

Self-healing juvenile cutaneous mucinosis

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Self-healing juvenile cutaneous mucinosis is an extremely uncommon disorder characterized by the acute eruption of multiple papules and subcutaneous nodules. In this report, we describe one of the youngest patients reported to date with self-healing juvenile cutaneous mucinosis and further define several of the histologic and clinical characteristics unique to the disorder. Awareness of this disease is important because, despite an ominous presentation, all reported cases have resolved spontaneously. Therefore, aggressive therapy should be avoided. (J Am Acad Dermatol 2004;50:S97-100.)

CASE REPORT

A 3-year-old Caucasian boy was seen in the emergency department with a 1-week history of low-grade fevers, irritability, and rapidly enlarging skin lesions. Two weeks before evaluation he had been given the diagnosis of an upper respiratory tract infection, but he had no other significant medical history. He was admitted to the hospital with a diagnosis of erythema nodosum and treated with 40 mg of intravenous methylprednisolone. The following day he was discharged on 30 mg of oral prednisolone and was scheduled for skin biopsy by pediatric surgery. Nine days later the child returned to the emergency department with enlargement of his existing lesions and the development of multiple new nodules. By this time, his prednisolone had been tapered to 15 mg, but he had refused the medication for the last 2 days. In addition, the patient had refused to walk for the last 24 hours. Dermatology consultation was requested at that time.

On examination, the child appeared fatigued and irritable, but was in no acute distress. Vital signs were within normal limits except for mild hypertension (maximum pressure 158/86 mm Hg). Cutaneous examination was remarkable for several firm, painless, subcutaneous, flesh-colored nodules ranging from 0.5 to 2 cm on the pretibial legs, axillae, scalp, and left forehead. A large, deep-seated mass was appreciated just lateral to the midline lower aspect of his back. Smaller flesh-colored papules were present on the extensor knees and distributed symmetrically overlying the joints of the back of his hands (Fig 1).

The patient was admitted for further evaluation. Three days after hospitalization, the patient's irritability, low-grade fevers, and hypertension had resolved without treatment. An excisional biopsy to deep fascia was performed of the large nodule on the



Fig 1. Firm, flesh-colored papules localized over proximal and distal interphalangeal joints of hand.

left pretibial leg. Subsequent deep biopsies were also performed 2 months later from the left occiput, left gluteal fold, and right pretibial leg.

Laboratory workup including complete blood cell count, C-reactive protein, anti-streptolysin O titer, erythrocyte sedimentation rate, liver transaminases, creatinine, and urinalysis were within normal limits. Immunologic workup included antinuclear antibody, anti-RNP, anti-Sm, anti-Ro, anti-La, C3, C4, IgA, IgG, IgM, creatine kinase, rheumatoid factor, and aldolase. All were within normal limits except for an elevated serum aldolase level at 13.6 U/L (normal: 1.2-7.6 U/L). Repeated aldolase testing 1 month later was within normal limits. Skeletal survey and abdominal ultrasound were unremarkable. Magnetic resonance imaging of the chest, abdomen, and pelvis identified several areas of increased signal on T2-weighted images involving the skeletal muscle and subcutaneous tissue consistent with myositis and subcutaneous edema.

The patient was discharged from the hospital for further observation after the majority of his diagnostic workup had been completed. Over the next several weeks, however, he developed new deep-seated nodules at previously uninvolved areas including large periarticular nodules (Fig 2). In addition, he developed a new striking periorbital eruption consisting of bright-pink erythema and rock-hard firm nodules (Fig 3). Despite the deforming appearance of the eruption, the patient remained in good health otherwise and appeared unbothered by his cutaneous eruption. Spontaneous resolution of the smaller papules on the hands was first noticed approximately 3 months after presentation (Fig 4). Other areas soon followed, but the patient continued to develop new lesions in previously unaffected areas. Nearly every cutaneous surface of his body was

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Fig 2. Large, firm subcutaneous nodule affecting medial knee.



Fig 3. One month after presentation. Rapid development of periorbital swelling with marked erythema. Small ivory-white papules are clustered on central forehead.



Fig 4. Six months after presentation. Complete resolution of periarticular papules on hands. Hand lesions were among first cutaneous lesions to improve.

affected with deep nodules at some time during the course of his disease. Eight months after his initial presentation, all lesions had resolved spontaneously without scarring or other apparent sequelae (Fig 5).

A total of 4 excisional biopsies were performed and all specimens showed essentially the same findings. Hematoxylin and eosin-stained sections revealed that the changes were in the subcutaneous tissue. The dermis was present for evaluation in each of the biopsy specimens and was normal with the exception of a very mildly increased amount of mucin. Sections showed a lobular array of stellate, spindled and in some cases rhabdoid or straplike cells embedded in a mucinous stroma within the subcutis, which stained strongly with Alcian blue at



Fig 5. Six months after presentation, there is marked improvement in periorbital swelling. Smaller papules on forehead have resolved without scarring.



Fig 6. Alcian blue stain highlights abundant amount of mucin present in lesion. (Original magnification $\times 20$.)

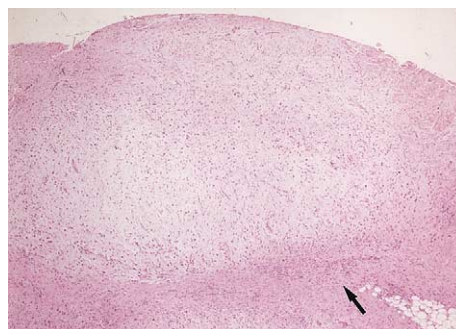


Fig 7. Low-power view of subcutaneous tissue from excisional biopsy specimen. Lesion is distinctly lobular with broad bands of fibrous tissue (*arrow*) demarcating highly mucinous areas. (Hematoxylin-eosin stain; original magnification $\times 4$.)

ph 2.5 (Fig 6). Dense fibrous tissue in large bands separated the mucinous islands and contained a sparse population of fibroblastic-like spindled cells (Fig 7). Mitotic figures were present but were sparse (less than 1/5 high-power fields), and no atypical mitotic figures were seen. There was a sparse associated lymphocytic infiltrate. The epidermis was without significant changes. Immunocytochemical stains showed that the cellular component of the lesion stained strongly for vimentin and weakly for desmin. Stains for cytokeratins, CD34, smooth-muscle actin, muscle-specific actin, and epithelial membrane antigen were negative. Direct immunofluorescence was negative.

DISCUSSION

Self-healing juvenile cutaneous mucinosis (SHJCM) was first reported in France by Colomb, Racouchot, and Vittori¹ in 1973. Eight subsequent cases have been described in the literature in the last 30 years, only 2 of which have been from the United States.²⁻⁹ Of the 9 reported patients, 6 have been male. Early reports described patients between 5 and 15 years of age.²⁻⁷ However, in the last year 2 younger patients have been reported with disease onset at 14 and 23 months.^{8,9}

Bonerandi et al⁷ proposed that SHJCM is a distinct mucinosis characterized by the following criteria: young age at onset; peculiar distribution of cutaneous lesions; presence of deep nodules on face and periarticular regions; absence of systemic findings (dysglobulinemia, bone marrow plasmacytosis, or thyroid dysfunction); and acute onset followed by spontaneous resolution. Cutaneous lesions are of several types. Small, non-tender, flesh-colored papules are commonly seen on the head, neck, trunk, and periarticular areas and may have a corrugated appearance.^{1-6,8} In our patient, these lesions were most pronounced over the knuckles of the hands, on the forehead, and extensor surfaces of the knees. Deep nodules typically develop on the face, scalp, and periarticular regions.^{2,5-9} Our patient initially presented with several large subcutaneous nodules localized to the scalp, but these lesions became generalized over the ensuing months. Finally, hard periorbital edema developed, similar to that described by Caputo, Grimalt, and Gelmetti.³ This was perhaps the most striking clinical finding in our patient.

Most skin biopsy specimens from patients with SHJCM have been taken from papular lesions rather than deep nodules. Histology from these lesions demonstrates separation of collagen bundles of the papillary and reticular dermis. A mild perivascular or diffuse mononuclear cell infiltrate is seen.^{2,3,6} In most cases, alcian blue staining at pH of 2.5 has identified the mucinous material to be predominantly hyaluronic acid. Alcian blue at pH 0.5 and periodic acid-Schiff staining are usually negative.^{2-4,6,9}

The proliferative histology characteristic of the nodules of our patient differs significantly from these previous reports. Only the report by Wadee, Roode, and Schulz⁵ describes similar cellular proliferation of nodular lesions that is distinct from the papular lesions. Similar to the deep biopsy specimens taken by Wadee, Roode, and Schulz⁵, the deep nodules in our patient appeared adherent to underlying periosteum. In both cases, prominent fibroblastic proliferation was seen and cells varied in appearance from spindle to plump with a few mitotic figures observed. However, biopsy specimens of papules in the case of Wadee, Roode, and Schulz⁵ demonstrated myxomatous tissue and mild inflammatory infiltrate only, and a small increase in fibroblasts. We believe the expansile architecture, marked variation in cell morphology, and mitoses of the deep nodules are an important histologic variant of this disorder. Three experts in soft-tissue pathology were consulted on this case and offered a differential diagnosis that included erythema nodosum, proliferative fasciitis, and nodular fasciitis. Although angiomyxoma displays prominent mucinous changes, the relative paucity of vascularity of this case made this diagnosis less likely.

Fibroblastic proliferation is seen in other generalized mucinoses, particularly scleromyxedema and pretibial myxedema, and may account for the thickening and hardening of the skin characteristic of these disorders.¹⁰ We believe our patient's firm nodules correlate well with the extent of fibroblast proliferation observed histologically.

Systemic symptoms associated with the acute phase of

SHJCM include fever, arthralgias, weakness, and muscle tenderness. In addition, transient hypertension, as seen in our case, was also observed in the case described by Bonerandi et al.⁷

Our patient's refusal to walk, elevated aldolase level (13.6 U/L; normal, 1.2-7.6 U/L), and muscle findings on magnetic resonance imaging are consistent with an acute myositis, suggesting a possible relationship between SHJCM and juvenile dermatomyositis. This is the second report of an elevated aldolase level in association with SHJCM. Pucevich et al⁶ described a 13-year-old boy with arthralgias, muscle tenderness, weakness, hoarseness, and decreased appetite who had an aldolase level of 13 U/L (normal: 1-6 U/L). Electromyogram in this case did not show evidence of myopathy. Caputo, Grimalt, and Gelmetti³ also describe a history of muscle weakness in his patient, but apparently no further diagnostic testing was performed.

Mucin deposition in collagen vascular disease is most often associated with systemic lupus erythematosus, but is also a common finding in skin lesions of patients with dermatomyositis.¹¹ Periorbital edema secondary to mucin deposition, a striking finding in several patients reported with SHJCM, may also be an important clinical clue to the diagnosis of juvenile dermatomyositis.¹² In addition, patients with dermatomyositis may develop atypical clinical lesions secondary to cutaneous mucin deposition.¹³

To date, markers of autoimmune disease including antinuclear antibody, rheumatoid factor, and complement levels in several of the reported cases of SHJCM have not revealed evidence of autoimmunity.^{3,4,6-8} Taken together, however, we believe patients suggested to have SHJCM should at minimum be evaluated with creatine kinase and aldolase testing for the presence of elevated muscle enzymes.

A common pathogenesis between SHJCM and other cutaneous mucinosis has been proposed, but evidence is lacking. The mucinoses are a group of poorly understood diseases and include scleredema of Buschke, papular mucinosis/lichen myxedematosus/scleromyxedema, and reticular erythematous mucinosis syndrome, and less common disorders including acral persistent papular mucinosis, cutaneous focal mucinosis, and cutaneous mucinosis of infancy. Unlike several of the acquired mucinoses, including scleromyxedema and some cases of scleredema of Buschke, there is no known association between SHJCM and paraproteinemia. However, there does appear to be some overlap in clinical appearance with other mucinoses, particularly the resemblance of corrugated papules of SHJCM to lichenoid lesions of papular mucinosis/lichen myxedematosus. In addition, the transient systemic findings in our patient of hypertension, elevated muscle enzymes, and arthralgias are all known associated systemic complications of scleromyxedema.¹⁴ Although lichen myxedematosus usually runs a protracted, unremitting course, exceptional cases of spontaneous resolution have been reported.¹⁵⁻¹⁷ Interestingly, the 29-year-old patient described by Kwon et al¹⁷ presented with lichenoid skin lesion on the back of his hands, extensor surfaces, and periorbital region, common sites of involvement in SHJCM. Stephens et al¹⁸ also reported spontaneous resolution of papular mucinosis in a patient with associated carpal tunnel syndrome.

A clear distinction between mucinoses on a histologic basis is also fraught with difficulty. Given the relative rarity of these diseases, establishing reliable diagnostic criteria can be a significant challenge. Podda et al¹⁹ recently described the evolution of histologic findings in a 9-year-old girl given the diagnosis of cutaneous mucinosis of infancy. Early lesions were composed primarily of mucin deposition characteristic of cutaneous mucin-

nosis of infancy, whereas lesions present for a year demonstrated less mucin and more dermal fibrosis and fibroblast proliferation. The authors suggest that cutaneous mucinosis of infancy may actually be the infantile presentation of lichen myxedematosus.¹⁹ In their 1991 classification of cutaneous mucinoses, Rongioletti and Rebora²⁰ suggest that SHJCM is a distinct entity for which diagnosis must be based on both clinical and pathologic criteria. In a more recent review, the authors categorized the entity as a subtype of localized mucinosis, grouping juvenile and adult variants under the subset "self-healing papular mucinosis."¹⁴ Four case reports are cited as examples of the adult variant. Unlike the distinct presentation of SHJCM, these patients had heterogeneous clinical presentations that ranged from a single isolated hand lesion, to a patient with a distinct cutaneous eruption with arthralgias similar to SHJCM, to a patient with lichen myxedematosus with polyclonal gammopathy.^{17,21-23} We believe the unique generalized clinical presentation and presence of both papular and characteristic deep-seated nodular lesions warrants that SHJCM be categorized as an entity distinct from other the other localized/papular mucinoses.

The cause of SHJCM is unknown, but is hypothesized to arise from a yet undetermined trigger that results in fibroblast proliferation and mucin production. SHJCM has been observed in a patient receiving chemotherapy for nephroblastoma raising the possibility of antigenic stimulation by the tumor or effect of chemotherapy.⁵ A preceding upper respiratory tract infection may have served as a possible trigger in our patient. The ominous eruptive presentation, associated symptoms, and aggressive histology of our patient appeared worrisome, but in all reported cases of SHJCM spontaneous resolution over several months to years is the rule. Sampling of multiple deep nodules has allowed us to better characterize the proliferative histologic findings of this disorder. Finally, it is important to be aware of the unique clinical pattern of the eruption, allowing an accurate and timely diagnosis to be rendered to avoid unnecessary testing or aggressive therapy for a self-limited disorder.

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