

# Primary Cutaneous Dermal Mucinosis on Herpes Zoster Scars

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## PRACTICE POINTS

- Focal mucinosis is a histopathologic finding that may be seen in different cutaneous disorders. It is an exceptional histopathologic finding that has rarely been described in herpes zoster scars.
- In most cases, focal mucinosis is just a histopathologic finding with no therapeutic consequences.

*The term isotopic response refers to the appearance of a new skin disease at the site of another unrelated and already healed skin disorder. Often, the first disease is herpes zoster (HZ). Several cutaneous reactions have been described in a dermatome recently affected by HZ. We present the case of a 33-year-old man who developed whitish papules with a zosteriform distribution on HZ scars. Histopathologic study with hematoxylin and eosin and Alcian blue (pH 2.5) staining demonstrated abundant deposits of mucin interstitially arranged between collagen bundles of the papillary dermis. Cutaneous dermal mucinosis as a postherpetic isotopic response is rare, but it should be added to the list of cutaneous reactions arising in HZ scars.*

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Mucin is an amorphous gelatinous substance that is found in a large variety of tissues. There are 2 types of cutaneous mucin: dermal and epithelial. Both types appear as basophilic shreds and granules with hematoxylin and eosin stain.<sup>1</sup> Epithelial mucin (sialomucin) is found mainly in the gastrointestinal tract and lungs. In the skin, it is present in the cytoplasm of the dark cells of the eccrine glands and in the apocrine secretory cells. Epithelial mucin contains both neutral and acid glycosaminoglycans, stains positive with Alcian blue (pH 2.5) and periodic acid–Schiff, is resistant to hyaluronidase, and does not stain metachromatically with toluidine blue. Dermal mucin is composed of acid glycosaminoglycans (eg, dermatan sulfate, chondroitin 6-sulfate, chondroitin 4-sulfate, hyaluronic acid) and normally is produced by dermal fibroblasts. Dermal mucin stains positive with Alcian blue (pH 2.5); is periodic acid–Schiff negative and sensitive to hyaluronidase; and shows metachromasia with toluidine blue, methylene blue, and thionine.

Cutaneous mucinosis comprises a heterogeneous group of skin disorders characterized by the deposition of mucin in the interstices of the dermis. These diseases may be classified as primary mucinosis with the mucin deposition as the main histologic feature resulting in clinically distinctive lesions and secondary mucinosis with the mucin deposition as an additional histologic finding within the context of an independent skin disease or lesion (eg, basal cell carcinoma) with deposits of mucin in the

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stroma. Primary cutaneous mucinosis may be subclassified into 2 groups: degenerative-inflammatory mucinosis and neoplastic-hamartomatous mucinosis. According to the histologic features, the degenerative-inflammatory mucinosis are better divided into dermal and follicular mucinosis.<sup>2</sup> We describe a case of primary cutaneous dermal mucinosis on herpes zoster (HZ) scars as an isotopic response.

### Case Report

A 33-year-old man presented to the dermatology department with slightly pruritic lesions on the left side of the chest and back that had appeared progressively at the site of HZ scars that had healed without treatment 9 months prior. Dermatologic examination revealed sharply defined whitish papules (Figure 1) measuring 2 to 4 mm in diameter with a smooth surface and linear distribution over the area of the left T8 and T9 dermatomes. The patient reported no postherpetic neuralgia and was otherwise healthy. Laboratory tests including a complete blood cell count, biochemistry, urinalysis, and determination of free thyroid hormones were within reference range. Serologic tests for human immunodeficiency virus, hepatitis B and C viruses, and syphilis were negative. Antinuclear antibodies also were negative.

Histopathology demonstrated abundant bluish granular material between collagen bundles of the papillary dermis (Figure 2). No cytopathologic signs of active herpetic infection were seen. The Alcian blue stain at pH 2.5 was strongly positive for mucin, which confirmed the diagnosis of primary cutaneous dermal mucinosis.

Topical corticosteroids were applied for 2 months with no notable improvement. The lesions gradually improved without any other therapy during the subsequent 6 months.



**Figure 1.** Linear distribution of small whitish papules with a smooth surface on the left side of the chest.

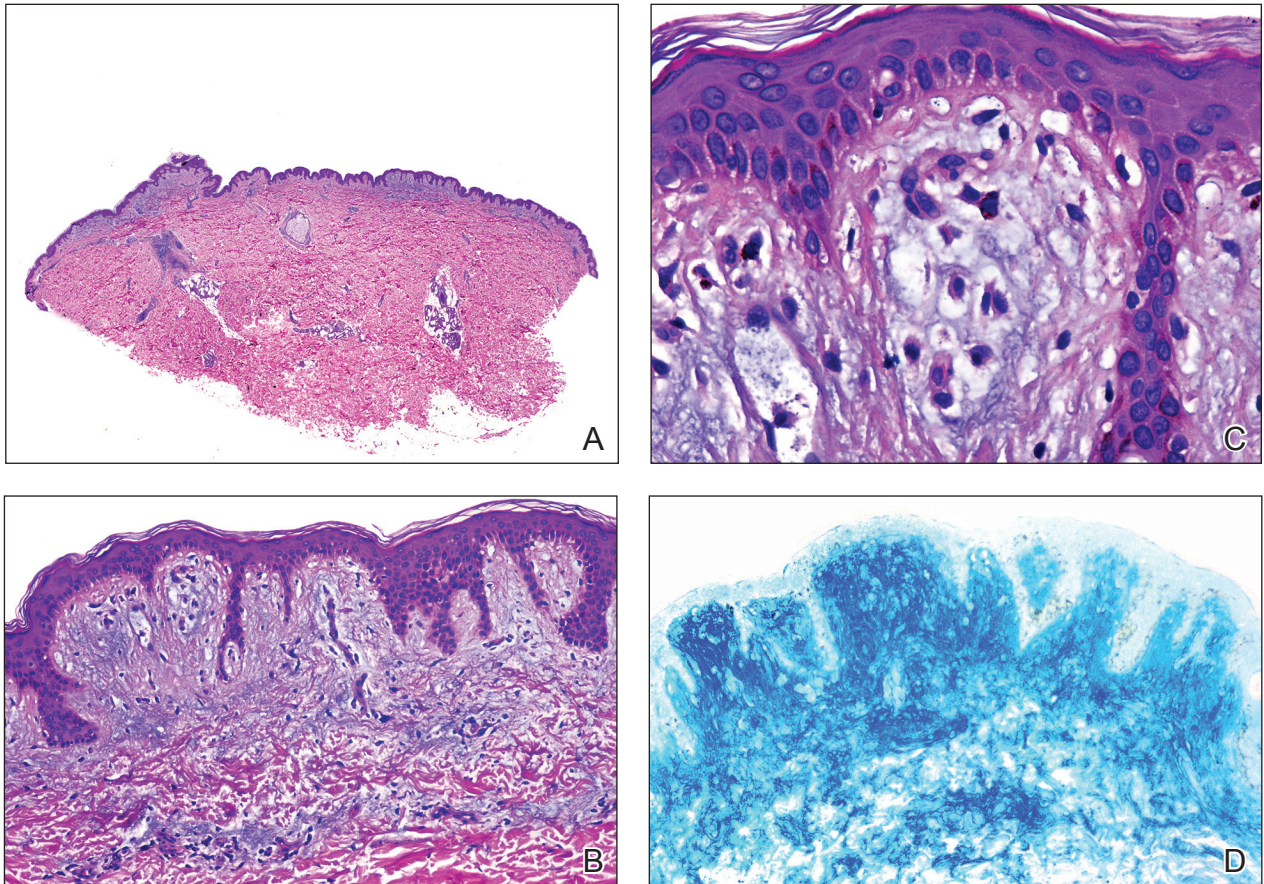
### Comment

The occurrence of a new skin disease at the exact site of a prior unrelated cutaneous disorder that had already resolved was first reported by Wyburn-Mason<sup>3</sup> in 1955. Forty years later, the term *isotopic response* was coined by Wolf et al<sup>4</sup> to describe this phenomenon. Diverse types of skin diseases such as herpes simplex virus,<sup>5</sup> varicella-zoster infections,<sup>4</sup> and thrombophlebitis<sup>4</sup> have been implicated in cases of isotopic response, but the most frequently associated primary disorder by far is cutaneous HZ.

Several benign and malignant disorders may occur at sites of resolved HZ lesions, including granulomatous dermatitis,<sup>6</sup> granuloma annulare,<sup>7</sup> fungal granuloma,<sup>8</sup> fungal folliculitis,<sup>9</sup> psoriasis,<sup>10</sup> morphea,<sup>11</sup> lichen sclerosus,<sup>12</sup> Kaposi sarcoma,<sup>13</sup> the lichenoid variant of chronic graft-versus-host disease,<sup>14</sup> cutaneous sarcoidosis,<sup>15</sup> granulomatous folliculitis,<sup>16</sup> comedones,<sup>17</sup> furuncles,<sup>18</sup> erythema annulare centrifugum,<sup>19</sup> eosinophilic dermatosis,<sup>20</sup> cutaneous pseudolymphoma,<sup>21</sup> granulomatous vasculitis,<sup>22</sup> Rosai-Dorfman disease,<sup>12</sup> xanthomatous changes,<sup>23</sup> tuberculoid granulomas,<sup>24</sup> acneiform eruption,<sup>25</sup> lichen planus,<sup>26</sup> acquired reactive perforating collagenosis,<sup>27</sup> lymphoma,<sup>28</sup> leukemia,<sup>29</sup> angiosarcoma,<sup>30</sup> basal cell carcinoma,<sup>31</sup> squamous cell carcinoma, and cutaneous metastasis from internal carcinoma.<sup>32</sup> The interval between the acute HZ episode and presentation of the second disease is quite variable, ranging from days to several months. Postzoster isotopic response has been described in individuals with varying degrees of immune response, affecting both immunocompetent<sup>12</sup> and immunocompromised patients.<sup>14</sup> There is no predilection for age, sex, or race. It also seems that antiviral treatment during the active episode does not prevent the development of secondary reactions.

Kim et al<sup>33</sup> reported a 59-year-old woman who developed flesh-colored or erythematous papules on HZ scars over the area of the left T1 and T2 dermatomes 1 week after the active viral process. Histopathologic study demonstrated deposition of mucin between collagen bundles in the dermis. The authors established the diagnosis of secondary cutaneous mucinosis as an isotopic response.<sup>33</sup> Nevertheless, we believe that based on the aforementioned classification of cutaneous mucinosis,<sup>2</sup> both this case and our case are better considered as primary cutaneous dermal mucinosis, as the mucin deposition in the dermis was the main histologic finding resulting in a distinctive cutaneous disorder. In the case reported by Kim et al,<sup>33</sup> a possible relationship between cutaneous mucinosis and postherpetic neuralgia was suggested based on the slow regression





**Figure 2.** Histopathology showed bluish granular material between collagen bundles of the papillary dermis (A) (H&E, original magnification  $\times 10$ ). Higher magnification showed abundant mucin in the papillary dermis (B), as well as mucin, fibroblasts, and some melanophages filling the dermal papilla (C) (H&E, original magnifications  $\times 100$  and  $\times 400$ ). Mucin was strongly positive on Alcian blue (pH 2.5) stain (D) (original magnification  $\times 100$ ).

of skin lesions in accordance with the improvement of the neuralgic pain; however, our patient did not have postherpetic neuralgia and the lesions persisted unchanged several months after the acute HZ episode. In the literature, there are reports of primary cutaneous dermal mucinosis associated with altered thyroid function<sup>34</sup>; autoimmune connective tissue diseases, mostly lupus erythematosus<sup>35</sup>; monoclonal gammopathy<sup>36</sup>; and human immunodeficiency virus infection,<sup>37</sup> but these possibilities were ruled out in our patient by pertinent laboratory studies.

The pathogenesis of the postherpetic isotopic response remains unknown, but several mechanisms have been proposed. Some authors have suggested that postzoster dermatoses may represent isomorphic response of Köbner phenomenon.<sup>13,15</sup> Although isomorphic and isotopic responses share some similarities, these terms describe 2 different phenomena: the first refers to the appearance of the same cutaneous

disorder at a different site favored by trauma, while the second manifests a new and unrelated disease at the same location.<sup>38</sup> Local anatomic changes such as altered microcirculation, collagen rearrangement, and an imperfect skin barrier may promote a prolonged local inflammatory response. Moreover, the destruction of nerve fibers by the varicella-zoster virus may indirectly influence the local immune system through the release of specific neuropeptides in the skin.<sup>39</sup> It has been speculated that some secondary reactions may be the result of type III and type IV hypersensitivity reactions<sup>40</sup> to viral antigens or to tissue antigens modified by the virus, inducing either immune hypersensitivity or local immune suppression.<sup>41</sup> Some authors have documented the presence of varicella-zoster DNA within early postzoster lesions<sup>6,7</sup> by using polymerase chain reaction in early lesions but not in late-stage and residual lesions.<sup>12,22</sup> Nikkels et al<sup>42</sup> studied early

granulomatous lesions by immunohistochemistry and in situ hybridization techniques and concluded that major viral envelope glycoproteins (glycoproteins I and II) rather than complete viral particles could be responsible for delayed-type hypersensitivity reactions. All these findings suggest that secondary reactions presenting on HZ scars are mainly the result of atypical immune reactions to local antigenic stimuli.

The pathogenesis of our case is unknown. From a theoretical point of view, it is possible that varicella-zoster virus may induce fibroblastic proliferation and mucin production on HZ scars; however, if HZ is a frequent process and the virus may induce mucin production, then focal dermal mucinosis in an HZ scar should be a common finding. In our patient, there was no associated disease favoring the development of the cutaneous mucinosis. These localized variants of primary cutaneous mucinosis usually do not require therapy, and a wait-and-see approach is recommended. Topical applications of corticosteroids, pimecrolimus, or tacrolimus, as well as oral isotretinoin, may have some benefit,<sup>43</sup> but spontaneous resolution may occur.<sup>44</sup> In our patient, topical corticosteroids were applied 2 months following initial presentation without any benefit and the cutaneous lesions gradually improved without any therapy during the subsequent 6 months. Focal dermal mucinosis should be added to the list of cutaneous reactions that may develop in HZ scars.

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