

Copyright Information of the Article Published Online

TITLE	Successful lower leg microsurgical reconstruction in homozygous sickle cell disease: Case report
AUTHOR(s)	Carolina Posso, Francisco Cuéllar-Ambrosi
CITATION	Posso C, Cuéllar-Ambrosi F. Successful lower leg microsurgical reconstruction in homozygous sickle cell disease: Case report. <i>World J Hematol</i> 2016; 5(4): 94-98
URL	http://www.wjgnet.com/2218-6204/full/v5/i4/94.htm
DOI	http://dx.doi.org/10.5315/wjh.v5.i4.94
OPEN ACCESS	<p>This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See:</p> <p>http://creativecommons.org/licenses/by-nc/4.0/</p>
CORE TIP	<p>This is a case report of a successful microsurgical reconstruction in a patient with sickle cell disease who presented with an extensive lower leg ulcer during a 12-year course of the disease. We provide several recommendations for plasmapheresis and blood transfusions before the surgical reconstruction, and the anticoagulation protocol during the procedure and the</p>

	postoperative period. This case description is intended to increase our colleagues' motivation to perform microsurgical reconstruction with a safer approach in the presence of hematologic diseases with elevated risk of thrombosis.
KEY WORDS	Sickle cell disease; Free flaps; Success rate; Microsurgical reconstruction; Ulcer
COPYRIGHT	© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.
NAME OF JOURNAL	World Journal of Hematology
ISSN	2218-6204 (online)
PUBLISHER	Baishideng Publishing Group Inc, 8226 Regency Drive, Pleasanton, CA 94588, USA
WEBSITE	http://www.wjgnet.com

Successful lower leg microsurgical reconstruction in homozygous sickle cell disease: Case report

Carolina Posso, Francisco Cuéllar-Ambrosi

Carolina Posso, Plastic and Reconstructive Surgery Service, University of Antioquia, Antioquia, Medellín 050010238, Colombia

Francisco Cuéllar-Ambrosi, Hematology Service, León XII Clinic, IPS Universitaria, Antioquia, Medellín 050010204, Colombia

Author contributions: Posso C and Cuéllar-Ambrosi F contributed to the acquisition of data and writing of the manuscript.

Correspondence to: Carolina Posso, MD, Plastic Surgeon-Microsurgeon, Plastic and Reconstructive Surgery Service, University of Antioquia, Antioquia, Medellín 050010238, Colombia. carolina.posso@gmail.com

Telephone: +57-4-3861283

Received: May 21, 2016 Revised: October 12, 2016 Accepted: October 25, 2016

Published online: November 6, 2016

Abstract

We present an 18-year-old female with sickle cell disease, who presented with an extensive lower leg ulcer over a 12-year course of the disease. Definitive reconstruction was made using a free latissimus dorsi flap and split-skin grafts. One week before the surgery, the plasmapheresis protocol and blood transfusion were administered, in order to achieve a hemoglobin S level of $\leq 30\%$. Intraoperatively, the flap pedicle was rinsed with plasminogen activator inhibitor-1 until the thrombolytic agent was obtained from the comitant vein; after the arterial flow had been released, an intravenous bolus dose of heparin (2000 U) was administered. No vascular complications occurred. Postoperatively, the patient received a 10-d course of hemodilution and a 14-d course of full-dose anticoagulation. After 8 mo postoperatively, the patient was able to walk and run, and showed complete wound healing. This case indicates that sickle cell disease is not a contraindication to free tissue transfer; however, the complications, their rate and overall outcomes for these cases are not yet clear. Herein, we provide an algorithm based on our clinical experience in this type of case and treatment, including several recommendations that may help to reduce thrombosis risk and systemic complications.

Key words: Sickle cell disease; Free flaps; Success rate; Microsurgical reconstruction; Ulcer

Posso C, Cuéllar-Ambrosi F. Successful lower leg microsurgical reconstruction in homozygous sickle cell disease: Case report. *World J Hematol* 2016; 5(4): 94-98 Available from: URL: <http://www.wjgnet.com/2218-6204/full/v5/i4/94.htm> DOI: <http://dx.doi.org/10.5315/wjh.v5.i4.94>

Core tip: This is a case report of a successful microsurgical reconstruction in a patient with sickle cell disease who presented with an extensive lower leg ulcer during a 12-year course of the disease. We provide several recommendations for plasmapheresis and blood transfusions before the surgical reconstruction, and the anticoagulation protocol during the procedure and the postoperative period. This case description is intended to increase our colleagues' motivation to perform microsurgical reconstruction with a safer approach in the presence of hematologic diseases with elevated risk of thrombosis.

INTRODUCTION

The introduction of microsurgery has opened new fields for the reconstructive surgeon, so that we are now prepared to face even more challenging cases. During vascular anastomosis in microsurgical procedures, there is always risk of thrombosis, even in experienced hands and at prestigious institutions^[1,2], but especially in cases of lower leg reconstruction. Patients with hematologic diseases and hypercoagulability are usually associated with high rates of complications, including anastomotic thrombosis and flap loss^[3]. Clinical experience with free flaps and sickle cell disease is limited, and clear recommendations are not available.

Herein, we describe our clinical experience with a patient with sickle cell disease, who presented with a chronic ischemic lower leg ulcer that was reconstructed successfully with a free flap.

CASE REPORT

An 18-year-old Afro-American female from Chocó, Colombia, with known homozygous sickle cell disease consulted with our department regarding an extensive lower leg ulcer that had presented during a 12-year period. During that time, the patient had also presented with multiple episodes of limited osteomyelitis and soft tissue infections, for which she had been treated with systemic antibiotics; however, at no time had a real debridement and definitive reconstruction been performed because of the risk of complications (Figure 1).



Figure 1 Ulcer on lower leg of the patient with sickle cell disease. A: Soft tissue defect; B: Detail of bone exposure; C: After extensive bone and soft tissue debridement.

One week before the microsurgical reconstruction, we started the patient on a plasmapheresis protocol and blood transfusion, with the aim of achieving a hemoglobin S level of $\leq 30\%$. An extensive soft tissue debridement and an anterior tibial decortication were performed subsequently, and no obvious bone defect was created. Bone and soft tissue cultures were taken; the analysis of which provided negative results. One week later, a free

latissimus dorsi flap surgery was performed to cover the soft tissue defect (20 cm × 8 cm; Figure 2). The anterior tibial vessels were determined to be compromised at the middle-third of the lower leg. Before the anastomosis, the flap pedicle was rinsed using plasminogen activator inhibitor-1 (commonly known as PAI-1), until the thrombolytic agent was obtained from the comitant vein. An end-to-end anastomosis was then made between the posterior tibial artery and the thoracodorsal artery, and only one comitant vein was anastomosed. The venous anastomosis was made first following the arterial anastomosis, and later on an intravenous bolus dose of heparin (2000 U) was administered. The total ischemia time was 40 min. A partial skin graft was made to cover the muscle (Figure 3).

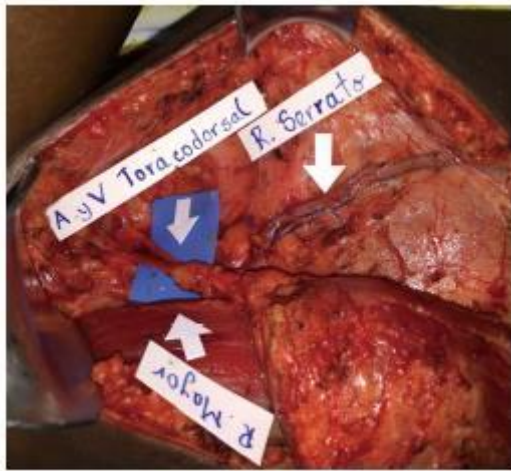


Figure 2 Vascular anatomy of the free flap.



Figure 3 Immediate postoperative result. The muscle is shown from two angles covered with the split-thickness skin graft.

During the postoperative period, hemodilution was administered over a 10-d course; no vascular complications occurred. A 14-d course of full-dose anticoagulation (low-molecular-weight heparins) was administered as well. After 3 wk, the patient presented partial loss of the skin graft due to a superficial infection. The patient was admitted to the hospital for intravenous treatment with ciprofloxacin (400 mg/d). After 10 d, a second skin graft was made and complete healing was achieved. The final clinical result is shown in Figure 4, after 3 mo and 8 mo of follow-up.



Figure 4 Follow-up postoperative results. A: After 3 mo of follow-up; B: After 8 mo of follow-up.

DISCUSSION

The sickle cell trait (SCT) results from the inheritance of one normal hemoglobin gene (HbA) and one mutated beta-globin gene (a sickle hemoglobin gene, HbS). In sickle cell disease, however, two sickle hemoglobin genes are inherited. The incidence of SCT and sickle cell disease in individuals living in the geographic region of Chocó, a Northwest Colombian area with a high density of Afro-American peoples, is 11%; intriguingly, vascular events are less frequent in these cases due to geographic adaptations of the sickle gene^[4]. Increased erythrocyte sickling occurs under conditions of hypoxia, acidosis, dehydration and hypothermia^[5]. SCT has been associated with an increased rate of exercise-related deaths, fetal loss, pre-eclampsia and venous thromboembolism.

Patients with SCT or sickle cell disease are usually considered a higher risk group for microsurgical reconstructions, and there is some pessimism among microsurgeons when these procedures are required^[6]. In particular, rates of free flap loss in lower extremity reconstructions are higher compared to those in head and neck reconstruction, where the accepted rate of failure can be up to 5%. Failure rates reported in lower leg reconstruction, in contrast, varies from 6% to 15%, depending on the case series^[7].

There is growing evidence from reports of clinical experiences involving patients with hematologic diseases and microsurgery^[8], but most of the case series have thus far included patients with very different types of disorders (*i.e.*, various etiologies and risks of thrombosis or bleeding), such as an increased number of blood elements responsible for hemostasis, abnormal blood elements or abnormality within the coagulation cascade. If we consider patients with sickle cell disease exclusively, only a few cases have been reported to date, some of which include flap loss^[9,10]; hence, the question remains: Can we compare different hematologic diseases and outcomes in microsurgery?

According to our experience, there are several recommendations that should be included in this particular group of patients undergoing microsurgical reconstruction (Figure 5). In the first place, control of the medical condition is essential and the hematologist should work closely with the reconstructive surgeon. Normally, the patient receives multiple transfusions to maintain the HbS level well below the recommended 30% level for a free flap surgery so that the risk of anastomosis occlusion can be minimized^[11]. On the other hand, it has been strongly recommended to use prophylactic anticoagulation therapy, but there is no evidence that this treatment will avoid any type of vascular complication. The ideal duration and type of therapy are not yet known.

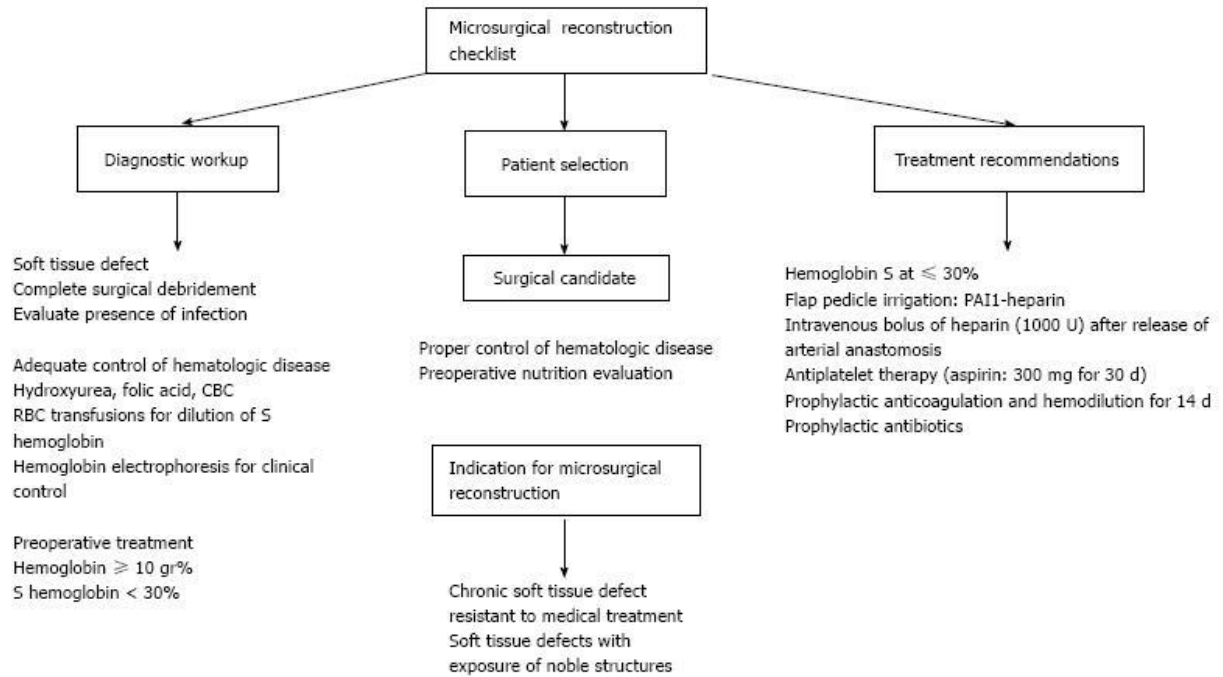


Figure 5 Algorithm treatment strategies for sickle cell disease.

Regarding the microsurgical technique, Ozkan *et al*^[12] reported some strategies that would help to avoid complications, but we disagree on some of them. First, proper flap selection does not depend on whether or not your patient has any hematologic disease; reliable anatomy is always desirable, but donor site morbidity, extension and location of the soft tissue defect should be always considered. Ozkan *et al*^[12] also recommended large recipient vessels, but what it is really important is to perform the vascular anastomosis in a healthy zone, avoiding inflammation of the vessel wall.

In conclusion, microsurgery transfer provides a well-vascularized tissue to solve extensive soft-tissue defects in a single procedure. In patients with SCT or sickle cell disease, complications such as thrombosis, bleeding, infection or poor wound healing may occur. This particular group of patients should be evaluated carefully before surgery so as to modify any potential risk factor. We have now demonstrated that it is possible to perform a successful free flap in one of these patients, but more extensive and closer monitoring in the postoperative period and a longer regimen of anticoagulation agents might be indicated. Moreover, this is a single-case report and larger case series are needed to clearly establish outcomes and rate of complications.

COMMENTS

Case characteristics

An 18-year-old female with medical history of sickle cell disease presented with a 12-year history of skin ulcer in her left leg and multiple episodes of limited osteomyelitis and soft tissue infections. The ulcer was reconstructed using a free flap.

Clinical diagnosis

A soft tissue defect was located over the anterior surface of the lower leg with bone exposure (20 cm × 8 cm).

Differential diagnosis

Chronic osteomyelitis, vascular ulcer.

Laboratory diagnosis

The hemoglobin level at admission was consistent with severe anemia.

Imaging diagnosis

A vascular occlusion was present in the anterior tibial artery.

Pathological diagnosis

After surgical debridement, bone culture was negative.

Treatment

Definitive soft tissue reconstruction was made using a free muscular flap and split-thickness skin graft.

Related reports

Microsurgical reconstruction in patients with hematologic diseases has not been reported frequently in the medical literature. Furthermore, if the authors consider patients with sickle cell disease exclusively, very few case reports are available, some of which include flap loss. There are no clear recommendations on how to decrease the risk of pedicle thrombosis in this patient population.

Term explanation

Sickle cell disease is an inherited red blood cell disorder, in which two sickle hemoglobin genes (HbS) are inherited. Increased erythrocyte sickling and secondary thrombosis occurs under special conditions, such as hypoxia, acidosis, dehydration and hypothermia, causing vascular compromise and skin necrosis in some cases. Patients with the sickle cell trait or disease are usually considered a higher risk group for microsurgical reconstructions, and preoperative control of the disease and a different surgical protocol should be included in order to avoid vascular complications.

Peer-review

This is an interesting and well written clinical case report.

REFERENCES

- 1 **Spence RJ.** The use of a free flap in homozygous sickle cell disease. *Plast Reconstr Surg* 1985; **76**: 616-619 [PMID: 4034781 DOI: 10.1097/00006534-198510000-00026]
- 2 **Khouri RK,** Upton J. Bilateral lower limb salvage with free flaps in a patient with sickle cell ulcers. *Ann Plast Surg* 1991; **27**: 574-576 [PMID: 1793245 DOI: 10.1097/00000637-199112000-00011]
- 3 **Richards RS,** Bowen CV, Glynn MF. Microsurgical free flap transfer in sickle cell disease. *Ann Plast Surg* 1992; **29**: 278-281 [PMID: 1524382 DOI: 10.1097/00000637-199209000-00017]
- 4 **Cuéllar-Ambrosi F,** Mondragón MC, Figueroa M, Préhu C, Galactéros F, Ruiz-Linares A. Sickle cell anemia and beta-globin gene cluster haplotypes in Colombia. *Hemoglobin* 2000; **24**: 221-225 [PMID: 10975441 DOI: 10.3109/036302600008997529]
- 5 **Novelli EM,** Gladwin MT. Crises in Sickle Cell Disease. *Chest* 2016; **149**: 1082-1093 [PMID: 26836899]
- 6 **McAnney A,** Durden F, Pearson GD, Tiwari P. Intra-flap thrombosis secondary to acute sickle crisis: a case report. *Microsurgery* 2012; **32**: 585-587 [PMID: 22976171 DOI: 10.1002/micr.22024]
- 7 **Hill JB,** Vogel JE, Sexton KW, Guillaumondegui OD, Corral GA, Shack RB. Re-evaluating the paradigm of early free flap coverage in lower extremity trauma. *Microsurgery* 2013; **33**: 9-13 [PMID: 22730189 DOI: 10.1002/micr.21994]
- 8 **Lin PY,** Cabrera R, Chew KY, Kuo YR. The outcome of free tissue transfers in patients with hematological diseases: 20-year experiences in single microsurgical center. *Microsurgery* 2014; **34**: 505-510 [PMID: 24648370 DOI: 10.1002/micr.22243]
- 9 **Weinzweig N,** Schuler J, Marschall M, Koshy M. Lower limb salvage by microvascular free-tissue transfer in patients with homozygous sickle cell disease. *Plast Reconstr Surg* 1995; **96**: 1154-1161 [PMID: 7568493 DOI: 10.1097/00006534-199510000-00024]
- 10 **Platt AJ,** Robertson A, Batchelor AG. Successful free flap transfer and salvage in sickle cell trait. *Br J Plast Surg* 2000; **53**: 707-708 [PMID: 11090333 DOI: 10.1054/bjps.2000.3446]

- 11 **Koshy M**, Weiner SJ, Miller ST, Sleeper LA, Vichinsky E, Brown AK, Khakoo Y, Kinney TR. Surgery and anesthesia in sickle cell disease. Cooperative Study of Sickle Cell Diseases. *Blood* 1995; **86**: 3676-3684 [PMID: 7579333]
- 12 **Ozkan O**, Chen HC, Mardini S, Cigna E, Hao SP, Hung KF, Chen HS. Microvascular free tissue transfer in patients with hematological disorders. *Plast Reconstr Surg* 2006; **118**: 936-944 [PMID: 16980855 DOI: 10.1097/01.prs.0000232371.69606.61]

FIGURE LEGENDS

Figure 1 Ulcer on lower leg of the patient with sickle cell disease. A: Soft tissue defect; B: Detail of bone exposure; C: After extensive bone and soft tissue debridement.

Figure 2 Vascular anatomy of the free flap.

Figure 3 Immediate postoperative result. The muscle is shown from two angles covered with the split-thickness skin graft.

Figure 4 Follow-up postoperative results. A: After 3 mo of follow-up; B: After 8 mo of follow-up.

Figure 5 Algorithm treatment strategies for sickle cell disease.

FOOTNOTES

Institutional review board statement: This case report was reviewed by and adhered to the standards set forth by the Institutional Review Board of the Clinic León XIII Ips University of Antioquia, Colombia.

Informed consent statement: The anonymity of the identity of the patient involved in this study was not compromised in the case report. The patient provided written informed consent for publication of these data.

Conflict-of-interest statement: Both authors declare no conflicts of interests in relation to this study or its publication.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Peer-review started: May 23, 2016

First decision: July 27, 2016

Article in press: October 27, 2016

P- Reviewer: Carter WG, Siddiqui AH **S- Editor:** Kong JX **L- Editor:** A **E- Editor:** Lu YJ