

Pruritus Ani As a Manifestation of Systemic Contact Dermatitis: Resolution with Dietary Nickel Restriction

Dianne L. Silvestri and Sara Barmettler

Pruritus ani is a common distressing problem with numerous possible causes. When locally applied agents trigger irritation or allergic response, skin changes of dermatitis usually accompany the itch. Focal pruritus in the absence of dermatitis is not generally considered to be a manifestation of contact allergy. Furthermore, focal pruritus is not listed among the possible diverse presentations of the systemic delivery of a proven contact allergen. We report a case of a gentleman with a 1.5-year history of treatment-resistant pruritus ani. When patch testing revealed a positive reaction to nickel sulfate, he admitted to daily peanut butter consumption. His symptoms resolved with dietary nickel restriction. Patch testing may be useful in patients with pruritus of the anogenital region, not only to elucidate potential contact exposures contributing to the symptom but also to suggest possible dietary precipitants.

“SYSTEMIC CONTACT DERMATITIS” is a term used to describe a cutaneous or mucosal reaction that follows systemic exposure to a contact allergen. A variety of such eruptions have been reported,¹ including flare of previous patch-test sites, deep-seated vesicles on the fingers and palms, symmetrical intertriginous and flexural exanthem, widespread dermatitis, exfoliative erythroderma, and (as recently reported) labial lichen planus.² Focal pruritus is not reported among these reactions. We report a patient with no other local or systemic causes of pruritus ani whose symptoms resolved with dietary avoidance of his patch test–proven allergens.

Case Report

A 59-year-old man was referred to our contact dermatitis clinic with an 18-month history of itching and occasional pain around the anus. He was initially seen by a colorectal surgeon, who recommended diphenhydramine cream and topical lidocaine, which afforded temporary relief. When the problem recurred, he was evaluated by a dermatologist, who noted a small fissure. Sitz baths were prescribed, along with ketoconazole 2% cream, hydrocortisone valerate 0.2% cream, and mupirocin ointment twice daily. His

symptoms improved, allowing him to reduce his application of topical lidocaine from every 2 hours to once daily. He took oral diphenhydramine at bedtime for itching. One month prior to his clinic visit, with worsening symptoms, he resumed applying topical diphenhydramine cream and lidocaine 5% ointment twice daily, occasionally adding Calmoseptine barrier cream (Calmo Manufacturing Inc, Huntington Beach, CA). He used white toilet tissue and moistened towelettes to cleanse after defecating. His usual diet was free of spices, alcohol, and coffee, and he denied any association between his anal symptoms and foods or medications.

The result of a colonoscopy 4 years earlier was normal. His medical history was significant for common variable immunodeficiency, which was treated with monthly intravenous immunoglobulin. His daily medications were simvastatin, fenofibrate, omeprazole, calcium, and fluticasone propionate nasal spray.

On examination, the patient appeared well. Mild perianal erythema was present, but there were no fissures or involvement of the scrotum or inguinal creases. The results of the remainder of the examination were normal.

To exclude contact allergy as the cause of his pruritus, he was patch-tested with a modified North American extended series-65 (Chemotechnique Diagnostics AB, Malmö, Sweden) and 22 additional test substances, including 8 personal products. All allergens were applied to the upper back through a standard technique with 8 mm Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Norgesplaster Alpha A/S, Venne, Norway). Patches were removed after 48 hours, and

From the Division of Dermatology, University of Massachusetts Medical School, Worcester, MA.

Reprints not available.

DOI 10.2310/6620.2011.10062

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readings were performed at 48 and 96 hours. Examination of the patch-test sites revealed a +++ reaction to bisphenol A epoxy resin, a +++ reaction to bisphenol F epoxy resin, a ++ reaction to nickel sulfate, and a + reaction to potassium dichromate.

The patient was given information on all positive allergens, and relevance was sought. The patient knew of no occupational or hobby-related exposure to epoxy. He denied using plastic beverage bottles. His symptoms were not temporally related to his monthly intravenous infusions. In reviewing the nickel avoidance instructions, the patient acknowledged eating a peanut butter sandwich at every lunch. He agreed to stop eating nuts and to begin restricting other foods with high nickel or chromate content (Table 1).

At a follow-up visit 3 months later, the patient reported dramatic improvement. He was symptom free with no treatments except his dietary restriction of nickel and chromate. Physical examination revealed a normal perianal area. Because of the marked relief from his symptoms, the patient was initially unwilling to undertake a dietary nickel challenge test. One year later, he remained free of symptoms while on his restricted diet. When reached by telephone nearly 2 years later, the patient reported that eating peanut butter on 2 consecutive days caused recurrence of his anal pruritus. Furthermore, consuming foods high in nickel or chromate produced a previously ignored intermittent hand itch and tiny vesicles. However, dietary chromate did not produce anal itching.

Discussion

Pruritus ani (defined as itch localized to the anus and perianal skin) has been associated with a number of causes, including systemic diseases and underlying colorectal abnormalities (Table 2). Primary cutaneous disorders such as psoriasis and lichen planus are other possible causes (Table 3). In many instances, however, symptoms are perpetuated by (if not produced by) contact irritants and allergens. Many efforts to delineate inciting agents have examined populations with "anogenital" complaints rather than solely pruritus ani, and cutaneous findings vary. Table 3 lists cited topical irritants, such as harsh cleansers, paper preservatives,³ and suppository oils.⁴ Table 4 lists both common and unusual implicated allergens, including peppermint oil,⁵ nail polish resin,⁶ and hair dye.⁷

Not all positive patch-test results in patients with anogenital pruritus are considered clinically relevant. Of 32 pruritus ani patients with diverse clinical findings, Dasan and colleagues⁷ observed positive patch-test reactions in 18,

but they interpreted none as relevant except a single reaction to para-phenylenediamine (present in the patient's bath water, from his wife's shampooing). Other positive reactions were to fragrance mix, preservatives, and topical antibiotics, and there were three reactions to nickel.

In another study, which examined 1,008 patients with anogenital complaints who were patch-tested during a 5-year period,³ the authors concluded that allergic contact dermatitis accounted for these conditions in only 351 of the 483 patients who had positive patch-test results; in those patients, topical medications and preservatives were the most frequent culprits. The numerous positive reactions to nickel sulfate were considered not likely to be relevant in regard to anogenital dermatitis.³

Warshaw and colleagues summarized the North American Contact Dermatitis Group patch-test results for patients with anogenital dermatitis who were patch-tested from 1994 to 2004.⁸ Of 347 patients with solely anogenital involvement, 73 had at least one relevant positive reaction. The most common significant allergens were fragrance, neomycin, caines, propylene glycol, corticosteroids, bacitracin, and preservatives. Although the reaction to nickel was positive in 5.76% of these patients, it was considered irrelevant except in one patient for whom there was evidence of transfer from jewelry. When vulvar complaints are evaluated separately from anal complaints, the results are similar. Nickel allergy is frequently present but only rarely felt to be relevant.⁹⁻¹¹

A few investigators have considered the possibility that systemic exposure to an allergen might produce anogenital pruritus. This may occur as a "recall" reaction, such as the pruritic vulvitis that developed when intravenous diazepam containing propylene glycol was administered to a woman who had been previously sensitized to propylene glycol in her vaginal lubricant.¹² Giordano-Labadie and colleagues reported on a man whose persistent perianal and buttock eczema cleared when sorbic acid was eliminated from his diet. A positive patch-test reaction to sorbic acid suggested the patient's prior sensitization by local use of a cream containing that ingredient.¹³

In addition to direct allergen contact and systemically evoked recall reactions, allergen exposure enterally may occasionally produce perineal symptoms. In their review of contact allergy to foods, Brancaccio and Alvarez noted that consumption of ginkgo can lead to perianal dermatitis.¹⁴ Salam and Fowler evaluated the usefulness of a diet that eliminated balsam of Peru for 71 patients who were patch test positive to balsam of Peru, fragrance mix, cinnamic aldehyde, or balsam of Tolu.¹⁵ Forty-five patients received instruction in the diet; 21 of the 35 who complied

Table 1. Dietary Guidelines for Restricting Nickel and Chromate

<i>Foods to Avoid</i>		<i>Allowed Foods*</i>
Egg yolks (C)	Green beans (NC)	Spaghetti
Bran and fiber products (NC)	Mushrooms (C)	Wheat flour
High-bran cereals (NC)	Sprouts (beans, alfalfa) (N)	Beets (red)
Wheat bran (NC)	Beans (brown, white, red kidney, soya) (N)	Cauliflower
Buckwheat (NC)	Asparagus (N)	Cabbage (white, Chinese)
Rye bran (NC)	Kale (N)	Cucumber
Muesli; similar breakfast products (NC)	Leeks (N)	Eggplant
Oats; oatmeal (N)	Lentils (N)	Peppers (red, green)
Multigrain bread (N)	Lettuce (N)	Squash (yellow)
Rice, unpolished (N)	Peas (green, split) (N)	Tomatoes
Corn (C)	Watercress (C)	Carrots
Corn flakes (C)	Onions (C)	Garlic
Millet (N)	Spinach (N)	Dill
Corn meal (C)	Salad dressings (N)	Parsley
Cornstarch (C)	Soy sauce (N)	Peeled apples
Strong tea (NC)	Black pepper (C)	Bananas
Coffee (C)	Cloves (C)	Berries (no raspberries)
Wine (C)	Thyme (C)	Peaches
Beer (C)	Canned and frozen fruits (C)	Pears
Chicken (C)	Canned plums (C)	Raisins
Lunch meats (NC)	Figs (N)	Rice (polished)
Sausage (N)	Raspberries (N)	Macaroni
Processed beef (C)	Prunes (N)	Milk
Canned tuna (N)	Dates (N)	Yogurt
Shellfish [†] (NC)	Pineapples (N)	Cheese
Potatoes (C)	Apple peel (C)	Butter
Baked beans (NC)	Rhubarb (N)	Margarine
Frozen and canned vegetables (C)	Jello (gelatin) (N)	Egg whites
Broccoli (C)	Soup concentrates (N)	Wheat flour (refined)
Licorice (N)	Bouillon (N)	White bread made with yeast
Chocolate; cocoa (NC)	Soy protein powder (N)	Yeast
Sunflower and sesame seeds (N)	Tofu (N)	Breakfast foods made from rice
Nuts [‡] (N)	Vitamin supplements (N)	Carbonated beverages
Peanut butter (N)	Nutritional supplements (N)	Alcoholic beverages
Popcorn (C)		Lamb
		Beef
		Pork
		Veal
		Fin fish
		Turkey

C = chromate; N = nickel; NC = both nickel and chromate.

*All fruits and vegetables must be fresh, not canned or frozen.

[†]Oysters, mussels, clams, cockles, crayfish, shrimp and lobsters.

[‡]Almonds, hazelnuts, peanuts, walnuts, and cashews.

experienced a complete or significant improvement in symptoms. In one-third of these individuals, the dermatitis was anogenital.

Dietary allergen exposure was also deemed important by Vermaat and colleagues, who examined 53 women with

chronic anogenital dermatitis.¹⁶ Seven of 35 positive patch-test results were considered clinically relevant. Three patients responded to oral elimination of spices to which they had tested positive (ie, nutmeg, coriander, onion powder, and curry). One patient who was sensitive

Table 2. Extracutaneous Causes of Pruritus Ani

Infestations
Pinworm (<i>Enterobius vermicularis</i>)
Scabies (<i>Sarcoptes scabiei</i>)
Pediculosis (<i>Phthirus pubis</i>)
Infections
Bacterial (<i>Corynebacterium minutissimum</i> [erythrasma], <i>Staphylococcus</i> , <i>Streptococcus</i> , <i>Neisseria gonorrhoeae</i> , <i>Treponema pallidum</i>)
Yeast (<i>Candida</i> species)
Dermatophyte (tinea cruris)
Viral (papilloma, herpes)
Parasitic
Colorectal disorders
Diarrhea (eg, inflammatory bowel disease, irritable bowel syndrome, lactose intolerance, laxative abuse)
Hemorrhoids
Rectal prolapse
Fistula in ano
Cryptitis
Anal abrasions or fissures
Colorectal adenocarcinoma
Metabolic diseases
Diabetes mellitus
Leukemia, lymphoma
Thyroid disorder
Liver disease (hyperbilirubinemia)
Pellagra
Hypovitaminosis (A and D)
Uremia
Anemia (including iron deficiency anemia)
Polycythemia vera

to peppermint oil had relief of symptoms after avoiding peppermint tea and experienced recurrence upon rechallenge, suggesting allergen excretion, allergen secretion, or systemic contact dermatitis.⁵ Of the 18 reactions to nickel sulfate in Vermaat and colleagues' group, none was felt to be relevant based on direct contact. However, the authors acknowledged that a nickel-free diet or urinary nickel analysis might have helped elucidate a role for nickel ingestion in anogenital dermatitis.¹⁶ Lucke and colleagues¹⁷ patch-tested 55 women who had primarily vulvar itching; 36 had at least one positive reaction, and 17 reacted to nickel sulfate. Although avoidance of contact with fragrances, topical medications, and dyes was prescribed for patients allergic to those substances, nickel was also considered possibly significant because of its high prevalence (31%) as an allergen in this group. Although half the nickel-positive patients improved after avoiding

Table 3. Nonallergic Cutaneous Causes of Pruritus Ani

Cutaneous disease
Psoriasis
Lichen planus
Seborrheic dermatitis
Lichen simplex chronicus
Lichen sclerosis
Atopic dermatitis
Fixed drug eruption
Acanthosis nigricans
Vitiligo
Benign familial chronic pemphigus (Hailey-Hailey disease)
Pityriasis rosea
Local malignancy (extramammary Paget's disease, Bowen's disease)
Irritant contact dermatitis
Dry skin (atopy, aging)
Persistent moisture (perspiration; leakage of mucous, stool, or suppository oils; prolapse; skin tags)
Harsh cleansers (soaps, moistened wipes)
Abrasives (washcloths, clothing fibers, seams)
Laundry detergent retained in garments
Occlusive fabrics, tight styles
Retained bath soap or shampoo
Fragrance (personal lubricant, contraceptive, cologne, douche, cream, oil, paper products)
Formaldehyde (paper, cream)
Dye (paper products, underwear)
Foreign body
Eliminated ingestants
Medications (antibiotics, colchicine, quinidine)
Vitamin C tablets
Nuts, seeds
Alcohol
Coffee, tea, acidic beverages
Chocolate, spices
Prawns, shellfish

contact with the metal, one patient failed to improve until both contact and ingestion of nickel were eliminated. The authors suggested that "nickel may be a more important allergen than has generally been thought."¹⁷

Our patient's proven epoxy allergy did not seem to explain his symptoms. There have been several reports of contact dermatitis from epoxy resin in hemodialysis catheters, including a local reaction accompanied by eosinophilia.¹⁸ Our patient's sensitization may have developed from prior exposure to epoxy in catheters used for his regular intravenous immunoglobulin (IVIG) infusions, although he recalled only a few local reactions to early infusions. He had no anogenital epoxy exposure,

Table 4. Contact Allergens Implicated in Anogenital Pruritus

Balsam of Peru
Benzocaine
Benzalkonium chloride
Clioquinol
Clotrimazole
Cobalt chloride
Colophony
Compositae
Coriander
Corticosteroids
Curry
Dibucaine
Formaldehyde-releasing preservatives
Fragrance mix I
Iodopropynyl butyl carbamate
Lanolin
Methyldibromoglutaronitrile
Methylchloroisothiazolinone/methylisothiazolinone
Neomycin
Nickel sulfate
Parabens
para-Phenylenediamine
para-tert-Butylphenol formaldehyde resin
Peppermint oil
Propolis
Propylene glycol
Sorbic acid
Thimerosal
Thiuram mix
Tosylamide formaldehyde resin

nor was there occupational or hobby-related contact that would allow hand transfer of allergen. Furthermore, the affected area had had no direct contact with nickel or chromate, his other positive allergens. However, the patient had been consuming a significant quantity of nickel¹ in his daily peanut butter sandwiches, and his symptoms cleared after he began avoiding dietary nickel. Although nickel is measurable in serum, urine, and hair, it seems to be eliminated preferentially in feces and sweat.¹⁹ Thus, it is possible that fecal excretion or sweat secretion of nickel could have accounted for his perianal pruritus, although he had no visible local dermatitis.

It is interesting to note that an elimination diet is sometimes recommended in the management of pruritus ani. One such diet prohibits coffee, cola, citrus fruit and oils, chocolate, alcoholic beverages (especially beer), tomatoes, ketchup, pork, milk, nuts, spices, and tea.²⁰ This diet is strikingly similar to the balsam of Peru–restrictive diet published by Salam and Fowler¹⁵ but also

includes restriction of nuts, thereby substantially reducing nickel consumption as well.

Conclusion

“Systemic contact dermatitis” is a term that has been used to describe varied cutaneous reactions that follow oral, transcutaneous, intramuscular, intravenous, inhalational, or implantation exposure to an allergen in a person with prior cutaneous sensitization.²¹ Although there is a large body of evidence that dietary nickel can produce pompholyx as well as other manifestations of systemic contact dermatitis,^{1,21} little attention has been focused on anal, scrotal, and vulvar pruritus as possible systemic expressions of an allergic response. Our case report and the summarized evidence suggest that patients with anogenital pruritus with no apparent cause should undergo patch testing. If avoidance of cutaneous exposure to allergens fails to give relief, a diagnosis of systemic contact dermatitis should be considered, and patients should be advised to restrict dietary sources of their allergen(s) for at least 4 weeks.²²

Acknowledgments

Dr. Silvestri received funding from Stiefel Laboratories through a grant from the American Contact Dermatitis Society for work unrelated to this report. No research support was used for the writing of this article. No commercial benefits related to the subject of this article were received. The authors have no conflicts of interest to report.

The authors gratefully acknowledge Nancy T. Harris, BS, RD (Ret.), for her assistance with Table 1.

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