

Bromangiomas-ipratropium bromide–associated angiomas



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INTRODUCTION

Cherry angioma is one of the most common cutaneous vascular proliferations, and little is known about why they occur. Angiomas associated with bromides were first reported by Cohen et al¹ in 2 patients exposed to bromides in industrial settings. We report angiomas in 2 patients with chronic administration of ipratropium bromide for treatment of asthma. We were unable to find similar cases reported in the literature.

CASE 1

A 60-year-old white man presented for evaluation of blood blisters on his arms and legs, present for more than 2 years and becoming progressively worse. Some lesions resolved spontaneously. He noted working outside for many years. His medical history was remarkable for gout, hypertension, hyperlipidemia, diabetes, and long-standing asthma. His medications included budesonide, losartan, atorvastatin, tamsulosin HCL, allopurinol, albuterol, pantoprazole, and ipratropium bromide (1-3 puffs per day for more than 6 years). On clinical examination, there were numerous red-to-violaceous papules and plaques within a photodistribution (Figs 1 and 2). There was marked sparing over the watch area (Fig 2) and absence of truncal, back, and facial involvement. There were multiple violaceous papules and plaques involving bilateral pretibial regions (Fig 3). Multiple biopsies of the arms and legs found histologic features consistent with the diagnosis of cherry angiomas.

CASE 2

A 77-year-old white woman presented for routine treatment of actinic keratosis. The patient complained of numerous red bumps on her arms, stating that she “hates how they look.” She had a long history of asthma for which she took albuterol and ipratropium bromide (3 puffs per day for 5-6 years). Her medical history was remarkable for chronic obstructive pulmonary disease and congestive heart failure. Additional medications included pregabalin, atorvastatin, and carvedilol. On clinical examination, there were numerous red-to-violaceous papules and plaques within a photodistribution involving both arms and complete sparing of the watch area (Fig 4). There was no truncal, back, facial, or lower extremity involvement. A biopsy found them to be cherry angiomas.

DISCUSSION

Cherry angiomas have been associated with chemical exposures, such as sulfur mustard gas^{1,2} and 2-butoxyethanol, a glycol ether solvent.³ To our knowledge, cyclosporine⁴ and topical nitrogen mustard⁵ are the only medications reported to induce angiomas. Conditions and therapeutic interventions associated with angiomas include chronic graft-versus-host disease,⁶ multiple myeloma,⁷ multicentric Castleman disease,⁸ and argon laser therapy.¹ None of these conditions or treatments were found in our 2 patients, and the lack of central truncal or back involvement with

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Fig 1. Angiomas on arms in a photodistribution, sparing the trunk and watch area.



Fig 2. Left arm, sparing of proximal arm and wrist.

angiomas would argue against inherited or age-related causes observed in patients with eruptive angiomas.

Bromides were first used medicinally dating back to 1826 in the form of potassium bromide to treat splenomegaly. Numerous xenobiotics contain bromides in the form of basic salts, bromoureaides, and other medications.⁹ Throughout the years, bromides were used to treat epilepsy, as a hypnotic and as a nerve tonic marketed as Bromo-Seltzer, Bromo-Quinine, and Dr Miles' Nervine. Abuse of such agents resulted in altered mental status, psychiatric complaints, and coma resulting in the US Food and Drug Administration banning bromide salts from over-the-counter products in 1975 and all sleep

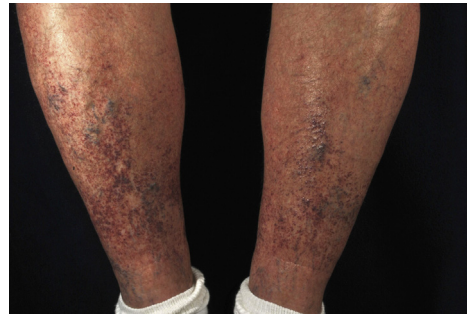


Fig 3. Angiomas, bilateral pretibial regions.



Fig 4. Left arm angiomas, sparing of proximal arm and wrist.

products in 1989.⁹ The symptoms of bromide toxicity became known as *bromism*.

Chronic bromide toxicity manifests predominantly as neurologic depression—lethargy, slurred speech, confusion, and ataxia, progressing to coma in severe cases. Cutaneous findings in chronic bromide use are referred to as *bromoderma* and manifest as an acneiform eruption, pustules, granulomatous plaques, ulcers, and/or bulla.⁹

The 2 patients with industrial exposure to bromides reported by Cohen et al¹ presented differently. Both patients had diffuse cherry angiomas involving the trunk and extremities. The lesions were described as red in color and between 1 and 4 mm in diameter.

We report here 2 cases of ipratropium bromide associated with angiomas in a photodistribution with unique features. The angiomas in both cases were larger and more violaceous than those observed in patients with common cherry angiomas. There was dramatic sparing of the truncal, back, and non-sun-exposed areas of both patients, particularly the watch area. Although both patients were also treated with atorvastatin, no association of angiomas has ever been reported with this ubiquitous drug, and atorvastatin is currently being evaluated for the treatment of cavernous angiomas through inhibition of RhoA kinase (ROCK).¹⁰ The distribution suggests

a possible photo-induced drug eruption that is more chronic in nature.

The cause of angiomas remains elusive and likely multifactorial.¹¹ Angiomas associated with ipratropium bromide therapy, although previously unreported, are likely more common than currently known. We hope that further observations will confirm this association. We introduce the term *bromangiomas* to refer to this unique presentation.

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