

# Pityriasis Rosea–Like Eruption Due to Bismuth

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*We report a case of bismuth-induced pityriasis rosea–like drug eruption. Although historical accounts of bismuth hypersensitivity exist, contemporary reports are lacking. Given the frequency of bismuth administration, a modern review of this phenomenon would seem prudent.*

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**B**ismuth has been used for the treatment of acute gastrointestinal complaints since the 18th century.<sup>1</sup> Bismuth subsalicylate, is currently the most common formulation of bismuth marketed in the United States and is indicated for the treatment of mild dyspepsia, diarrhea, and peptic ulcer disease. Although the literature contains some historical descriptions of cutaneous manifestations of bismuth hypersensitivity, contemporary documentation is limited.<sup>2–4</sup> We report a case of a papulosquamous eruption reminiscent of pityriasis rosea following multiple doses of bismuth subsalicylate.

## Case Report

A 67-year-old woman developed a pruritic eruption while admitted to the Pain Treatment Center for narcotic detoxification and depression. The rash started on her abdomen and spread to her chest, back, and upper extremities within 24 hours. The patient's medical history was significant for chronic peripheral neuropathy and hypothyroidism. Medications that she had been taking for longer than one year at a constant dose included oxycodone, zolpidem, mirtazapine, alprazolam, furosemide, liotrix, estrogen,

and psyllium fiber. During admission, she was started on bupropion and given as-needed doses of bismuth subsalicylate, clonidine, acetaminophen, and dicyclomine (Table).

Results of the patient's physical examination showed multiple oval patches, papules, and plaques primarily on the abdomen, chest, back, and buttock, with some involvement of the bilateral upper extremities (Figure 1). The inframammary folds were diffusely erythematous. The face and lower extremities were spared. The lesions ranged in size from 2 to 3 cm, with the largest found on the lower abdomen. This latter lesion appeared first and possessed a fine collarette of scale. Other lesions also displayed fine scale but lacked collarette formation. The lesions showed no particular distribution on the trunk. Further examination of the inguinal creases revealed intensely erythematous plaques with scant scale.

Results of a potassium hydroxide preparation of scale from the inguinal region revealed pseudohyphae; however, a similar examination of the abdominal lesions was completely negative. The patient was prescribed nystatin cream twice daily, which she applied to all her lesions, with improvement of only the inguinal eruption. Her medical team was advised to discontinue bismuth administration because of the possibility of a bismuth-associated cutaneous hypersensitivity reaction; however, the patient received an additional dose of bismuth subsalicylate on day 2 of the eruption. Her rash worsened significantly by day 3 and the dermatology department was again consulted on day 4. At this time, a 4-mm punch biopsy specimen was taken from one of the smaller abdominal lesions. Hematoxylin-eosin (H&E) staining of the specimen revealed a perivascular, interstitial inflammatory infiltrate composed of eosinophils and lymphocytes (Figure 2). A mild diffuse pattern of spongiosis with minimal focal parakeratosis and mild exocytosis was observed within the epidermis. There was a basket-weave appearance to the stratum corneum. Periodic acid–Schiff staining of the specimen was negative for fungal elements.

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The authors report no conflict of interest.

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### Medical Administration Record Describing Doses of New Medications

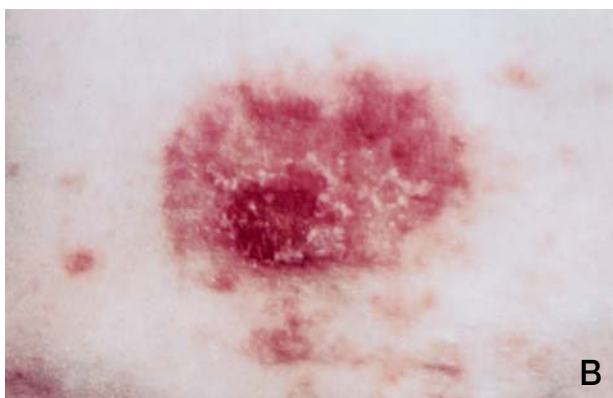
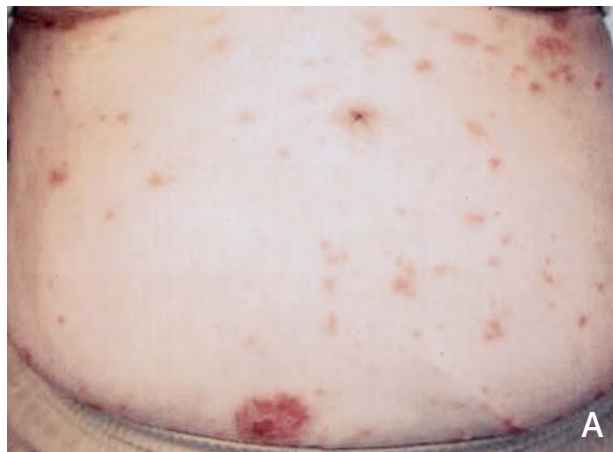
	Day																	
	1	2	3	4	5	6	7	8	9	10	11*	12*	13*	14†	15†	16†	17*	18*
Bupropion‡	2	2	2	2	2	2	2	2	2	2	2	2	1			2		
Bismuth subsalicylate‡					1	2				1		1	1					
Clonidine‡	2	1																
Acetaminophen‡	1			1							1	1						
Dicyclomine‡										2	3							

\*Days with mild rash.

†Days with severe rash.

‡Numbers represent number of doses.

The patient was started on fluocinonide ointment twice daily and hydroxyzine. The rash began to improve by day 6 and had completely resolved by week 3, with minimal postinflammatory hyperpigmentation.



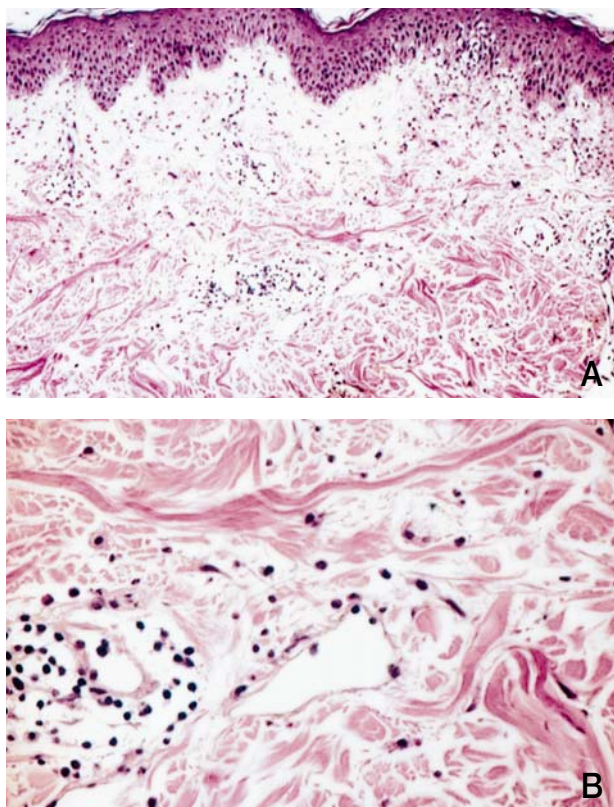
**Figure 1.** Multiple patches, papules, and plaques with fine scale located mainly on the trunk of the patient (A). The largest lesion, found on the lower abdomen, possesses a fine collarette of scale (B).

### Comment

Pityriasis rosea–like eruptions secondary to bismuth administration were first reported in the 1930s during the treatment of syphilis.<sup>2,3</sup> Pityriasis rosea–like eruptions were most frequent in this population, with urticarial, folliculopapular, and exfoliative eruptions also observed. Less commonly, chronic bismuth therapy was associated with a lichen planus–like eruption.

These early investigators based their diagnosis of a bismuth-induced rash on 3 criteria: (1) development of the eruption during bismuth therapy, (2) resolution of the rash with treatment withdrawal, and (3) recurrence of the lesions with reinitiation of bismuth therapy.<sup>2,4</sup> In this report, we describe a patient who developed an atypical pityriasis rosea–like eruption following multiple doses of bismuth subsalicylate; the eruption was exacerbated by additional doses of the agent and resolved rapidly upon its discontinuation. Although the patient was on other medications, the rash resolved despite continuation of these drugs, including the more recently initiated bupropion (Table). Other diagnoses were considered, including widespread cutaneous candidiasis; however, the negative results of the potassium hydroxide examination in areas outside the inguinal region and the absence of fungal elements on the biopsy results effectively ruled out these options. Inverse psoriasis and secondary syphilis may mimic pityriasis rosea clinically; however, the rapid resolution of lesions observed in this case would not be typical of either of these conditions.

Results of histopathologic examination of the lesions revealed characteristics of a drug hypersensitivity reaction due to the increased numbers of dermal eosinophils, not characteristically observed



**Figure 2.** Results of an intraslesional biopsy revealed both perivascular and interstitial inflammation with a mixed lymphocytic and eosinophilic infiltrate (A and B)(H&E original magnifications  $\times 10$  and  $\times 40$ , respectively).

in pityriasis rosea. This dermal infiltrate was associated with subtle changes in the epidermis reminiscent of pityriasis rosea, leading to a pathologic diagnosis of pityriasis rosea-like drug eruption, with bismuth as the most likely offending agent given the medical administration record.

Drug-induced pityriasis rosea has been observed secondary to a variety of agents including gold,<sup>5</sup> captopril,<sup>6</sup> barbiturates,<sup>6</sup> clonidine,<sup>6</sup> tripelenamine,<sup>6</sup> terbinafine,<sup>7</sup> isotretinoin,<sup>8</sup> metronidazole,<sup>9</sup> ketotifen,<sup>10</sup> D-penicillamine,<sup>11</sup> levamisole,<sup>11</sup> arsenicals,<sup>11</sup> herbicides,<sup>11</sup> methoxypropazine,<sup>11</sup> and omeprazole.<sup>12</sup> Various vaccinations including smallpox,<sup>11</sup> Bacillus Calmette-Guerin,<sup>13,14</sup> diphtheria toxoid,<sup>15</sup> and hepatitis B,<sup>16</sup> also have been implicated. In general, pityriasis rosea-like drug eruptions may occur days to weeks following initiation of therapy.<sup>17</sup> The classic fur tree distribution is often absent, and fewer larger lesions, persistent lesions, and even oral lesions may be observed.<sup>17</sup>

Although a few reports from the early 1930s and 1940s briefly describe the variety of skin eruptions that may occur in the setting of bismuth

therapy, this phenomenon has been largely ignored by the contemporary dermatologic literature. We suggest that, given the already high and increasing frequency of bismuth administration as an antiemetic and antimicrobial agent, heightened awareness of possible bismuth-associated reactions would seem prudent.

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