[10].

In conclusion, we present a new case of PEL, characterized by the massive proliferation of proerythroblasts and a markedly complex karyotype, with a very poor outcome in an advanced breast cancer patient.

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Received on Nov. 20, 2013; Revised on Jan. 6, 2014; Accepted on Mar. 4, 2014

http://dx.doi.org/10.5045/br.2014.49.1.69

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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Efficacy and safety of combined oral iron chelation therapy with deferasirox and deferiprone in a patient with beta-thalassemia major and persistent iron overload

TO THE EDITOR: Patients with beta-thalassemia major who need regular blood transfusions develop iron overload, because the body is unable to excrete the excess iron. Prevalence of complications resulting from iron overload is different in various regions [1]. Numerous management strategies have been proposed to decrease iron overload in thalassemic patients, among which deferoxamine (DFO) has been used for about 40 years. In contrast to the well-known benefits of deferoxamine, patients' compliance adversely affects the efficacy of this medication [2].

Oral iron chelators that are accompanied by better compliance have been proposed and examined during the past 2 decades. The first oral chelator was approved in 2005 for human use; deferasirox (DFX) is administered once daily and is approved for use in children aged ≥2 years. The second oral iron chelator, deferiprone (DFP), was approved for human use on October 14, 2011, in the United States [3].

Although combined oral and parenteral chelation therapy has been reported as an effective method to decrease iron overload [4], reports on combined oral iron chelation with both DFP and DFX are rare. Here, we describe a patient with thalassemia major who received a combination treatment with 2 oral chelating agents with significantly positive effects.

The patient is a 25-year-old woman with thalassemia major who has been receiving regular blood transfusions since 3 years of age in our thalassemia comprehensive center. She started chelation therapy with DFO by subcutaneous infusion in early childhood. She could not comply with the medication since the past few years because of difficulty in handling the drug and owing to the skin reactions at the insertion site of the implantable device. During the past 3 years, her serum ferritin level had an increasing trend that reached a maximum of 4,200 ng/mL at about 22 years of age. Liver and heart magnetic resonance imaging (MRI-T2*) at this time were 1.7 and 10.3 milliseconds (msec), respectively (normal values: cardiac MRI-T2* >20 msec, liver MRI-T2* >6.2 msec). Because of the lack of patient compliance and refusal to receive subcutaneous infusions of DFO, the patient commenced DFX at 25 mg/kg/day. Her serum ferritin level decreased significantly to 1,596 ng/mL

after 1 year of treatment. Liver and heart MRI-T2* increased to 6.78 and 15 msec, respectively. After availability of DFP and published reports regarding safety of the drug and because of moderate degrees of cardiac iron loading on the cardiac MRI (15 msec at this time), DFP 75 mg/kg/day in 3 doses/day was added to a single dose of DFX after obtaining the patient's informed consent. After 8 months of combined treatment, the serum ferritin level dropped to less than 100 ng/mL, and liver and heart MRI-T2* increased to 9.0 and 23.1 msec, respectively. As a result of the ensuing hypoferritinemia and normalization of liver and cardiac MRI indices, the combined regimen was then modified to DFX 15 mg/kg/day 3 times per week and DFP 50 mg/kg/day 4 days per week. No adverse effect or toxicity was reported during the combined treatment. Complete blood counts were checked every 15 days for the first 3 months and then monthly thereafter.

Review of the literature shows that there are few reports of treatment of iron overload with a combination of oral iron chelators. There is a report of successful monotherapy with DFP in pediatric patients, although adverse effects such as gastrointestinal irritation and neutropenia were important concerns [5]. Combined intensive therapy with DFO and DFP has shown a significant decrease in iron overload and profound improvement in cardiac siderosis [6, 7]. Since the past decade, cardiac MRI-T2* has been extensively used as a noninvasive tool to measure iron deposits in the heart. At present, this technique has been recognized as the most sensitive index to evaluate cardiac iron burden [8]; meanwhile, liver MRI-T2* correlates well with hepatic iron concentration. Alternate treatment with DFP and DFX has been reported with significant effect mainly on serum ferritin and liver iron levels in 2 patients [9]. The drugs' doses used by the researchers were similar to ours (75 mg/kg/day for DFP and 30 mg/kg/day for DFX). Voskaridou *et al.* [10] reported successful combined oral chelation therapy in a 34-year-old woman. Compared with our patient, their patient had a lower serum ferritin level as well as less severe indices in the liver and cardiac MRI-T2*. Although we used approximately similar doses of both drugs for combination therapy, our patient's response to the treatment was so significant that it led to hypoferritinemia, which has not previously been reported, and normal cardiac index in the follow-up imaging. Finally, we continued both drugs on an alternative schedule for each, compared with the daily doses used by Voskaridou *et al.* [10].

Continuous chelation achieved by using combined oral iron chelators might be promising in alleviating iron overload in patients who do not comply with DFO and also have developed high cardiac siderosis. However, it is difficult to make a final judgment based on a single case report. Larger studies through clinical trials are recommended to confirm the safety of combining these 2 drugs.

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Received on Jan. 2, 2014; Revised on Feb. 20, 2014; Accepted on Mar. 4, 2014

http://dx.doi.org/10.5045/br.2014.49.1.72

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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