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Abstract Topic: - Molecular effects of genetic variation

Abstract Title: - Association of CTLA4 Single nucleotide polymorphism with vasculitis

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Aims: - The aim of the study is

* To analyze association of CTLA-4 gene (Cytotoxic T-lymphocyte associated antigen 4) single nucleotide polymorphism (rs3087243G>A) with vasculitis.

* To correlate the CTLA4 SNP expression with ANCA positive and ANCA negative cases of vasculitis. The expression is compared among cases and controls between A/A, A/G, G/G genotypes.

Methods: - This case-control study was conducted among 100 subjects who were divided into cases and controls as follows: CASES: 50 patients of vasculitis with clinical, radiological or histological evidence. CONTROL: 50 age and sex matched healthy volunteers from general population. Polymorphism in genes were analyzed by ARMS PCR amplification of DNA. Serum urea and creatinine, WBC count, ESR and hemoglobin are compared among cases and controls. Statistical analysis was done by SPSS-16 software.

Results: - The age, sex, BMI, serum urea, serum creatinine, hemoglobin, white blood cell count, erythrocyte sedimentation rate , ANCA positivity among cases, genotype of 50 cases and 50 controls.

1.The levels of serum urea and creatinine, ESR, WBC count are higher among cases than controls.

2.The expected genotype frequency according to Hardy Weinberg principle is calculated and chi-square test revealed that the CT60 (rs3087243) loci was in the balance of Hardy-Weinberg equilibrium (χ^2 test = 16.213, P=0.001). The CT60 (rs3087243) SNP loci can be used as a marker to study the association between the CTLA4 gene and vasculitis.

3.There is no significant difference in frequencies of genotype in cases (AA, 18% ; AG,31% ; GG,10%) and controls (AA,14% ;AG,39% ; GG, 4%) indicated by the p value (0.154).

4.The frequency of genotype in ANCA associated vasculitis (AA,15.4%; AG,30.8%; GG,53.8%) were significantly different from those in ANCA negative cases. It is evident that GG genotype is higher among cases of ANCA associated vasculitis (χ^2 test=12.429, P value=0.002*). Inversely the frequency of AG genotype is lower in ANCA associated vasculitis.

5. Univariate analysis is done to assess the risk of development of vasculitis if 'G' allele is present. Odds ratio, which is the measure of exposure and outcome, proves that there is 1.2 times higher frequency of 'G' allele among ANCA- associated vasculitis than ANCA negative vasculitis.

Hence individuals with polymorphism in 3'-untranslated region of CTLA4

Conclusions: - We evaluated the association of CTLA4 rs3087243 single nucleotide polymorphism with vasculitis.

1. We found that 26% of cases were ANCA positive and 37% of cases were ANCA negative.
2. There is no significant difference in frequency of genotype among vasculitis group and controls.
3. There is an increased frequency of patients homozygous for CTLA4 CT60 (rs3087243) single nucleotide polymorphism in ANCA associated vasculitis (53.8%).
4. The G allele of CT60 indicated a positive role in susceptibility to autoimmune vasculitis.
5. Lifestyle changes to minimize the environmental hazards can delay the occurrence of vasculitis among susceptible individuals.

The study warrants detailed investigation of larger cohorts among subgroups of vasculitis to support the hypothesis.

Keywords: - The age, sex, BMI, serum urea, serum creatinine, hemoglobin, white blood cell count, erythrocyte sedimentation rate, ANCA positivity among cases, genotype of 50 cases and 50 controls.

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Hence individuals with polymorphism in 3'-untranslated region of CTLA4