral diclofenac 12.5 mg/day to control her residual pain.

	Feb 2018	Jul 2018
Endometrial thickness	12.5 mm	7 mm
RA factor	342.1 IU/ml	123.8 IU/ml
hsCRP	32.69 mg/L	1.84 mg/L
ESR	70 mm/first hour	25 mm/first hour

Discussion:

The current issue with autoimmune disorders is finding the relevant molecular target for the patients. By SNP testing we can identify the molecular targets for that particular case and low dose cytokine therapy could be a safe, cheap therapeutic option in future.

References:

1. Martin-Martin LS, Giovannangeli F, Bizzi E, et al. An open randomized active-controlled clinical trial with low-dose SKA cytokines versus DMARDs evaluating low disease activity maintenance in patients with rheumatoid arthritis. *Drug Des Devel Ther*. 2017;11:985-994.

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