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Transfused neutrophils home to a joint with fungal infection

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Granulocyte collection from donors stimulated by G-CSF and dexamethasone is well established¹ and allogeneic granulocyte transfusions may bridge periods of neutropenia or marrow suppression.² The published evidence of its effectiveness is limited.³ Here we document the migration of transfused granulocytes in a severely neutropenic patient to a suspected *Fusarium* seeded joint.

A 9-year-old Jamaican boy with sickle cell trait developed neutropenia with an absolute neutrophil count (ANC) of $0.00 \times 10^3/\mu\text{l}$. Cultures of peripheral blood and skin lesion biopsies grew *Fusarium solani*. He was diagnosed with severe aplastic anemia (SAA) and his abbreviated clinical history has been reported as part of a single-center case series of invasive fusariosis (patient no. 10).² Magnetic resonance imaging (MRI) showed osteomyelitis in several joints. He received horse antithymocyte globulin (hATG) and cyclosporine followed by the transplantation of hematopoietic progenitor cell (HPC) grafts. His neutropenia and marrow suppression was bridged by granulocyte transfusions from unrelated donors stimulated with 480 μg G-CSF and 8 mg dexamethasone.

After 17 granulocyte transfusions over 36 days and therapeutic doses (mean $\pm$ SD) of $6.29 \pm 1.90 \times 10^{10}$ granulocytes per transfusion, yielding a mean post-transfusion ANC of $1.94 \pm 1.14 \times 10^3/\mu\text{l}$ without signs of engraftment, he complained about pain and stiffness in several joints. The right knee joint was drained of a yellow cloudy purulent fluid. Numerous neutrophils were found in this aspirate (Fig. 1, left panel; Diff-Quick staining), of which a paraffin-embedded cell block was prepared (right panel; hematoxylin and eosin staining). No fungi were identified in this aspirate (Grocott's methenamine silver (GMS) staining, photomicrograph not shown) and no bacteria intra- or extracellularly, while signs of infection remained at different sites. The neutrophil morphology appeared well preserved in this joint inflammation associated with fungal osteomyelitis in contrast to the often frail morphology found, for instance, in rheumatoid arthritis.

The symptoms in his joints improved moderately as a total of 39 granulocyte products were administered over 70 days. The HPC grafts were rejected in association with the development of new HLA antibodies, possibly induced by exposure to allogeneic

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granulocytes from multiple donors. The patient eventually succumbed² to overwhelming adenoviral infection.

Transfused granulocytes have been known to home to bacterially infected solid tissues.^{4,5} The photomicrographs document that such mobilized transfused neutrophils also retain their ability to migrate into joint cavities inflamed by fungal infection. Granulocyte transfusions may be underutilized⁴ because this blood product is produced only upon special request, although they could become an adjunct to anti-microbial therapy in any life-threatening non-viral infection associated with neutropenia.⁶

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References

1. Dale DC, Liles WC, Llewellyn C, Rodger E, Price TH. Neutrophil transfusions: kinetics and functions of neutrophils mobilized with granulocyte-colony-stimulating factor and dexamethasone. *Transfusion*. 1998; 38:713–21. [PubMed: 9709778]
2. Kadri SS, Remy KE, Strich JR, Gea-Banacloche J, Leitman SF. Role of granulocyte transfusions in invasive fusariosis: systematic review and single-center experience. *Transfusion*. 2015; 55:2076–85. [PubMed: 25857209]
3. Estcourt LJ, Stanworth S, Doree C, Blanco P, Hopewell S, Trivella M, Massey E. Granulocyte transfusions for preventing infections in people with neutropenia or neutrophil dysfunction. *Cochrane Database Syst Rev*. 2015(6):CD005341.
4. Ein-Gal S, Pepkowitz SH, Hurvitz CH, Goldfinger D. Dramatic tissue response after a single granulocyte transfusion. *Transfusion*. 2007; 47:2185–6. [PubMed: 17714424]
5. Lee JJ, Song HC, Chung JJ, Bom HS, Cho D, Kim HJ. Clinical efficacy and prediction of response to granulocyte transfusion therapy for patients with neutropenia-related infections. *Haematologica*. 2004; 89:632–3. [PubMed: 15136239]
6. Marfin AA, Price TH. Granulocyte transfusion therapy. *J Intensive Care Med*. 2015; 30:79–88. [PubMed: 23920161]

Fig. 1.