ORIGINAL ARTICLE

Treatment of classic Kaposi’s sarcoma-associated lymphedema with elastic stockings

Lucia BRAMBILLA, Athanasia TOURLAKI, Silvia FERRUCCI, Marinella BRAMBATI, Vinicio BONESCHI

Institute of Dermatological Sciences, University of Milan, Fondazione IRCCS Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena, Milan, Italy

ABSTRACT

Lymphedema of the lower extremities is a frequent complication of Kaposi’s sarcoma (KS). Compressive therapy is the basis of treatment for lymphatic disorders, but to the authors’ knowledge, there are no controlled trials to evaluate its effectiveness in KS-related lymphedema. Sixty-five patients with classic KS-associated lymphedema limited to below the knee were studied. Fifty patients received below-knee elastic stockings, whereas the remaining 15 did not use any compressive device. Among treated patients, 60% (30/50) experienced a limb volume reduction, while 40% (20/50) had an increase of limb volume. In contrast, all patients (15/15) of the untreated group had an increase of limb volume. No correlation between lymphedema reduction and systemic or local chemotherapy was observed, supporting compressive therapy as the major strategy for the treatment of this condition. Our results suggest that elastic stockings may be important tools for the management of lymphedema associated to classic KS.

Key words: circumference measurements, compression therapy, elastic stockings, Kaposi’s sarcoma, lymphedema.

INTRODUCTION

In 1872, the Hungarian dermatologist Moritz Kaposi first described “idiopathic multiple pigmented sarcoma of the skin” which later became known as Kaposi’s sarcoma (KS). To this day, the precise origin cell of this unusual neoplastic disorder is still controversial, even if most ultrastructural and immunohistochemical observations strongly support derivation from either lymphatic endothelium or a cell type capable of undergoing lymphatic differentiation. Moreover, a lymphatic endothelial source is sustained by the unique distribution of cutaneous lesions along the lines of lymphatics, the predilection of KS for lymph nodes, and the absence of lesions in organs which are devoid of lymphatics.

There are four recognized epidemiological forms of this entity: (i) classic; (ii) endemic or African; (iii) KS associated with immunosuppressive therapy; and (iv) AIDS-related or epidemic KS. While there is some clinical variability among these groups, histological features are quite uniform and they consist of small, irregular, endothelial-lined spaces that surround normal blood vessels in the early patch-stage, and of sheets of spindle cells and slit-like vascular spaces in the late nodular-stage. Human herpes virus (HHV)-8 has an etiopathogenetic role in all KS variants, but the specific mechanism by which the virus participates in the oncogenic process is uncertain. Notably, KS may begin as a polyclonal hyperplasia that develops into a monoclonal tumor, and paracrine effects may be important in the progression of the disease.

Classic KS mainly occurs in elderly men and, especially in patients with long-standing classic KS, lymphedema of the involved lower extremities...
frequently develops as a complication of the disease. A variety of mechanisms have been involved in the development of KS-associated lymphedema, such as distal lymphatic obliteration, proximal nodal obstruction, and increased normal vessel permeability, due to exuberant endothelial proliferation, reticuloendothelial hyperplasia, and elaboration of permeability factors by KS lesions, respectively.

Lymphedema sometimes precedes the appearance of visible KS lesions. Chronic lymph stasis may impair local immune surveillance by disrupting trafficking of the immunocompetent cells, and it may also stimulate angiogenesis in the lymphedematous areas. Consequently, lymphedema may not only complicate KS, but also facilitate the onset of this HHV-8-associated neoplasm.

Management of this condition includes manual lymph drainage, compression therapy, exercise programs, skin care and occasionally surgical treatment. Compression therapy with bandages or stockings is the basis of treatment for venous and lymphatic disorders, because it assists in decreasing the size of excess interstitial fluid. The aim of this work is to evaluate the efficacy of compressive therapy for the treatment of classic KS-associated lymphedema.

MATERIALS AND METHODS

A total of 65 patients with classic KS-associated lymphedema limited to below the knee were enrolled in this study. Fifty patients accepted the use of elastic stockings, while the remaining 15 were randomly selected to form the control group. Forty of the 50 patients who received the stocking were males, and 10 were females. The mean age was of 71 years (range: 39–91). The control group was composed of 15 patients with mean age of 74 years (range: 44–89), 13 males and two females.

They all had a grade II lymphedema, according to the classification of the International Society for Lymphology. In particular, no pitting after digital compression was observed, edema was not spontaneously reversible by elevation of the limb, and elephantiasis was absent. Lymphedema was unilateral, and limited to below the knee.

The diagnosis of lymphedema was based on physical examination and medical history. Sixty-two patients developed lymphedema after the appearance of visible KS lesions, and three patients developed the first KS lesion in a lymphedematous limb. Among this latter group, the first patient had a history of primary lymphedema praecox, and the second presented with lymphedema 6 years before the first KS manifestation, after two episodes of erysipelas. In the third patient, limb swelling appeared 7 months before KS, after a traumatic injury.

Each compressive stocking we prescribed was ordered after individual measurements of the limb (custom-made stocking) taken as early in the morning as possible. In order to calculate volume, the limb was divided into 1.5-cm height sections, with each section representing a truncated cone. Total limb volume was determined by adding the volumes of the various sections together. The estimation of partial volumes was based on circumference measurements at the top and at the bottom of each section, and then by using the truncated cone formula, that is, \( \frac{1}{3} \pi h (R^2 + rR + r^2) \), with height \( h \) of 1.5 cm and radius \( R \) (of the small base) and \( r \) (of the large base). Circumferences were taken using a paper tape positioned along the limb from the base of the great toe to the knee, and provided with several horizontal equidistant adhesive tapes that embraced the limb at intervals of 1.5 cm (Fig. 1). Thus, every horizontal tape measured the limb circumference at a fixed point.

Follow-up physical examinations were performed within a minimum of bimonthly intervals, whereas measurements considered for statistical analysis were repeated after 15 months on average.

We proposed below-knee elastic stockings made of synthetic (61% nylon and 39% Lycra Spandex), latex-free, washable material, quite easy to put on and to remove thanks to zipper openings (BSN-Jobst, Tipperary, Ireland). For most of the patients, the compression level was 40 mmHg at the ankle with gradual reduction from ankle to knee. Patients were asked to wear their stockings from morning (before taking the upright position) until bedtime. Stockings were replaced every 6 months. In order to avoid complications, skin care advice and stocking washing instructions were given. No additional treatment, for example physical massage or diuretics, were prescribed.
Figure 1. Measuring tape for lower limb circumferences at multiple points.
During the observation period, 20 of the 50 patients remained without any treatment for KS, 10 patients were treated locally with intralesional injections of vincristine, and 18 patients were treated with systemic chemotherapy. We had no reliable information in relation to KS treatment for the remaining two patients. Concerning the control group, four patients were not treated for KS, three were treated locally with injections of vincristine, and eight were treated with systemic chemotherapy. None underwent surgery or radiation therapy.

RESULTS

The mean observation period was 66 weeks for patients treated with elastic stockings, and 64 weeks for the control group. Sixty percent (30/50) of all patients treated with elastic stockings had a limb volume reduction of $6.9\% \pm 5.1$ (range: 0.6–19.1%). This improvement was arbitrarily considered “good” for values higher than the mean plus one standard deviation (SD; $> 12\%$) while it was considered “poor” in patients with a limb volume reduction lower than the mean value minus one SD ($< 1.8\%$). A good improvement was achieved in 16.67% (5/30) of cases, and a poor improvement in 13.33% (4/30). Intermediate values were recorded in the rest of the patients (70%, 21/30). The mean volume reduction for the 30 improved limbs was of 89.3 ml (range: 6.5–341 ml). Notably, circumferences were reduced in an irregular manner along some limbs.

The remaining 40% (20/50) of elastic stocking-treated patients presented an increase of limb volume of $6.7\% \pm 6.2$ (range: 0.7–26.1%), although it was higher than the mean value plus one SD (> 12.9%). The mean value of the limb volume increase was of 78.7 ml (range: 6.5–341 ml). Notably, circumferences were reduced in an irregular manner along some limbs.

Table 1. Results of treatment with elastic stockings for classic Kaposi’s sarcoma-associated lymphedema

<table>
<thead>
<tr>
<th>Chemotherapy</th>
<th>Elastic Stockings</th>
<th>Reduced LV</th>
<th>Increased LV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic (26)</td>
<td>Yes (18)</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>No (8)</td>
<td>0</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Local (13)</td>
<td>Yes (10)</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>No (3)</td>
<td>0</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>None (24)</td>
<td>Yes (20)</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>No (4)</td>
<td>0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Not available (2)</td>
<td>Yes (2)</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Numbers in parentheses represent the number of patients. LV, limb volume; significant difference between patients treated with systemic chemotherapy plus elastic stockings vs systemic chemotherapy alone ($p = 0.002239$, Fisher’s exact test). A trend toward LV reduction is also present among patients treated with local chemotherapy plus elastic stockings and with elastic stockings alone.

50 patients who used elastic stockings. The number of improved limbs was not significantly different in patients who received both elastic stockings and systemic chemotherapy (18/48), or in patients treated with elastic stockings and local chemotherapy (10/48) compared with patients treated with elastic stockings alone (20/48), because limb volumes were reduced in 12, five and 12 patients, respectively ($P > 0.05$, $\chi^2$ test). On the other hand, an increase in limb volume was observed in eight of eight (100%) and in six of 18 (33%) patients treated with systemic chemotherapy alone or with systemic chemotherapy plus elastic stockings, respectively ($P = 0.002239$, Fisher’s exact test), further supporting the uncertain relevance of chemotherapy in the treatment of KS-associated lymphedema (Table 1).

DISCUSSION

Lymphedema is a frequent complication of KS, most likely due to lymphatic obliteration, nodal obstruction, and increased vessel permeability secondary to the HHV-8 infection of various cell types. Moreover, as for other types of neoplasms, KS may be preceded by local lymphedema, suggesting that abnormalities of the lymph drainage may facilitate the development of this malignancy. Swelling most often involves lower extremities, but it can also manifest in other areas of the body, such as the groin, genitals or periorbital regions. Many patients have sensations of tightness, heaviness and pain in their affected limbs. Chronic congestion
Elastic stockings for lymphedema in Kaposi's sarcoma

leads to skin changes (e.g. fibrosis, papillomas, ulceration) causing aggravation of lymph stasis, and increased bacterial and fungal infection risk. In fact, recurrent cellulitis is a quite common complication that further damages the cutaneous lymphatics, worsens the skin quality, and aggravates the edema. In severe cases, impaired mobility, reduced capacity for self-care, and unsatisfactory appearance complicate health conditions and social life.

Because the classic variant of KS is a slowly progressive disease, management of lymphedema in patients with this disorder may be useful to improve their quality of life. Unfortunately, there is no cure for lymphedema, so treatment focuses on reducing symptoms and complications. Compressive treatment with elastic stockings is one of the main therapeutic options, either for acute or chronic lymphedema. Although compressive therapy is largely used for lymphatic system disorders, there are no controlled trials to evaluate its effectiveness in KS-related lymphedema. To document the outcome of this treatment, accurate and consistent measurement techniques are mandatory to examine limb volume over time, although other factors than lymphedema (e.g. weight gain and muscle hypertrophy) can influence limb volume. Volume changes can be measured either directly by water-displacement volumetry (measuring the amount of water displaced by the limb when immersed) or by various indirect methods often based on circumference measurements. Either direct or indirect methods can be confidently used, as they seem to be equally efficacious in detecting volume changes. However, because each method may produce different measurements, they should not be mixed or substituted in a single patient or in a single study. Circumferential measurements have been the most commonly used methods, probably because of the simplicity of application mode, the low cost, and the ability to produce quantitative data. Limb volume can be quickly calculated using circumferential measurements at two or three points, but measurements at multiple points may be more appropriate, especially when grossly localized bulges are present. Two basic formulas (cylinder and truncated cone) are used to calculate volume based on circumferential measurements. The truncated cone formula is intrinsically the most accurate, because most extremities are shaped like a cone rather than like a cylinder. In our study, 1.5-cm segments with a truncated cone formula were used, although 10-cm intervals seem to be sufficient for routine measurements of the limb.

More than half of patients who used elastic stockings experienced a lymphedema reduction, and only a few patients had a severe increase of limb volume. In contrast, a deterioration of lymphedema was noticed in all patients who did not wear elastic stockings. Furthermore, the lymphedema reduction seemed to be independent of systemic or local chemotherapy, supporting compressive therapy as the major strategy for the treatment of this condition.

The stockings were well-tolerated; no allergies were observed. Some patients found them uncomfortable to wear during hot weather, especially during walking or doing other exercise. Even if there were zipper openings, elderly patients sometimes had difficulty putting their stockings on. Unlike other patients with lymphedema, no patient found the stocking anesthetic, probably because evident KS lesions pre-existed.

Finally, although no prospective data are still available, limb volume reduction could be useful to improve the prognosis of classic KS, because lymphedema may compromise immune response against neoplastic cells. Within this context, the employment of elastic stockings in the management of KS-related lymphedema is further encouraged.

REFERENCES