



## Case Report

# Compression stockings as an effective treatment for erythema nodosum: Case series <sup>☆,☆☆</sup>



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## ABSTRACT

Erythema nodosum (EN) is a septal panniculitis that is characterized clinically by tender, erythematous, subcutaneous nodules that are predominately localized on the pretibial lower legs. EN affects women more than men and can be idiopathic or secondary to another disease process such as infection or an immune response. Treatment options for erythema nodosum are suboptimal and often involve significant side effects or require a change in lifestyle. We investigated the effects of moderate 20 mmHg to 30 mmHg compression stockings as an alternative treatment method in two female patients with recurrent erythema nodosum. In both cases, the patients wore the compression stockings daily. At the follow-up visit, the EN lesions were no longer tender to the touch, and postinflammatory hyperpigmentation changes had started. Both patients had a lasting clinical resolution.

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## Introduction

Erythema nodosum (EN), a septal panniculitis, presents as tender, warm, erythematous, subcutaneous nodules that are predominantly localized on the pretibial lower legs. EN is more prevalent in female patients with a peak presentation in the late teenage years to the mid-thirties (Blake et al., 2014; Bohn et al., 1997; Cribier et al., 1998). The histology is characterized by lymphohistiocytic septal inflammation in the subcutaneous adipose tissue with occasional presence of giant cells (Requena and SanchezYus, 2008; Scarpa et al., 1989).

EN is suspected to be a delayed type IV hypersensitivity reaction that is associated with infectious or inflammatory diseases such as streptococcus, sarcoidosis, coccidioidomycosis, and tuberculosis (Bohn et al., 1997; Cribier et al., 1998). EN may also occur as a result of a drug reaction, pregnancy, or malignancy (Bohn et al., 1997). Clinical plans in these cases involve the identification of the underlying causative agent and prescription of the appropriate treatment with the EN clearing secondarily. Necessary laboratory studies and imaging should be obtained to rule out probable causes.

More than half of EN cases are considered idiopathic (Cribier et al., 1998). In these cases, the treatment plan is less concrete and more challenging. The current recommendation is supportive care with nonsteroidal anti-inflammatory drugs to reduce inflammation and pain as well as bed rest and elevation to decrease edema (Ubogy and Persellin, 1982). Treatment with medications such as steroids or saturated solutions of potassium iodide (SSKI) depends on the treating physician (Blake et al., 2014). SSKI has various side effects, including hypothyroidism, and may require thyroid function monitoring (Johnson and Rapini, 1988). Systemic corticosteroid drugs are indicated as a second-line agent due to adverse side effects from long-term use (Requena and SanchezYus, 2008).

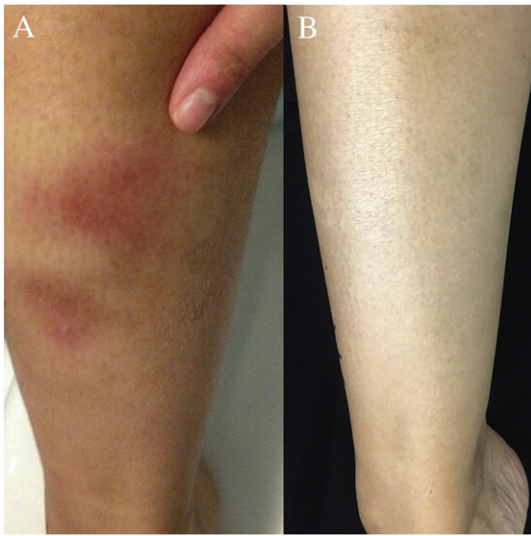
In idiopathic cases, a more optimal treatment plan is warranted, especially in cases that are recurrent or of longer duration. Compression stockings have been suggested as a form of supportive care but have not been investigated as a primary form of treatment (Blake et al., 2014). Compression stockings are beneficial because they provide a prolonged mechanism to decrease swelling while also allowing little disruption to the patient's schedule and quality of life. In young female patients, who are the typical demographic for EN, it is important to consider a treatment that does not disrupt daily activities. We report on the cases of two female patients with recurrent idiopathic EN whose lesions resolved after wearing moderate 20 mmHg to 30 mmHg compression stockings.

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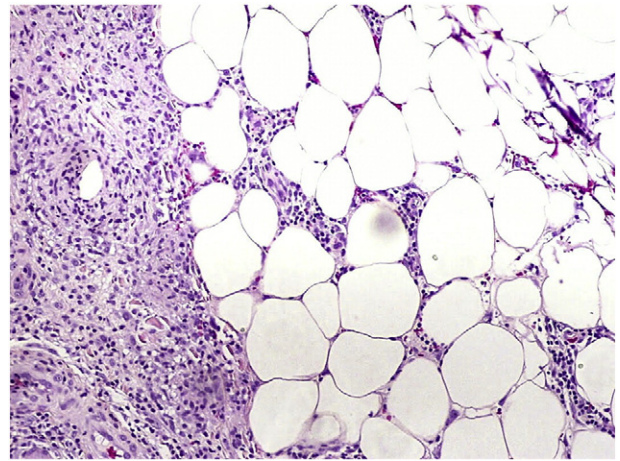
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**Fig. 1.** (A) Persistent pretibial erythematous nodules on the right lower leg in Patient 1 despite treatment with ibuprofen and topical steroid medications. (B) Photograph taken approximately 2 years later, during which period the patient did not have any recurrences.



**Fig. 2.** Biopsy from Patient 2 with features of septal panniculitis: subcutaneous fat with widened fibrous septum that has been completely replaced by lymphohistiocytic inflammation (hematoxylin and eosin,  $\times 400$ ).

## Case Report

### Patient 1

A 28-year-old female patient presented in January 2013 with 5 months of persistent EN. The patient's medical history was significant for two previous flare-ups (in 2007 and 2010) with negative coccidioidomycosis titers and clear chest x-ray images. In both past instances, the EN lasted 10 weeks, and treatment had been initiated with ibuprofen 600 mg three times daily in addition to a twice-daily application of class II topical steroid medications.

At the time of the presentation of the third flare, the patient reported persistent EN despite the same previously successful treatment regimen (Fig. 1A). This prompted a more detailed workup, including testing for complete blood count, complete metabolic panel, antinuclear antibodies, rheumatoid factor, human immunodeficiency virus, and coccidioidomycosis, all with negative results. A biopsy was conducted, and the results confirmed EN.

During the development of a treatment plan, other options were preferred over SSKI or systemic steroids to minimize side effects. The patient was prescribed moderate 20 to 30 mmHg compression stockings daily for prolonged and controlled decreased swelling of her lower legs. When the patient returned 2.5 weeks later, the EN had completely resolved. A photograph taken approximately 2 years later (Fig. 1B) shows no scarring and no evidence of prior bouts of EN. The patient shares that she has not had any recurrences since the third flare-up.

### Patient 2

A 24-year-old female patient with a significant history of previous EN episodes presented in November 2015 with 4 months of recurrent, painful, erythematous lesions on the bilateral lower legs. Physical examination findings showed multiple erythematous subcutaneous nodules that were warm to the touch and tender to palpation on the bilateral shins and left medial calf. Test results showed negative immunoglobulins M and G cocci titers and chest x-ray images with no acute abnormalities. A deep surgical incisional biopsy of the right shin revealed a septal granulomatous inflammation with giant

cells and focal lobular spill-over in the surrounding adipose tissue with a marked neutrophilic infiltrate (Fig. 2). Periodic acid-Schiff, Grocott's methenamine silver, and acid fast bacilli stains were negative for fungi and mycobacteria. A diagnosis of EN was made. When discussing treatment options, the patient expressed the importance of continuing daily activities as normally as possible and that she did not want to take medications that carried a high risk of adverse effects. The patient was prescribed daily use of moderate 20 to 30 mmHg compression stockings. At the time of follow-up 1 month later, a physical examination showed that the EN had completely resolved with negligible erythema and early postinflammatory hyperpigmentation changes (Fig. 3). The warmth of the skin and tenderness to the touch had also resolved. Patient 2 also has not had any recurrences of EN lesions for the past year and a half.



**Fig. 3.** Appearance of early postinflammatory hyperpigmentation changes on the right pretibial lower leg in Patient 2. During the physical examination, no warmth or tenderness to the touch of the skin previously affected with erythema nodosum was observed. Note: surgical scar on the right mid shin from the diagnostic biopsy.

## Discussion

Our case series demonstrates the positive benefits and effectiveness of compression stockings as an alternative treatment method for patients with EN. The timeline of EN does not follow a definitive course because it may wax and wane or spontaneously resolve, but idiopathic cases have a tendency to persist for longer durations. In most cases, EN plaques and nodules are rapid in onset, progress to bruise-like lesions, and eventually fully resolve spontaneously over a period of various weeks (Requena and SanchezYus, 2008). A retrospective study showed that 77% of patients with EN secondary to infection had symptom resolution in 7 weeks, and the longest duration was 18 weeks. However, 30% of patients with idiopathic EN had symptoms for more than 6 months (Bohn et al., 1997). In both of our idiopathic cases, after months of little to no improvement, a dramatic clearing of the lesions occurred with daily use of moderate 20 to 30 mmHg compression stockings.

Although compression stockings are prescribed for various disease processes, the mechanism of action remains unclear throughout the literature. A recent systematic review identified 25 recommendations for acute and chronic venous disorders (Rabe et al., 2017). Inflammatory conditions are mentioned under other possible indications, and one paper concludes that more research is warranted on disease processes such as EN (Rabe et al., 2017). One study that investigated chronic venous insufficiency ulcers demonstrated that compression therapy reduces pro-inflammatory cytokine levels to promote healing (Beidler et al., 2009). It is plausible that a similar mechanism occurs with the inflammatory process in EN.

Treatment options for EN, a disease that often affects young women, have been suboptimal and involve significant side effects or a decreased quality of life. Although bedrest is normally recommended as a supportive form of care alongside SSKI, topical, or oral steroid medications for treatment, other options also should be explored. This is especially important for active patients or in EN cases that are recurrent and/or persistent for months. Because there is no substantial evidence of consistent treatment regimens for patients with idiopathic EN, compression stockings should be considered because they allow patients to maintain a good quality of life and have minimal side effects.

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