LP-110 DEVELOPMENT OF GSTA1, CYP2C19, AND CYP2B6 GENE POLYMORPHISM DETECTION METHODS ON THE RESPONSE OF CYCLOPHOSPHAMIDE THERAPY FOR LUPUS NEPHRITIS PATIENTS

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Background Cyclophosphamide, an immunosuppressant in patients with lupus nephritis, aims to prevent recurrence and is a steroid-sparing agent. The clinical response (efficacy and toxicity) of lupus nephritis patients receiving cyclophosphamide varied.[1] Cyclophosphamide is a pro-drug metabolized by hydroxylation via the CYP2C19 and CYP2B6 enzymes and detoxification via the glutathione-S-transferase (GST) enzyme.[2] The most common type of mutation that occurs is single nucleotide polymorphism (SNP). Several SNPs from previous studies associated with cyclophosphamide response, metabolism, and toxicity in patients with lupus nephritis, namely rs3957356 in the GSTA1, rs4244285 in the CYP2C19, rs7254579 and rs4802101 in the CYP2B6.[3] Therefore, detecting and screening SNP genotypes in lupus nephritis patients can help analyze cyclophosphamide response variation. This study aims to develop a method for detecting the genotypes of the four target SNPs and several surrounding SNPs using PCR-Sanger sequencing.

Methods The gene polymorphism analysis method was optimized before taking patient samples at the hospital. PCR and Sanger sequencing methods are used for gene polymorphism analysis because they produce chromatograms with target amplicon base lengths and several SNPs that can be analyzed simultaneously.

Results The analysis results of the four target SNPs of the GSTA1, CYP2C19, and CYP2B6 (rs3957356, rs4244285, rs7254579, and rs4802101) showed one synonymous SNP and three SNPs (regulatory and intergenic). We have developed an SNP detection assay using four fragments from the GSTA1, CYP2C19, and CYP2B6 that can detect 15 SNPs simultaneously (figure 1). In addition, this method succeeded in distinguishing wild-type, heterozygous and homozygous genotypes. Furthermore, this method can be used to analyze GSTA1, CYP2C19, and CYP2B6 gene polymorphisms in lupus nephritis patients receiving cyclophosphamide therapy, especially in a population in West Java, Indonesia.

Conclusions PCR-sanger sequencing is a reliable, accurate, and simple method for determining SNP genotypes from blood samples.

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8. Miscellaneous conditions associated with SLE

LP-112 A CASE OF MACROPHAGE ACTIVATION SYNDROME IN NEONATAL LUPUS

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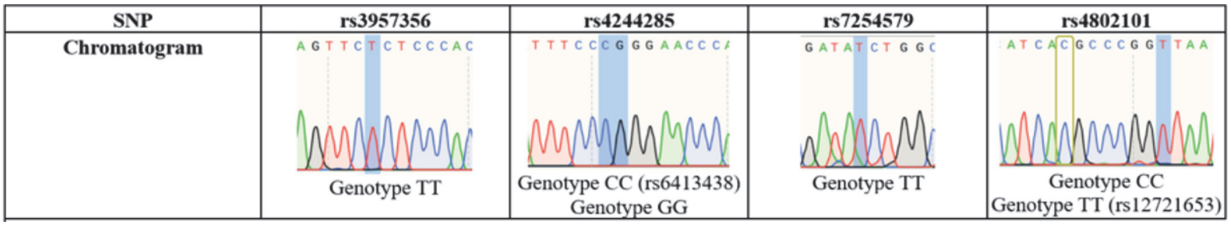
Description Neonatal lupus was developed in infants born from mother with autoimmune disorders through transplacental autoimmune antibodies. Macrophage activation syndrome (MAS) occur in autoimmune diseases and is fatal complication that led to death if not promptly diagnosed and treated appropriately. MAS in neonatal lupus is very rare.

A 33 days-old female was admitted due to fever with pancytopenia. Her skin was showed multiple erythema marginatum like rash on whole body. She was born from primipara mother without any autoimmune disorders. She was admitted at another hospital due to skin rash at post-natal 5 days and diagnosed with neonatal lupus because her mother auto immune study had positive anti-nuclear antibody (ANA) and anti-SSA (+), SSB (+). On admission, laboratory data were shown as 5.6 g/dL hemoglobin, 1,100/μL white blood cells (absolute neutrophil count: 110/μL), and 71,000/μL platelet. Inflammatory biomarkers showed C-reactive protein was 9.17mg/dL, and procalcitonin 1.88 ng/mL, and ferritin 1,507 ng/mL. DIC profiles were showed that INR of prothrombin time was over 5, aPTT over 120 seconds, and antithrombin III 64.2%, fibrinogen 401 mg/dL. We began empirical antibiotics for septicemia and high dose methylprednisolone (mPD) therapy for MAS. She received supportive care with packed red cell transfusion, fresh frozen plasma, and anti-thrombin. Body temperature decreased 3 days later after mPD treatment,



Abstract LP-110 Figure 1 Chromatogram depicting four genotypes SNP target and adjacent SNP simultaneously