

# Calcium Citrate for Vulvar Vestibulitis

## A Case Report

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*A woman had suffered from vulvar vestibulitis (vulvodynia) for four years. Pain from the disorder had disrupted her ability to function at work and home as well as sexually. An initial full range of treatments, including multiple operations, had produced no relief. Examination of the urine for evidence of excess oxalate, which has been shown to cause epithelial reactions similar to those found in vulvodynia, showed periodic hyperoxaluria and pH elevations related to the symptoms. Calcium citrate was given to modify the oxalate crystalluria. The symptoms were significantly reduced in three months, and the patient was pain free after one year. She was able to resume normal work, family, sexual and recreational activities. Withdrawal of the calcium citrate resulted in a return of the symptoms; reinstitution alleviated them. These findings suggest that further study of individualized metabolic factors that may underlie vulvodynia is warranted.*

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## Introduction

Treatment of vulvodynia has included local surgical incision and attempts to destroy the painful lesions with laser vaporization and cryotherapy.<sup>1-5</sup> Antibacterial, antiviral and antiinflammatory agents plus a variety of topical hormonal preparations have all been tried, as have highly irritating substances, such as capsaicin.<sup>6</sup> Antidepressants have had limited success.<sup>7</sup> These methods involve considerable discomfort and risk to the patient, are expensive and have produced disappointing results.<sup>4,5</sup>

A basic need in the therapeutic approach to this condition is an understanding of the factors leading to vulvodynia. Although attempts have been made to explain the mechanism of the pain,<sup>8</sup> all the therapeutic approaches utilized to date have been empirical, directed at controlling the secondary symptomatology rather than the underlying causes.

We decided to examine the urine of women with vulvodynia for evidence of any substances irritating to the vulvar epithelium and to search for biochemical and/or metabolic factors that might give a clue to the etiology of the condition. We were particularly interested in the role of urinary oxalate because sharp oxalate crystals can cause severe burning and itching when in contact with epithelial surfaces.<sup>9-11</sup> Below is a report of one case.

## Case Report

A 32-year-old, white woman, gravida 2, para 2, was seen in February 1982 for a postpartum examination six weeks after her second cesarean section. She had regular menstrual periods every 30 days, lasting 5 days. She had never had any major illnesses, and her only previous operation was a cesarean section for her first pregnancy because of a breech presentation (May 1979). She complained of burning and stabbing pain at the introitus. She was unable to have intercourse, was preoccupied with and exhausted by the persistent pain and was unable to resume her usual professional responsibilities.

A physical examination revealed a low transverse abdominal scar and an exquisitely tender area of redness at the posterior fourchette. Colposcopic examination showed small, villuslike projections associated with human papillomavirus (HPV). The vagina and cervix were nulliparous. The uterus was parous, anteverted and mobile. The adnexa were small and nontender. The rectovaginal examination was unremarkable.

Biopsy of the painful areas showed findings "suggestive of flat condyloma."<sup>12,13</sup> After the biopsy the

painful area was treated unsuccessfully with electrocautery. Because the pain became disabling, the patient consulted two dermatologists, two gynecologists and a psychologist. In April 1982 she was treated for an episode of monilial vaginitis, but that treatment did not alleviate the pain.

Initial treatments included antibacterial and antiviral agents, steroids and hormonal preparations locally and systemically, all to no avail. The patient was referred to two major gynecologic centers for further treatment. In November 1982 she underwent removal of minor vestibular glands and perineoplasty, as described by Woodruff et al.<sup>1</sup> The excision was unsuccessful in relieving the pain, and subsequently the patient underwent laser surgery on the painful areas, which were located between the external urethral meatus and the clitoris, on six occasions at approximately three-month intervals. The laser surgery was followed by two operations involving local excision of the painful areas, which included the area around the external urethral meatus and around the clitoris. The last operation was performed in December 1984.

The patient experienced continued pain but received no treatment for the next two years. Her sexual activity ceased with the associated strain on her marriage.<sup>14</sup> She underwent counseling for depression, including periods of suicidal ideation. Although she tried to maintain as normal a life as possible, chronic fatigue and irritability caused by the pain plus depression engendered by the belief that the pain would never stop interfered with her ability to function at her job or with her family. Although the pain varied throughout this time, it was always present; although at times a little better, it was always disabling. Three types were present: (1) an intensely painful, stabbing pain occurred spontaneously at random intervals; (2) a constant aching and burning sensation accompanied by red and swollen vulvar tissues fluctuated with the menstrual cycle and was worse premenstrually; (3) tiny, red dots were present that were exquisitely painful if touched with a cotton-tipped swab on examination, contacted by underwear or touched when attempting intercourse.

The patient was referred for a urinary biochemical evaluation for the purpose of developing a new approach to therapy. The pattern of her pain episodes was studied in relation to her urinary pH and oxalate excretion.

#### Biochemical Evaluation

Each voiding urine (specimen) was collected separately over a 24-hour period and individually an-

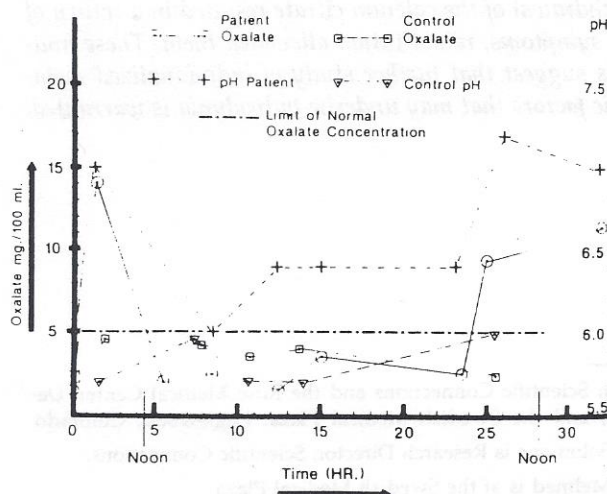
alyzed as previously described.<sup>15</sup> This analysis revealed several instances of transient hyperoxaluria (three times normal) often accompanied by microscopic oxalocrystalluria as well as increased pH values (6.5–8.5) in the absence of infection. These changes, especially the increased pH values, consistently preceded the typical symptoms of stabbing and burning pain. Both related (three sisters) and unrelated control subjects (three) did not show this degree of fluctuation in their urinary constituents (Figure 1).

#### Management

Baseline values for daily pain frequency were meticulously recorded for several months. On the basis of the abnormal urinary findings it was decided to attempt to control the intake of dietary oxalates and modify the physical chemistry of the urine with regard to oxalate.<sup>16</sup> Accordingly, a nutritionally balanced, low-oxalate diet was prescribed, and calcium citrate without vitamin D was given orally at a dosage of six tablets daily, each containing 200 mg of calcium and 950 mg of citrate in divided doses. The fluid intake and urine output were significantly increased, and a trial of vitamin B<sub>6</sub> (200 mg/d) was carried out for a month. A low-carbohydrate, ketogenic diet was utilized for a week to reduce the pH values.

#### Clinical Course

The increased urine volume, vitamin B<sub>6</sub> administration and ketogenic diet had no significant effect on the



**Figure 1**

Urinary pH values and oxalate concentrations in the patient as compared to those in normal controls. ○ = patient's oxalate, □ = control oxalate, + = patient's pH, ▽ = control pH, --- = limit of normal oxalate concentration.

patient's symptoms. On calcium citrate alone her pain frequency decreased from an average of  $4.2 \pm 1.8$  SD episodes of stabbing pain per day to a mean of  $0.40 \pm 0.52$  episodes within three months. This decrease was highly statistically significant ( $P < .001$ ). Within one year the patient was completely pain free, sexually and athletically active and enjoying a normal life-style. Once the pain had decreased, her need for psychologic counseling was drastically reduced.

When, on two occasions, the medication was stopped, the pain returned within two weeks but disappeared after reinstitution of the calcium citrate. Periodic monitoring of the blood pressure, serum ionized calcium and urinary calcium revealed values within the normal range. At this writing the patient had received calcium citrate daily for over three years, with no discernible undesirable side effects. After three years the dose of calcium citrate was reduced to three tablets per day without an exacerbation of the symptoms.

## Discussion

Repeated surgical and topical treatment had failed to control the patient's pain over a period of three years, but therapy based on metabolic considerations was successful within three months.

Oxalate, citrate and hydrogen ion metabolism appear to be areas of importance to the understanding and management of vulvodynia. Citrate has been shown to retard the nucleation and crystal growth of calcium salts.<sup>17</sup> We tried to use the minimum effective dose of calcium citrate, although the doses used were within the range of the usually recommended daily calcium intake. An upper limit of nine tablets per day was adhered to. Magnesium citrate can be used therapeutically in place of calcium citrate but tends to cause diarrhea; patients in whom constipation is a problem may welcome that effect. Sodium and potassium citrate were not used because of their tendency to further alkalinize the urine.<sup>17</sup> Vitamin B<sub>6</sub> administration, 200 mg/d, temporary urinary acidification with a ketogenic diet and an increased urinary output were all ineffective in controlling the pain. Barrier creams used on a short-term basis were ineffective; they included one containing mineral oil, petrolatum and paraffin and another containing zinc oxide. Both were tried for approximately one month.

Dietary manipulation to decrease the oxalate intake was partially successful in reducing the symptoms in our patient. Since oxalate is an end product of metabolism, a reduced intake does not have a harmful effect. The patient reported a marked exacerbation of

her symptoms after an intake of high-oxalate-containing foods, such as rhubarb, peanuts, spinach and celery. A careful history will often reveal a dramatic episode of severe pain after a high oxalate intake. That effect might be useful as a diagnostic indicator.

Several hypotheses concerning the biochemical etiology are suggested by the findings. It has been shown that calcium oxalate crystals of plant origin cause stabbing and burning pain in the epithelium.<sup>10,11</sup> We have demonstrated periodic hyperoxaluria in association with the pain of vulvodynia. The therapeutic effectiveness of calcium citrate might result from the ability of citrate to inhibit calcium oxalate crystal formation without necessarily reducing the total amount of calcium and oxalate in the urine.<sup>17</sup> One of the main unanswered questions concerns the reasons for periodically elevated urinary pH values in the absence of infection. These elevations, over the long term, may set the stage for a variety of normally innocuous substances or procedures to cause pain. Although significant increases in urinary oxalate were observed in a few of the individual voidings, the total excretion of oxalate over a 24-hour period was often within normal limits. The peaks of elevated oxalate excretion would have been missed if the conventional protocol for a pooled 24-hour collection had been used.

Our patient had evidence of an HPV infection. She had "cactuslike" projections, and a biopsy showed changes suggestive of condyloma; the association has been well documented.<sup>5,12,13</sup> However, there was no evidence of cervical pathology, and the Papanicolaou smears were always normal. Future studies might attempt DNA hybridization of the HPV to determine if a particular HPV type is associated with vulvodynia, although a previous attempt was unproductive.<sup>13</sup> HPV may be one of the factors sensitizing patients to this syndrome,<sup>13</sup> but we doubt that it is the sole cause.

It appears that 60–85% of women with vulvodynia respond to surgical excision of the affected area. Those are the most optimistic results published, and many investigators have found the surgical results to be disappointing or have warned of possible worsening of symptoms in 10% of postsurgery patients.<sup>18</sup> Our patient responded poorly to multiple operations. Surgery yielded relief from her pain in only some areas of excision and/or laser treatment; new, painful areas emerged on the periphery of the surgical sites approximately six weeks after each operation.

While it is desirable to treat patients with noninva-

sive and inexpensive therapy, we must caution against the indiscriminate use of calcium citrate in all patients with vulvodynia without careful monitoring. Any medical condition or use of medication that causes sensitivity to calcium or magnesium citrate intake would necessitate caution. Further assessments of the metabolic and biochemical factors associated with vulvodynia may prove to be of significant benefit to patients with this disorder.

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