Use of darbepoetin alfa for myelodysplastic syndrome coincident with chronic kidney disease

Kei Nagai¹ · Kunihiro Yamagata¹

Received: 30 October 2015 / Accepted: 28 December 2015 / Published online: 22 January 2016
© Japanese Society of Nephrology 2016

To the Editor:

Darbepoetin alfa (DA) has been used in Japan since the end of 2014 to treat myelodysplastic syndrome (MDS) and is the only way apart from blood transfusion to improve these patients' anemia. Severe anemia is a suspected risk factor in progression of chronic kidney disease (CKD). It is therefore important to maintain appropriate hemoglobin levels in CKD patients, although it remains unclear whether administration of erythropoiesis-stimulating agents suppresses CKD progression [1]. Here, we show how using DA beyond the maximum dose for renal anemia appeared to improve renal function by maintaining hemoglobin levels in a patient with severe anemia caused by MDS coincident with CKD.

An 82-year-old man diagnosed with MDS by bone marrow examination had been treated at a local clinic. A low-dose continuous erythropoietin receptor activator was given, but had been stopped after 6 months because it was considered ineffective in improving his anemia. His serum creatinine level rose from 1.18 to 5.27 mg/dL in the 17 months after MDS diagnosis; he was then referred to our hospital (Fig. 1). We could not find out any exogenous causes to induce acute exacerbation of CKD such as administration of nephrotoxic reagents or clinical manifestation of infections. Although the patient's bodyweight and fluid volume were stably controlled, he felt general fatigue on mild exercise. We began treating him with high-dose DA (240 µg) and blood transfusions, because his

hemoglobin level had fallen below 6 g/dL and he was symptomatic. DA had just been approved for use in MDS in Japan; using it, we were able to maintain the patient's hemoglobin level at about 7 g/dL with infrequent blood transfusions. Interestingly, the patient's serum creatinine level simultaneously decreased to about 3 mg/dL (Fig. 1). We inferred that progression of the CKD had been suppressed by the aggressive use of DA to activate erythropoiesis.

We cannot clearly demonstrate why this man's renal function improved after DA administration. Urinalysis revealed a contentious, mild proteinuria with little hematuria, suggesting that the renal injury had been caused by

Fig. 1 Clinical course of the patient. The patient started to receive darbepoetin alfa 240 µg biweekly 18 months after being diagnosed with MDS. Serum creatinine and hemoglobin levels are demonstrated. Gray shading indicates hemoglobin level below 7.0 g/dL. CERA continuous erythropoietin receptor activator, DA darbepoetin alfa, MDS myelodysplastic syndrome, M months, W weeks

✉ Kei Nagai
knagai@md.tsukuba.ac.jp

¹ Department of Nephrology, Faculty of Medicine, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki 305-8575, Japan

renal ischemia associated with nephrosclerosis on which was superimposed progressive anemia. Although normalization of hemoglobin (to 12–13 g/dL) has not improved renal function in some clinical trials [2], severe anemia without treatment (Hct 25.3 ± 1.9 %) can worsen renal injury [3]. The patient's renal hypoperfusion with severe anemia seemed to have been alleviated by the blood transfusion and DA. Thus, this patient with both MDS and CKD benefited from high-dose DA.

Erythropoiesis-stimulating agents are often given to MDS patients with severe, symptomatic anemia requiring blood transfusion [4]. We suggest that avoiding severe anemia using high-dose DA (beyond the doses used in renal anemia: 120 µg per 2 weeks in Japan) in patients with MDS and CKD might be effective for preventing worsening of CKD.

Sincerely yours,
Kei Nagai, MD, PhD and Kunihiro Yamagata, MD, PhD

Compliance with ethical standards

Conflict of interest All the authors have declared no competing interest.

Source of funding None.

References

1. Chapter 3: use of ESAs and other agents to treat anemia in CKD. *Kidney Int Suppl.* 2012;2(4):299–310.
2. Palmer SC, Navaneethan SD, Craig JC, Johnson DW, Tonelli M, Garg AX, et al. Meta-analysis: erythropoiesis-stimulating agents in patients with chronic kidney disease. *Ann Int Med.* 2010;153(1):23–33.
3. Kuriyama S, Tomonari H, Yoshida H, Hashimoto T, Kawaguchi Y, Sakai O. Reversal of anemia by erythropoietin therapy retards the progression of chronic renal failure, especially in nondiabetic patients. *Nephron.* 1997;77(2):176–85.
4. Bowen D, Culligan D, Jowitt S, Kelsey S, Mufti G, Oscier D, et al. Guidelines for the diagnosis and therapy of adult myelodysplastic syndromes. *Br J Haematol.* 2003;120(2):187–200.