

VULVAR PAGET'S DISEASE: RECOVERY WITHOUT SURGERY FOLLOWING CHANGE TO VERY LOW-FLUORIDE SPRING AND WELL WATER

Michael P Connett^a

Burlington, Vermont, USA

SUMMARY: A case report of a Caucasian female born in 1927 is presented in which rapid recovery from vulvar extramammary Paget's disease (EMPD) without surgical intervention occurred following an abrupt change from fluoridated/chlorinated tap water (0.9- 1.0 mg F⁻/L) to low-fluoride spring and well water (both <0.1 mg F⁻/L) for drinking, cooking, bathing, and laundry purposes. Within weeks of switching from the tap water her condition completely cleared, with no recurrence after three years except when re-exposed to fluoridated tap water. EMPD primarily affects post-menopausal Caucasian women, but occasionally it also occurs in men. The condition presents as an itchy, rash-like condition that can be accompanied by invasive malignant changes to underlying dermal tissue, for which surgical excision of the affected region is the most common treatment. Possible reasons for recovery without surgery in this case are discussed.

Keywords: Chlorinated water; Extramammary Paget's Disease; Fluoridated water; Vulvar Paget's disease; Water disinfection by-products.

INTRODUCTION

Vulvar Paget's disease is the most common type of extramammary Paget's disease (EMPD).¹ Originating in the epidermal tissue of the vulva region, it is the most common type of skin-type Paget's disease, a form of adenocarcinoma (a carcinoma arising from glandular epithelial tissue). In the majority (80%) of cases, the malignant changes of the epidermis do not spread to the underlying dermal tissue.¹ When dermal invasion does occur, prognosis for survival worsens.²

Vulvar Paget's is a rare disease that primarily impacts Caucasian woman after menopause. The condition typically presents as a red, velvety, pruritic-like skin rash of the vulva region which may closely mimic a multitude of other, more common conditions.¹ As a result, vulvar Paget's (which requires a biopsy for definitive diagnosis) is frequently misdiagnosed, leading to an often lengthy lag-time (an average of about two to three years) between the onset of symptoms and diagnosis.¹⁻⁴ The causes of vulvar Paget's and EMPD in general remain poorly understood.

CASE REPORT

The patient, CH, is a post-menopausal Caucasian woman born in 1927. In 1994, she moved to a community in northwest Washington State (USA) where the water was fluoridated (0.9-1.0 mg/L) and chlorinated. Previously, she had lived in areas where the water was chlorinated but not in areas where the water was fluoridated. Within five years of moving to the fluoridated community, CH developed a small red itchy area in the perineum area that was initially diagnosed as a fungus infection, and later as a "chronic perianal and vulvar dermatitis." Anti-fungals and

^aFor correspondence: 82 Judson St, Canton NY 13617, USA. E-mail: michael@fluoridealert.org

topical creams proved ineffective, and the condition continued to “come and go” for years.

In 2003, CH underwent an operation for unrelated conditions, including a partial colectomy to treat diverticulitis and removal of an ovarian cyst. The surgery was uneventful, and the patient was home within a few days. However, over the course of the following month, CH's health began to deteriorate. The rash in the perineum area doubled in size, and became unbearably painful. According to CH's medical records: “Perianal area is red, macerated, with some whitish looking areas, and this area extends all the way up to perineum onto the right vulva.” In addition to the worsening of the “vulvar dermatitis,” CH experienced an onset of other symptoms including dry skin, rashes on her arms and torso, earaches, a buildup of a white wax-like substance in her tonsils (‘tonsil stones’), dizzy spells, and pain in her legs. Concurrent with the onset of these symptoms, she also developed an allergy to latex.⁵

Blood tests revealed high levels of calcium and parathyroid hormone (PTH), which led to a diagnosis of hyperparathyroidism. Elevated blood pressure was also noted in several readings, and hypertension was suspected. A biopsy of skin from the perianal area produced a diagnosis of extramammary Paget's Disease (EMPD). Medical records describe the microscopic findings of CH's biopsy:

“Punch biopsy of skin has a thickened epidermis with hyperkeratosis and underlying lichenoid chronic inflammation. Epidermis has intraepithelial spread of malignant cells disposed as clusters, nests, and as single cells. The differential diagnosis is Paget's disease versus intraepithelial amelanotic melanoma versus possibly poorly-differentiated intraepithelial squamous cell carcinoma. To resolve this differential, immunoperoxidase with low molecular weight cytokeratin 35BH11, CEA, CK5/6, and tyrosinase are performed. Malignant cells are positive with CEA, 35BH11 and negative with CK5/6 and tyrosinase. In addition, on mucicarmine stain, cells are focally positive. These results confirm that this is extramammary Paget's disease. No underlying structure has atypical change; specifically underlying sweat glands are not atypical.”

Following the biopsy, physicians recommended surgical intervention to remove the affected skin of the perineum and vulva. They also recommended medical treatment for the hyperparathyroidism and hypertension. CH declined treatment, however, as she suspected an allergy might be the source of her symptoms. According to CH:

“Some years ago I had nurses training. I think that helped me to analyze the situation and stay calm. I checked with my surgeon every six weeks to see if there was any sign of cancer. He gave me various ointments to try to help the pain but nothing helped. Knowing I had to be my own doctor, I started with the idea that it was an allergic reaction to something, maybe foods. I started keeping a journal of everything I ate everyday and would note any change in the itching and pain. This went on for about 6 months. There was no pattern that I could find. The pain would come and go, but it didn't connect with any food.”

Failing to identify any relationship between symptoms and food-intake patterns, CH eventually considered (in February 2004) whether the water supply might be the culprit. Having previously lived in nonfluoridated Wichita, KS, where a

fluoridation campaign had been waged, she was familiar with concerns that fluoridated water might be harmful to health. To test whether fluoride in water was affecting her condition, she purchased spring water from the store and used it as her sole source for drinking and cooking. Within three days, she noticed an “immediate” improvement in symptoms. As a result, she decided to prolong the use of nonfluoridated water. For the next six weeks, she had spring water (Mountain Mist, <0.1 mg F⁻/L) delivered to her house in 5-gallon jugs. Thereafter, for convenience, CH relied solely on well water (<0.1 mg F⁻/L) from her son's house nearby. According to her account:

“I stopped using the tap water for drinking and bathing, and the Paget's started clearing up immediately. I now use well water from my son's house and go there to bathe. I was free of symptoms within weeks—except the tonsil stones. It took about a year for those to completely go away.”

CH has continued to rely strictly on well water for drinking, bathing, and laundry purposes until the present day, and has limited her consumption of processed beverages. Her blood pressure and PTH levels have returned to normal, her blood calcium has reduced to high normal, and her vulvar Paget's has cleared completely with the exception of one brief recurrence. While she is now able to drink an “occasional espresso” with her city's tap water without ill effect, CH did experience a relapse of symptoms following repeated exposure to tap water over the course of several days¹. As she reported:

“In 2005 I had house guests and we were on the go a lot, and I didn't want to go to my kids' house to bathe so I showered at home. We ate out a lot at local restaurants that use the local tap water. I started itching and turning red in the same area. The symptoms cleared in 2 or 3 days after I stopped [using the tap water].”

DISCUSSION

Although some of the symptoms reported in this case are not commonly associated with EMPD (e.g. ‘tonsil stones’ and elevated PTH), the subject shares many of the typical characteristics reported in the literature.¹⁻⁴ She is a post-menopausal Caucasian woman; there was a significant lag-time (five years) between the onset of symptoms and diagnosis; and the neoplastic changes were confined to the epidermis without dermal invasion or underlying carcinoma.

Perhaps the most notably different feature of this case is that a full recovery was obtained without any surgical intervention, in sharp contrast to most cases recorded in the literature. For example, Fanning et al., reported that among 100 cases of vulvar Paget's retrospectively identified from eight hospitals, the condition was treated surgically in all 100 patients, and among them the recurrence rate was 34%.²

Since the only identifiable change made by the subject to her lifestyle/diet was an abrupt switch from fluoridated tap water to low-fluoride spring and well water, this case report points to the likelihood that fluoride, or possibly some other component of tap water (e.g., chlorinated disinfection by-products), may be a contributing cause of vulvar Paget's in some patients suffering from this rare disease.^a While a causal relationship between tap water and vulvar Paget's has not been previously reported, the evidence in this case strongly indicates a causal relationship with fluoridated or chlorinated water.^b

Case studies have previously reported that fluoride ingestion may cause rash-like conditions, including eczema, dermatitis, urticaria, and pruritus.⁷⁻¹¹ In Kuopio, Finland, the incidence of eczema, itchy skin, and dry skin decreased within one to three months following termination of the city's fluoridation program in 1992.¹² Additionally, studies on toothpaste have reported an association between fluoridated brands and perioral dermatitis in some users,¹³⁻¹⁶ while studies on animals report that topical fluoride can induce, or enhance, skin inflammation, particularly if the skin has been abraded prior to exposure.¹⁷⁻¹⁹ Other studies, including *in vitro* studies on cultured mammalian cells²⁰ and a limited number of *in vivo* studies,²¹ indicate that fluoride has a genotoxic potential as well.

In addition to fluoride, there is some evidence indicating a link between chlorinated water and skin lesions (e.g. atopic eczema & contact dermatitis).²²⁻²⁴ More convincing, however, is the evidence linking chlorinated water, along with its accompanying disinfection by-products (DBPs), to both genotoxic effects and cancer.²⁵⁻³⁰ Of particular interest are several epidemiological investigations that have found significant correlations between chlorinated DBPs and bladder cancer.²⁸⁻³⁰ Bladder cancer is one of the most common underlying cancers in vulvar Paget's and EMPD.¹⁻²

However, while it seems likely that fluoridated water and chlorinated water can, under certain conditions, cause adverse skin reactions, and while it seems possible that fluoride, and particularly DBPs, can cause genotoxic effects; there appears to be no direct evidence demonstrating that either chemical can produce the specific neoplastic changes diagnostic of Paget's disease. Thus, it remains to be determined whether fluoride, chlorinated DBPs, or some other component of tap water, could contribute to the development of the neoplastic changes in EMPD.

Nevertheless, based on the successful recovery documented here in the absence of surgical treatment, coupled with the seriousness of the disease, it may prove helpful for physicians and researchers to pay closer attention to the possible relationship between tap water and vulvar Paget's disease.

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^aRequests made by the author in the fall of 2006 for follow-up patch tests were declined, due to CH's concerns about a possible relapse of the EMPD.

^bAn alternative explanation for the recovery is that it was a result of a "placebo effect," whereby the patient's suspicion that fluoride may have been causing the problem promoted the body's recovery following cessation of exposure. A recent meta-review by Hrobjartsson and Gotzsche⁶ indicates, however, that such a "placebo effect" would be an unlikely explanation for this case, since the outcome (reversal of vulvar Paget's) was an "objective" outcome, not a "subjective" one. Lasting recovery from malignancies is not usually seen with a placebo effect. Moreover, a return of the condition upon reintroduction of fluoridated water, followed by clearing on subsequent removal of the affecting water, is equally difficult to attribute to a placebo effect.

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