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Letter to the Editor

Acquired Hemoglobin C Secondary to Transfusion With Antigen-Matched Red Blood Cells

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To the Editor:

Raciti et al. [1] recently described a patient with sickle cell disease requiring chronic transfusion support, who was passively transfused with hemoglobin C (HgbC), hemoglobin G-Philadelphia, and glucose-6-phosphate dehydrogenase deficient RBC units all of which were antigen-matched to reduce the likelihood of alloimmunization. We would like to share our experience with a similar patient.

The patient was a 13-year-old black male with sickle cell disease complicated by pain crises, priapism, silent brain infarcts, iron overload, and alloimmunization (anti-E), who receives simple blood transfusion every three weeks. Per institutional policy, the patient receives units matched for Rh and K1 antigens, with extended matching for Fy^a and S, if possible. Most recently, the patient was transfused with two antigen-matched, crossmatch-compatible RBC units (A-positive; E-, K1-, S-, Fy^a-) without incident and an appropriate post-transfusion increase in hemoglobin (pre: 8.2 g/dL, post: 9.6 g/dL). A post-transfusion hemoglobin fractionation and quantification was performed using high-performance liquid chromatography (HPLC, Bio-Rad Variant II System; Hercules, CA). The patient had the expected reduction in HgbS (18.8%); however, there was a new minor peak (5.05 minutes, 2.2% total) eluting in the "C-window," consistent with HgbC (Fig. 1A). This was confirmed by capillary zone electrophoresis (Sebia Capillarys, Fig. 1C). Sample contamination was excluded and a review of the patient's previous hemoglobin evaluations confirmed this was a new peak.

Because of the recent transfusion, retained segments from the two RBC units were subjected to HPLC analysis. The first unit demonstrated a normal chromatogram, while the second unit (Fig. 1B) disclosed a peak eluting at 5.16 min comprising 31.4% of the total hemoglobin, consistent with a HgbC heterozygous donor. The slightly later elution time seen in the donor (5.16 versus 5.05 min) is an artifact of the HPLC method whereby smaller peaks tend to elute slightly faster than large peaks. This artifact was confirmed with a titration study performed by the authors.

As mentioned by Raciti et al. [1], we too considered the consequences of antigen-matching for this patient. Donors negative for K1, S, and Fy^a antigens are significantly more common among black donors (60% versus 15% white) [2], thus increasing the likelihood of transfusion with HgbC. HgbC is present in 2.4% of African Americans and is particularly high among those of west Africa descent, where the incidence of HgbC reaches 25% of the general population [3]. Less commonly, HgbC may be seen in those of Middle Eastern and Mediterranean descent [4]. Interestingly, the donor in our case was a 62-year-old Caucasian female who was a long-time donor.

Clinically, individuals with HgbC trait are asymptomatic. Passive transfusion of donor RBC with HgbC trait is unlikely to adversely affect transfusion efficacy although it can confuse diagnostic testing. There are also ethical issues regarding the need to inform the donor. While HgbC trait is a benign disorder, homozygosity (HgbC disease) or inheritance with another hemoglobin variant such as HgbS (Hgb SC disease) can lead to a clinically relevant hemoglobinopathy with implications for genetic counseling.

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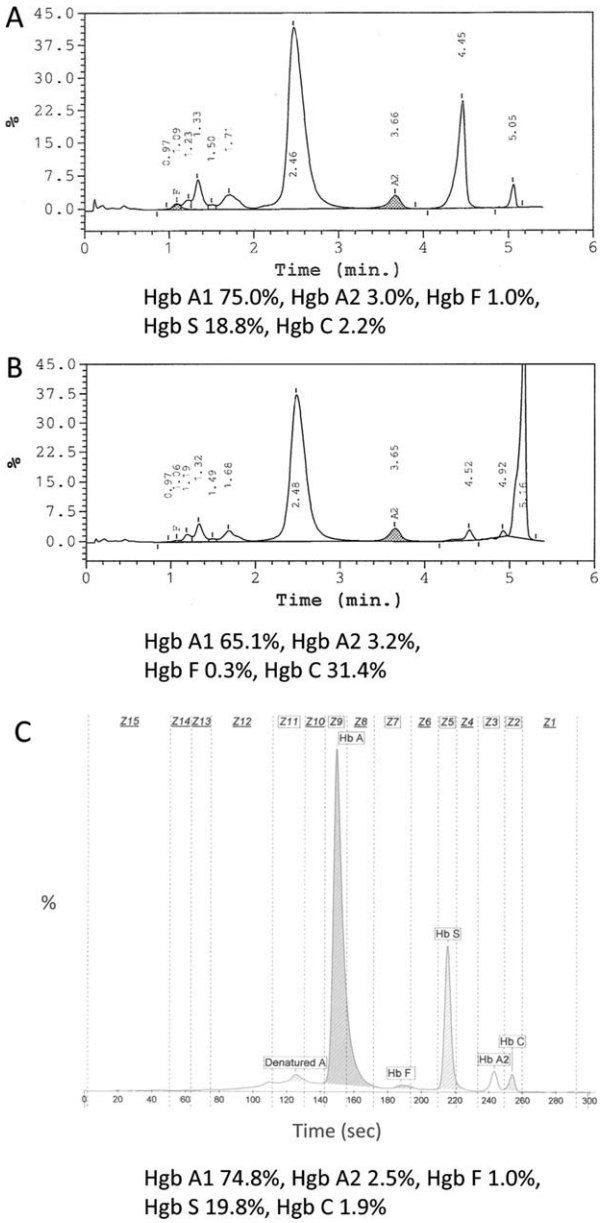

Fig. 1. Panel (**A**) is the patient's post-transfusion chromatogram demonstrating hemoglobins F, A1, A2, S, and a small amount of hemoglobin C (2.2%) eluting at 5.05 min. Panel (**B**) is the chromatogram of the donor unit demonstrating heterozygosity for hemoglobin C which elutes at 5.16 min, slightly later than seen in Panel (A). Panel (**C**) is the confirmatory capillary zone electrophoresis chromatogram of the patient's post-transfusion sample, demonstrating a small peak corresponding to hemoglobin C (1.9%).

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