CEN Case Reports (2018) 7:187–188
https://doi.org/10.1007/s13730-018-0322-5

LETTER TO THE EDITOR

Chronic nephritis associated with X-linked thrombocytopenia

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Received: 5 March 2018 / Accepted: 11 March 2018 / Published online: 16 March 2018

To the Editor,

A 31-year-old man was referred to our hospital due to thrombocytopenia and chronic kidney disease (CKD). His thrombocytopenia had been noticed since the age of 6 months, because of the bleeding diathesis. He had neither eczema nor deafness. He had been clinically diagnosed as chronic idiopathic thrombocytopenic purpura. At the age of 21, proteinuria and hematuria appeared, and thereafter his renal function deteriorated gradually. At the referral, his laboratory data were as follows: proteinuria 2.1 g/g creatinine, hematuria (3+), white blood cells 5100/μL, hemoglobin 10.3 g/dL, platelets 8000/μL, total protein 6.7 g/dL, albumin 4.1 g/dL, urea nitrogen 34.2 mg/dL, creatinine 2.92 mg/dL, C_3 74 mg/dL, C_4 28 mg/dL, CH-50 44.8 U/mL, and IgA 321 mg/dL. His autoantibodies were negative. By obtaining an informed consent from the patient, DNA sequencing analysis was performed using the next generation sequencer, MiSeq (Illumina, San Diego, CA) and TruSight One sequencing kit (Illumina). As a result of the analysis of 4813 genes, a missense mutation (c.223G > A, p.Val75Met) was found in the exon 2 in the *WAS* gene (Fig. 1). This mutation has already been reported to be responsible for a cause of X-linked thrombocytopenia (XLT) [1]. He was diagnosed as having XLT.

Mutations in the *WAS* gene cause either XLT or Wiskott–Aldrich syndrome (WAS). XLT is a mild form of WAS and characterized by congenital thrombocytopenia with small platelets, whereas WAS is associated with severe thrombocytopenia, small platelets, eczema, recurrent infection, and increased susceptibility to lymphoid malignancies. Chronic nephritis, such as IgA nephropathy, has been reported to be accompanied in 5–19% of XLT and WAS patients [1, 2]. Aberrant IgA production is considered to be a cause of chronic nephritis in these patients. In addition, results of recent studies have shown that WAS protein, relating to nephrin and Neph1, acts to the polymerization of actin in podocytes and plays an important role in the development of chronic nephritis [3, 4]. According to the previous studies [1, 2], a certain number of patients had developed to end-stage renal disease, requiring dialysis therapy. On the other hand, there are several cases in which hematopoietic stem cell transplantation (HSCT) was effective to improve chronic nephritis, as well as thrombocytopenia [5]. HSCT would be a therapeutic option in our case, if renal dysfunction progresses.

When a patient exhibits thrombocytopenia and renal dysfunction, it is important for nephrologists to think of XLT and to consider HSCT as an alternative therapy for CKD.

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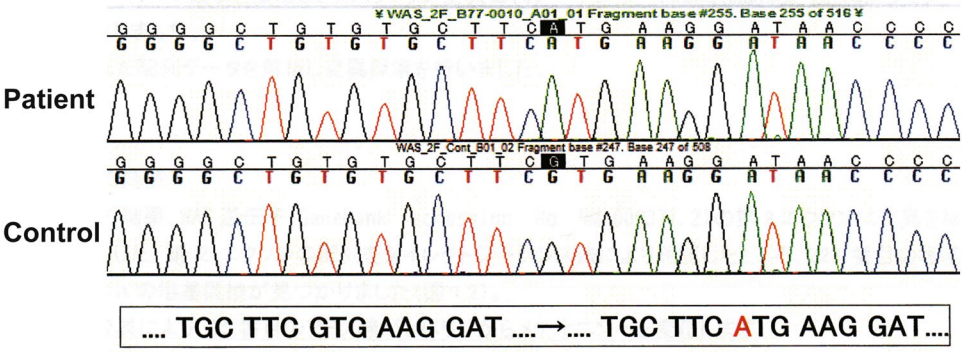

Fig. 1 A missense mutation (c.223G > A, p.Val75Met) in the exon 2 of the *WAS* gene. Top: patient, bottom: control

Compliance with ethical standards

Conflict of interest The authors have declared that no conflict of interest exists.

Human and animal rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee at which the studies were conducted (IRB Approval Number 20130388) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from an individual participant included in the study.

References

1. Imai K, Morio T, Zhu Y, Jin Y, Itoh S, Kajiwara M, Yata J, Mizutani S. Clinical course of patients with *WASP* gene mutations. Blood. 2004;103:456–64.
2. Albert MH, Bittner TC, Nonoyama S, Notarangelo LD, Burns S, Imai K, Espanol T, Fasth A, Pellier I, Strauss G, Morio T, Gathmann B, Noordzij JG, Fillat C, Hoenig M, Nathrath M, Meindl A, Pagel P, Wintergerst U, Fischer A, Thrasher AJ, Belohradsky BH, Ochs HD. X-linked thrombocytopenia (XLT) due to *WAS* mutations: clinical characteristics, long-term outcome, and treatment options. Blood. 2010;115:3231–8.
3. Fried S, Matalon O, Noy E, Barda-Saad M. WIP: more than a WASp-interacting protein. J Leukoc Biol. 2014;96:713–27.
4. Hattori S, Kanda S, Harita Y. Tyrosine kinase signaling in kidney glomerular podocytes. J Signal Transduct. 2011; 2011:317852.
5. Oshima K, Imai K, Albert MH, Bittner TC, Strauss G, Filipovich AH, Morio T, Kapoor N, Dalal J, Schultz KR, Casper JT, Notarangelo LD, Ochs HD, Nonoyama S. Hematopoietic stem cell transplantation for X-linked thrombocytopenia with mutations in the *WAS* gene. J Clin Immunol. 2015;35:15–21.