

Research Paper

## Evaluation of the Prevalence of Concomitant Idiopathic Cyclic Edema and Cellulite

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### Abstract

The aim of this study was to evaluate the prevalence of concomitant idiopathic cyclic edema with Grade II and III cellulite. All patients treated for Grade II and III cellulite were evaluated for idiopathic cyclic edema in a retrospective, quantitative and cross-sectional study. The study was carried out at the Godoy Clinic in the period from 2006 to 2010. All patients with body mass indexes > 25, Grade I cellulite and other causes of edema were excluded. The diagnosis of idiopathic cyclic edema was based on a clinical history and fluid retention throughout the day, in particular difficulty in removing rings on waking in the morning which improves later in the day. All patients with cyclic edema were treated with 75 mg aminaphtone three times daily. Statistical analysis considered the frequency of edema.

Of the 82 women evaluated with ages between 18 and 58 years old (mean of 34.9 years) 41 (50.0%) were diagnosed with idiopathic cyclic edema.

Idiopathic cyclic edema is an aggravating factor for cellulite and is frequently associated with the more advanced stages of the disease. Its control is essential in the treatment of cellulite.

Key words: Cellulite, idiopathic cyclic edema, aminaphtone, treatment

### Introduction

Cellulite is a common complex cosmetic problem for many post-adolescent women characterized by relief alterations of the skin surface, which give the skin an orange-peel appearance <sup>1</sup>.

It has been demonstrated that the angiotensin I-converting enzyme (ACE) and hypoxia-inducible factor-1 alpha (HIF1A) genes play an independent role in predisposing to cellulite. This may provide novel information on the pathophysiology of this

common cosmetic problem and offer a research topic for novel beautification interventions <sup>2</sup>.

Glycosaminoglycans (GAGs) have hydrophilic properties, which lead to excessive fluid retention in the dermis, adipocytes, and interlobular septae. Edema can also lead to vascular compression, hypoxia, and capillary neoformation, resulting in microhemorrhages that are noted upon histologic evaluation <sup>3,4</sup>.

Studies suggest that one pathophysiological hypothesis on the development of cellulite relates to interference in the lymphatic system and stimulation to produce substances in the interstitial space. This results in regional lymphostasis in the skin which impedes the mobilization of these substances leading to their accumulation. Among the factors that affect this system are female hormones and genetic predisposition<sup>5</sup>. Clinical studies employing a specific technique to stimulating the lymphatic system can lead to the reduction of these substances<sup>6</sup>.

Cellulite can be divided into three main grades based on the clinical severity. Grade I is characterized by smooth skin without any dimpling upon standing and laying down, but the skin adopts a mattress-like (orange peel) configuration upon pinching, which forces the fat into the reticular and papillary dermis. In grade II cellulite, a mattress-like appearance of cellulite is present upon standing but disappears when the patient is in the supine position. Grade III cellulite can be found in patients that exhibit skin dimpling upon standing and while they are in the supine position, which can be exacerbated by pinching the skin<sup>7</sup>.

In recent years an investigation of idiopathic cyclic edema began to be routine before starting treatment of cellulite.

Idiopathic cyclic edema syndrome was identified in 1955 by Mach and is related to a set of clinical states that involve vascular hyperpermeability associated with swelling due to retention of interstitial fluid<sup>8,9</sup>.

The aim of this study was to evaluate the prevalence of concomitant idiopathic cyclic edema and Grade II or III cellulite.

## Method

All patients treated for Grade II and III cellulite based on the Nurnberger-Muller scale<sup>7</sup> and idiopathic cyclic edema were evaluated in a retrospective, quantitative and cross-sectional study. The study was carried out at the Godoy Clinic in the period 2006 to 2010.

All patients who sought the clinic with complaints of any type of venous disease and had associated diagnoses of cellulite were included in the study.

Patients with body mass indexes > 25, Grade I cellulite and other causes of edema were excluded.

An evaluation for idiopathic cyclic edema is routinely made in the diagnosis of cellulite, in obesity and in other evident causes of clinical edema.

The diagnosis of idiopathic cyclic edema was clinical based on the clinical history and fluid retention throughout the day and, in particular, difficulty

to remove rings on waking in the morning which improves later in the day. Some patients reported facial edema early in the morning and swelling of the legs at the end of the day. Participants were asked to weigh themselves using the same weighing scales at around 7 a.m. and 7 p.m. for three consecutive days. They were requested to use the same clothes in both evaluations during each day and not to eat before weighing. The patient was diagnosed with cyclical edema when the difference in weight between morning and afternoon was greater than 800 grams on all three days.

All patients with cyclic edema were treated with 75 mg aminaphtone three times daily. The treatment for cellulite began only after controlling the edema with the weight differences over 12 hours being reduced to less than 300 grams.

The frequency of edema was considered in the statistical analysis. The study was approved by the Research Ethics Committee of the Medical School in São José do Rio Preto (FAMERP number 460/2010).

## Results

Eighty-two women aged between 18 and 58 years old with a mean age of 34.9 years were evaluated between 2006 and 2010. Of the 82 women, 41 (50.0%) were diagnosed with idiopathic cyclic edema. The therapeutic approach with aminaphtone was effective in 32 (72%) patients and the other 9 (28%) required other types of treatments. Aminaphtone was the first drug of choice but when treatment failed ginkgo biloba was prescribed. For the 9 patients treated with the ginkgo biloba, the treatment of 6 patients was successful. In 3 patients this was associated with spironolactone and with the combination of drugs control of edema was attained.

## Discussion

This study illustrates the association of idiopathic cyclic edema with more advanced cases of cellulite. There are no data related to this observation in the PubMed, ISI and Scopus medical databases.

The identification of this association occurred from observations of phlebologic and lymphatic patients. It was observed that some of these patients may retain significant quantities of fluids throughout the day. Variations from 800 grams to up to 4 kilos can occur in patients that drink much liquid throughout the day. Diagnosis is suggested when there is a difference of more than 800 grams. However, there are no additional routine laboratory tests to diagnose this condition. Thus, diagnosis is clinical with the response to treatment using drugs that improve capillary permeability confirming the diagnosis.

The main drug used is aminaftone 75 mg. Although, no study has determined the optimal duration of therapy, it should be maintained for at least six months, as therapeutic failures have been observed after short treatment periods. If treatment with aminaftone fails other options exist with ginkgo biloba<sup>10</sup> and spironolactone<sup>11</sup> being the main most commonly used. In the literature dextroamphetamine sulfate is reported as an option in the treatment of cyclic edema.<sup>12,13</sup>

The treatment of cellulite in this study arose from reports of patients who were in treatment for lymphedema using a technique developed by the authors.<sup>5,6</sup> Some patients recognized that the cellulite, on the same limb as the lymphedema being treated, had disappeared. From this observation we started a line of research into the treatment of cellulite. Thus, all patients who were referred for treatment of cellulite were submitted to a detailed vascular assessment, specifically in relation to edema. The observation of cyclic edema demonstrated the success of the treatment and the need for its control, but we had no idea of the high prevalence of edema in the more advanced grades of cellulite. The lack of specific clinical and laboratory studies hinders research on cyclic edema and the dissemination of information on this disease. The fact that it is idiopathic is another limiting factor to its management as there are few reports about treatment in the literature.

During the evaluation of patients with cellulite, it was noted that many with edema with Grade II and III cellulite also had idiopathic cyclic edema which constituted the main reason for treatment failure. When the idiopathic cyclic edema is not previously treating, the failure and early relapse rates of treatment for cellulite is more than 80%. Once the edema is controlled it is possible to obtain better results in the treatment of cellulite. From this observation patients are nowadays routinely assessed for cyclic edema during the evaluation of cellulite; if diagnosed treatment for cellulite is not started until the edema is controlled.

Another important aspect to be analyzed is the assessment of all changes that may lead to tissue accumulation such as in obesity, lipedema and lymphedema; the pathophysiology of each association should be addressed in order to improve the aesthetic result. These associations constitute aggravating effects such as, for example, cyclic edema aggravates the symptoms of lipedema, cellulite and obesity.

These data offer a new research perspective in relation to the treatment of aggravating factors in cellulite.

## Conclusion

Idiopathic cyclic edema is an aggravating factor for cellulite and is frequently associated with the more advanced stages. The control of edema is essential in the treatment of cellulite.

## Conflict of Interest

The authors have declared that no conflict of interest exists.

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