Surgical Treatment of Persistent Macrocheilia in Patients With Melkersson-Rosenthal Syndrome and Cheilitis Granulomatosa

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Background: Various conservative methods for treatment of labial swelling in patients with cheilitis granulomatosa have been attempted, often with only moderate success and sometimes with persistent disfiguring lip swelling. Severe macrocheilia can produce an unaesthetic facial deformity associated with functional disturbances. In patients with persistent macrocheilia, reduction cheiloplasty with excision of excess tissue may be indicated when conservative treatment has proven ineffective in reducing swelling but may have been successful in stabilizing disease.

Objective: To evaluate long-term results after reduction cheiloplasty in patients with macrocheilia caused by Melkersson-Rosenthal syndrome or cheilitis granulomatosa.

Design: Follow-up study in 7 patients with severe persisting macrocheilia, including 3 patients with Melkersson-Rosenthal syndrome and 4 patients with cheilitis granulomatosa in a stable state of disease, treated by reduction cheiloplasty at our hospital between January 1, 1987, and December 31, 2002. Preoperative and postoperative medical histories were obtained, and criteria for the success of surgical treatment were evaluated by clinical examination. Different techniques of reduction cheiloplasty are described and demonstrated in representative cases of severe macrocheilia.

Results: Surgical treatment in all 7 patients showed satisfying aesthetic and functional outcomes that persisted throughout follow-up (median follow-up, 6.5 years).

Conclusions: Reduction cheiloplasty is an effective method to correct persistent macrocheilia and improve lip aesthetics in patients with Melkersson-Rosenthal syndrome or granulomatous cheilitis in the persistent state of disease. With careful planning, proper sequencing of treatment, and proficiency in the various surgical techniques, optimal results can be achieved.

Arch Dermatol. 2005;141:1085-1091

MINERSSON -ROSENTHAL syndrome (MRS) is characterized by recurrent or persistent orofacial swellings, intermittent peripheral facial nerve paralysis, and a fissured tongue.1 Reports on the mucocutaneous and neurologic manifestations of this disorder have been published.1-3 One variant, cheilitis granulomatosa of Miescher (CG), is generally accepted as a monosymptomatic form of MRS.4 Characteristic histologic findings are edema and noncaseating epithelioid cell granulomas, variably containing multinucleated giant cells and paravascular and perivascular mononuclear inflammatory infiltrates.1 In the early pathologic process, there may only be lymphocytic infiltrates. The etiology and pathogenesis are still uncertain, but parainfectious, autoimmune, and genetic causes have been proposed. Hornstein5 suggests that the disorder is a multicausal syndrome with a hereditary disposition to disturbances of the autonomic nervous system. The granulomatous reaction in the edematous tissue may be due to an allergic response to different agents. Macrocheilia can affect the upper or lower lip, with variable asymmetric deformity. Typically, the lips exhibit nontender swelling that fluctuates and eventually is persistent because of fibrosing lymphedema. Aesthetic deformity is caused by the increase in lip volume and eversion of the labial mucosa. Functional deficiency may include labial incompetence with resultant interference in speaking, drinking, salivary control, and mastication, which may become intolerable for many patients.

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Various methods of treating labial swelling have been established, often resulting in moderate success1; these include salazosulfapyridine, antihistamines, anti-
biodermics, and irradiation. Most commonly used are corticosteroids administered intraleisonally or systemically, as well as systemic treatment with clofazimine in the acute edematous phase, often resulting in only temporary relief. Whether elimination of infective sources, such as dental foci or other inflammatory processes, might reverse the labial swelling in CG is controversial. Nevertheless, any inflammatory sources should be eliminated in these patients. Potential allergens also should be identified by patch testing and eliminated. In patients to treat severe and persistent swelling of the upper or lower lip when the lip volume reached at least twice the normal lip size. At the time of surgical intervention, the patients were in a stable state of disease with a relapse-free period of 8 months or longer. The patients were reexamined in 2002. The age at onset of disease, symptoms, surgical treatment, and preoperative and postoperative medical histories were also updated. A clinical examination was performed to evaluate criteria for the success of surgical treatment, including frontal and profile aesthetics and soft tissue thickness. Factors representing a good outcome were symmetry of the lip, normal anterior projection, dimensional harmony between the upper and lower lips, inconspicuous cicatrices, oral continence, and normal lip sensation, interlabial distance, and lip thickness. With the lips relaxed, the normal interlabial distance is up to 3 mm. The mean ± SD normal lip thickness is approximately 12 ± 2 mm in white subjects and 15 ± 2 mm in black subjects. The surgical outcome was regarded as moderate if one of these factors was not fulfilled. A poor result was indicated in the absence of 2 or more of the criteria.

HISTORY

There were 3 patients with MRS and 4 with CG. All patients (6 males and 1 female) were referred to our institution because of cosmetic or functional discomfort due to persistent labial swelling. The median follow-up was 6.5 years (range, 3-15 years). All patients had had symptoms for a minimum of 16 months before their diagnosis. The median age at the time of surgical resection was 36 years (range, 20-61 years). The Table gives the medical histories, medical treatment, surgical methods, and long-term results. Previous conservative treatment included mainly intraleisonal corticosteroid injections or systemic treatment with corticosteroids and tetracyclines.

PREOPERATIVE CLINICAL FINDINGS

All 7 patients had severe persistent macrocheilia, with a lip volume more than twice the normal size. Facial palsy was observed in 1 patient with MRS, another patient with MRS had

Table. Summary of Patient Data

<table>
<thead>
<tr>
<th>Patient No./ Sex/Age at Onset, y</th>
<th>Diagnosis/Age at Surgery, y</th>
<th>Clinical Findings at First Examination</th>
<th>Clinical Findings at Latest Follow-up</th>
<th>Previous Therapy</th>
<th>Relapse-Free Period Before Surgery, mo</th>
<th>Surgical Method (Outcome/Cosmetic Result)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/55</td>
<td>CG/61</td>
<td>Severe MC (LL and UL)</td>
<td>Normal LL, minimal MC in UL at 5 y</td>
<td>IntraleSIONal and systemic corticosteroids</td>
<td>10</td>
<td>UL: Conway (remission/good)</td>
</tr>
<tr>
<td>2/M/20</td>
<td>CG/49</td>
<td>Gigantic MC (LL)</td>
<td>Minimal edema in LL at 6 y</td>
<td>NA</td>
<td>NA</td>
<td>LL: Conway (remission/good)</td>
</tr>
<tr>
<td>3/M/15</td>
<td>CG/20</td>
<td>Severe MC (LL)</td>
<td>Normal LL at 5 y</td>
<td>IntraleSIONal corticosteroids, tetracyclines</td>
<td>8</td>
<td>LL: Conway (remission/good)</td>
</tr>
<tr>
<td>4/M/30</td>
<td>MRS/36</td>
<td>Severe MC (UL and LL), gingival hyperplasia</td>
<td>Moderate edema in UL, gingival hyperplasia at 9 y</td>
<td>IntraleSIONal corticosteroids</td>
<td>12</td>
<td>UL: Conway, Mouly (partial recurrence/moderate)</td>
</tr>
<tr>
<td>5/M/18</td>
<td>MRS/23</td>
<td>Severe MC (LL), fissured tongue</td>
<td>Normal LL, fissured tongue at 15 y</td>
<td>IntraleSIONal and systemic corticosteroids</td>
<td>9</td>
<td>LL: Conway (remission/moderate)</td>
</tr>
<tr>
<td>6/M/38</td>
<td>CG/43 and 44</td>
<td>Severe MC (LL and UL)</td>
<td>Normal lips at 6½ y</td>
<td>IntraleSIONal corticosteroids</td>
<td>11</td>
<td>UL and LL: Conway (remission/good)</td>
</tr>
<tr>
<td>7/M/32</td>
<td>MRS/32 and 36</td>
<td>Severe MC (LL), facial palsy</td>
<td>Normal LL, facial palsy at 10½ y</td>
<td>IntraleSIONal corticosteroids, tetracyclines</td>
<td>10</td>
<td>LL: Conway, wedge resection, Z-plasty (remission/good)</td>
</tr>
</tbody>
</table>

Abbreviations: CG, cheilitis granulomatosa of Miescher; LL, lower lip; MC, macrocheilia; MRS, Melkersson-Rosenthal syndrome; NA, not available; UL, upper lip.

METHODS

PATIENTS

The study included 7 patients with MRS or CG who underwent surgical treatment at the Department of Cranio-Maxillofacial Surgery between January 1, 1987, and December 31, 2002. The diagnosis was confirmed by biopsy in all patients. Excision and reconstruction were performed in all patients to treat severe and persistent swelling of the upper or lower lip when the lip volume reached at least twice the normal lip size. At the time of surgical intervention, the patients were in a stable state of disease with a relapse-free period of 8 months or longer. The patients were reexamined in 2002. The age at onset of disease, symptoms, surgical treatment, and preoperative and postoperative medical histories were also updated. A clinical examination was performed to evaluate criteria for the success of surgical treatment, including frontal and profile aesthetics and soft tissue thickness. Factors representing a good outcome were symmetry of the lip, normal anterior projection, dimensional harmony between the upper and lower lips, inconspicuous cicatrices, oral continence, and normal lip sensation, interlabial distance, and lip thickness. With the lips relaxed, the normal interlabial distance is up to 3 mm. The mean ± SD normal lip thickness is approximately 12 ± 2 mm in white subjects and 15 ± 2 mm in black subjects. The surgical outcome was regarded as moderate if one of these factors was not fulfilled. A poor result was indicated in the absence of 2 or more of the criteria.

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a fissured tongue, and the third patient with MRS had gingival hyperplasia not related to any of its common causes. In addition to the cosmetic problems, some patients had difficulties in speaking and drinking, depending on the degree of lip swelling, hardening of the soft labial tissue, and relapsing fissures of the labial surface. Macrocheilia was found concomitantly in the upper lip and the lower lip in 3 patients. The ratio between upper and lower lip involvement was 3:7. Labial lesions were generally manifested as diffuse, pasty, nontender edema, with pronounced anterior projection of the lip. Some lesions were more solid, with bleaching of the vermillion border. All lip swellings were bilateral and almost symmetric at the time of surgery.

SURGICAL TREATMENT

In the normal lip, the seromucocutaneous line is coincident with the crest of the lip. In the presence of macrocheilia, the lip shows a pronounced anterior projection with eversion of the seromucocutaneous line and the vermillion border. All 7 patients had these clinical features, and reduction cheiloplasty was performed using different techniques (Figure 1). The basic surgical procedure was the Conway11 method, including a transverse sickle-shaped mucosal incision between 1 and 1½ cm dorsal to the vermillion border. Posteriorly, the incision was extended bilaterally into the cheek about 1 to 2 cm distal to the commissure to prevent scarring in the immediate vicinity of the angle. Depending on the degree of lip swelling, the excision was usually deepened to include a wedge of mucosa and various amounts of submucosal glandular tissue. In some cases, affected orbicularis oris muscle layer had to be excised. In 4 patients with severe lower lip macrocheilia, the procedure was supplemented with the excision of a central wedge. In 2 patients with severe and gigantic macrocheilia, the lip reduction was performed by combining the basic Conway procedure with a central sagittal excision of a large wedge, followed by reconstruction of the lower lip with a Z-plasty. In 1 patient with severe macrocheilia of the upper lip, a widely pronounced anterior projection of the lip was corrected with a combination of a sickle-shaped mucosal incision and a procedure described by Mouly.12 The method, which includes the excision of 2 sagittal triangular wedges at the lateral eminences of the philtrum, enables the natural protrusion of the eminences and the normal central depression of the upper lip to be preserved. The undermining of the wound edges should be limited to that needed for appropriate tissue apposition. Closure of the resection defects is usually performed in 2 layers, and sutures are removed 7 to 10 days after surgery. The type of resection in each patient and the time between last disease activity and surgery are listed in the Table. Patient 6 was treated by resection of the lower and upper lips, with a 1-year interval between procedures. In patients 1 and 4, reduction cheiloplasty of the upper and lower lips was performed in 1 surgical session.

HISTOLOGIC FINDINGS

In all resection specimens of the 7 patients, histologic examination showed typical features of the late phase of MRS and CG, namely, fibrosis, dilated lymph vessels, and scattered noncaseating epithelioid cell granulomas and paravascular lym-
phocytic infiltrates (Figure 2A). By contrast, diagnostic biopsy specimens in the early inflammatory phase of disease lacked fibrosing lymphedema (Figure 2B).

RESULTS

POSTOPERATIVE FINDINGS

The patients received no systemic application or local injection of corticosteroids or any other conservative treatment in the postoperative period. Temporary minimal recurrences of lip swelling 1 to 6 months after reduction cheiloplasty occurred in 3 of the 7 patients. Patient 3 developed minimal swelling of the resected lip 1 month after surgery, without further recurrence. In the other 2 patients (patients 1 and 4), the duration and severity of the exacerbations were minimal. The Table gives the postoperative courses of the patients.

LONG-TERM RESULTS AFTER SURGICAL TREATMENT

At the time of the last examination in 2002, the 7 patients were satisfied with the functional and cosmetic results of their corrected lips. Only patient 4 showed moderate swelling of the upper lip, with a minimally pronounced anterior projection, which did not surpass the previously recorded degree of swelling. We classified the long-term result of this patient as moderate because of persistent solid swelling and anterior projection of the upper lip. The clinical results in the other 6 patients were good, with no signs of lip swelling. Postoperative evaluation of the cicatrices in all patients revealed an inconspicuous outcome with soft scarring. In all patients, skin sensitivity was preserved. Figure 3 (patient 1) and Figure 4 (patient 2) show preoperative findings of severe and gigantic macrocheilia, respectively, and the postoperative results after follow-up.

The therapeutic regimen in patients with CG favors conservative treatment such as systemic application of corticosteroids, sulfones, and salazosulfapyridine; local corticosteroid injections; and removal of underlying allergies, infections, or inflammatory foci. However, such treatment varies in success rates.1,8,9 In cases of persistent and disfiguring lip swelling, surgical treatment is often essential. In recurrent lip swelling, the mucocutaneous soft tissues show a diffuse persistent edema with solid reorganization and long-term fissures because of fibrosing lymphedema. Severe macrocheilia may result in conspicuous facial deformity, sometimes associated with salivary and labial incompetence.

The timing of surgical treatment in macrocheilia is based on the underlying disease process. The method used for reduction cheiloplasty demands careful and critical assessment of lip swelling to avoid stimulation of the granulomatous inflammatory process, which might induce a more severe pathologic process. Surgical treatment should be deferred until the patient has been free of disease activity for about 1 year.9 Each of our 7 patients had had a minimum relapse-free preoperative period of 8 months. Ellitsgaard et al13 reported that disease persisted in 6 of their 13 patients operated on, but swelling never surpassed the preoperative degree, nor was it permanent. They did not recommend deferring resection until patients had remained relapse-free for a longer period. Our patients differed from those of Ellitsgaard et al in that they were treated by reduction cheiloplasty only during the nonactive period of the disease. In accord with Vistnes and Kernahan,9 we recommend surgical treatment of persistent macrocheilia in patients with MRS and CG after a relapse-free period of about 8 to 12 months, regardless of patient sex or age. Important factors are the anatomic condition and lip volume, including functional and aesthetic disorders and histologic proof of the persistent fibrosing state of the disease.

It is important that excision of hypertrophic fibroglandular tissue be as extensive as possible; this will ensure a postoperative outcome with normal lip dimensions by keeping the mass of the orbicularis oris muscle largely intact.9 In our study, the transverse lip length, including the central part of the orbicularis oris muscle, had to be shortened in 4 patients with pronounced macrocheilia by excising a median sagittal wedge. In 2 of these patients, Z-plasty on the lower lip was necessary.
to achieve a stable vertical median lip dimension. The pathophysiologic process following reduction cheiloplasty is not completely understood, especially in terms of how surgically induced alteration may lead to improvement even when disease still appears to be exacerbating. One reason may be that partial excision of the persistently altered and swollen tissue reduces the amount of tissue available for swelling. Reduction cheiloplasty might also reduce local vasomotor disturbances and rectify defective lymphatic drainage by creating lymphaticovenous anastomoses.14 In contrast to the multimodal therapeutic regimen of Glickman et al,15 our patients received no systemic application or local injections of corticosteroids in the postoperative period. Only 1 of our patients showed less than a good result, with middle-grade swelling of the upper lip at the latest follow-up.

General treatment principles for surgical correction of macrocheilia involve the following important aspects. Lip resection should be conservative, resulting in harmonious upper and lower lip balance, symmetry, and appropriate anterior projection. Furthermore, the surgical procedure should preserve oral continence, which is achieved through the interplay of lip sensation, strength of the orbicularis muscle, and height of the lip curtain. In their study of oral continence, Stranc and Fogel16 found the most important factor to be preservation of normal lip sensation. In patients presenting with severe macro-
cheilia with the pathologic process extending into the cheek and sulcus region, use of the Conway procedure must preserve near-maximal mental sensory function. For optimal results, an attempt should be made to establish a harmonious balance between the upper and lower lips instead of reducing the lips to a norm.

The results of our follow-up study, with no recidivism of lip swelling after surgical correction, indicate that reduction cheiloplasty may be performed in patients with disfiguring CG, not only to provide functional gain but also to achieve aesthetic remodeling of the lip and to assist in social reintegration in some cases. Although there is little risk of failure or relapse with the surgical principles described herein, the timing of surgical measures is important. Conservative treatment to bring the initial inflammatory phase of the disease under control should first be exhausted. Reduction cheiloplasty should be confined to patients in a stable condition but showing persisting disfigurement of the lips.

Accepted for Publication: November 15, 2004.
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Author Contributions: Study concept and design: Kruse-Lösler. Acquisition of data: Kruse-Lösler, Presser, Metze, and Joos. Analysis and interpretation of data: Kruse-

Figure 4. Gigantic macrocheilia of lower lip in a patient with cheilitis granulomatosa (patient 2 in the Table). A and C, Preoperative findings. B and D, Postoperative findings 6 years after Conway procedure, wedge resection, and Z-plasty.
Losler. Drafting of the manuscript: Kruse-Lösler. Critical revision of the manuscript for important intellectual content: Kruse-Lösler, Presser, Metze, and Joos. Statistical analysis: Kruse-Lösler. Obtained funding: Kruse-Lösler. Administrative, technical, and material support: Kruse-Lösler and Metze. Study supervision: Joos.

Financial Disclosure: None.

REFERENCES


Correction

Error in Reference List. In the Study by Kreuter et al titled “Pulsed High-Dose Corticosteroids Combined With Low-Dose Methotrexate in Severe Localized Scleroderma,” published in the July issue of the ARCHIVES (2005; 141:847-852), the following references were omitted from the reference list. This correction was made previously to online versions of this article.