Online First
Calcinoisis Cutis Occurring in Association With Autoimmune Connective Tissue Disease

The Mayo Clinic Experience With 78 Patients, 1996-2009

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Objective: To describe characteristics and treatment of patients with calcinosis cutis in the clinical setting of autoimmune connective tissue disease (ACTD).

Design: Retrospective study.

Setting: Tertiary referral center.

Patients: Seventy-eight patients with calcinosis cutis and ACTD between 1996 and 2009.

Main Outcome Measures: Clinical features, treatments, and outcomes of patients with calcinosis cutis in the clinical setting of ACTD.

Results: Of 78 patients (mean age at onset of calcinosis cutis, 40.1 years), 64 (82%) were female. The following diseases were associated with calcinosis cutis: dermatomyositis (n=30) with classic (n=15), juvenile (n=14), and amyopathic (n=1) subtypes; systemic sclerosis with limited cutaneous scleroderma (n=24); lupus panniculitis (n=4); systemic lupus erythematosus (n=2); mixed connective tissue disease (n=4); overlap connective tissue disease (n=6); undifferentiated connective tissue disease (n=6); polymyositis (n=1); and rheumatoid arthritis (n=1). Therapy for calcinosis cutis consisted of medical treatment alone (n=19), surgical therapy alone (n=11), combined medical and surgical treatment (n=17), no treatment (n=30), and unknown (n=1). Diltiazem hydrochloride was the most commonly used medical therapy, with 9 of 17 patients having a partial response. Twenty-eight patients had surgical excision of 1 or more lesions of calcinosis cutis: 22 had a complete response, 5 had a partial response, and 1 had no response.

Conclusions: Dermatomyositis and systemic sclerosis were the most common ACTDs associated with calcinosis cutis. Although no treatment was uniformly effective, surgical excision of symptomatic lesions and medical treatment with diltiazem provided benefit for some patients.

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Four subtypes of calcinosis cutis exist: dystrophic, metastatic, iatrogenic, and idiopathic.1,2 Of these subtypes, dystrophic calcinosis cutis is the most common, and it is most frequently seen in association with underlying autoimmune connective tissue disease (ACTD).3 The condition causes substantial morbidity and is associated with pain when the process involves areas close to joints or when ulceration occurs. Because of this substantial morbidity, treatment is often sought; however, the condition is exceedingly hard to treat.3,4 Descriptions of patients with calcinosis cutis in the clinical setting of underlying ACTD and their treatments have thus far been limited to small case series and case reports.

The objectives of this study were to elucidate the ACTDs associated with calcinosis cutis in a series of 78 patients seen at Mayo Clinic, Rochester, Minnesota, and to describe the clinical features, treatments, and outcomes of these patients.

Methods

Data Collection

We used the institutional medical index and text retrieval system to identify patients who received a diagnosis of (1) calcinosis cutis, cutaneous calcification, or calcinosis and (2) connective tissue disease, dermatomyositis, lupus, scleroderma, or systemic sclerosis at Mayo Clinic between January 1, 1996, and December 31, 2009. Patients who denied research authorization were excluded from the study. This study was approved by the Mayo Clinic Institutional Review Board.
Table 1. Characteristics and Prevalence of ACTD Associated With Calcinosis Cutis

<table>
<thead>
<tr>
<th>Underlying ACTD</th>
<th>Patients, No. (%) (N=78)</th>
<th>Age at Onset of Calcinosis Cutis, Mean (Range), y</th>
<th>Time to Onset of Calcinosis Cutis After Diagnosis of ACTD, Mean (Range), mo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female Sex</td>
<td>Male Sex</td>
<td>Total</td>
</tr>
<tr>
<td>Dermatomyositis</td>
<td>23 (77)</td>
<td>7 (23)</td>
<td>30 (38)</td>
</tr>
<tr>
<td>Classic</td>
<td>11 (73)</td>
<td>4 (27)</td>
<td>15 (19)</td>
</tr>
<tr>
<td>Amyopathic</td>
<td>1 (100)</td>
<td>0</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Juvenile</td>
<td>11 (79)</td>
<td>3 (21)</td>
<td>14 (18)</td>
</tr>
<tr>
<td>Systemic sclerosis with limited</td>
<td>21 (88)</td>
<td>3 (13)</td>
<td>24 (31)</td>
</tr>
<tr>
<td>cutaneous scleroderma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overlap CTD</td>
<td>5 (83)</td>
<td>1 (17)</td>
<td>6 (8)</td>
</tr>
<tr>
<td>Undifferentiated CTD</td>
<td>5 (83)</td>
<td>1 (17)</td>
<td>6 (8)</td>
</tr>
<tr>
<td>Lupus panniculitis</td>
<td>4 (100)</td>
<td>0</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Mixed CTD</td>
<td>2 (50)</td>
<td>2 (50)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>SLE</td>
<td>2 (100)</td>
<td>0</td>
<td>2 (3)</td>
</tr>
<tr>
<td>RA</td>
<td>1 (100)</td>
<td>0</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Polymyositis</td>
<td>1 (100)</td>
<td>0</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

Abbreviations: ACTD, autoimmune connective tissue disease; CTD, connective tissue disease; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

aCalcinosis cutis preceded the diagnosis of systemic sclerosis in 4 of the 24 patients. When these 4 patients are excluded from the analysis, the mean time to onset of calcinosis cutis in the other 20 patients becomes 109 months (range, 3-372 months).

bThe 6 patients in this cohort had overlap CTD of the following types: SLE and RA, SLE and systemic sclerosis, SLE and dermatomyositis, systemic sclerosis and dermatomyositis (n = 2), and systemic sclerosis, SLE, and RA.

cThe 6 patients in this cohort had features of the following ACTDs: dermatomyositis and systemic sclerosis (n = 2), SLE and systemic sclerosis, SLE, dermatomyositis and RA, and SLE and RA.

dIn 1 of the 6 patients, calcinosis cutis preceded the diagnosis of undifferentiated CTD.

The initial search identified 923 patients, and we examined the medical records of these patients to identify 78 who met the study inclusion criteria of calcinosis cutis occurring in association with ACTD. Patients who did not meet the criteria for ACTD were excluded. Patients with incidentally identified forms of calcinosis that were unrelated to ACTD (eg, cutaneous neoplasms with foci of calcification present on histopathologic examination and benign breast calcification identified on mammography) also were excluded. For this study, overlap connective tissue disease (CTD) was defined as 2 or more separate ACTDs where each disease complied with the classification criteria for that disorder. Similarly, we defined undifferentiated CTD as ACTD that had clinical or serologic features, or both, of CTD but had not yet developed into defined disease and did not meet the classification criteria for a particular disorder.

We abstracted the following information from the medical records of the 78 patients: patient characteristics (eg, sex and age), disease duration, clinical characteristics of calcinosis cutis (eg, pain, ulceration, and extent and location of the calcinosis), underlying ACTD, duration of ACTD until the onset of calcinosis cutis, histopathologic and imaging findings of calcinosis cutis, treatments used for the associated ACTD, treatments used for calcinosis cutis, response to treatments, and follow-up data since diagnosis.

RESPONSE TO THERAPY

Patient response to therapy was graded according to the response levels of complete, partial, none, or unknown. Total resolution of an individual lesion and lack of recurrence in that area indicated complete response. Regression or recurrence of a lesion that had previously regressed or completely healed indicated partial response. The persistence of old lesions with or without the occurrence of new lesions indicated no response.

STATISTICAL ANALYSIS

Overall survival rates were estimated using the Kaplan-Meier method and were compared with the expected survival of age- and sex-matched Minnesota residents through a log-rank test. Comparisons among the number of calcinosis locations, of therapies for calcinosis, and of therapies for CTD were evaluated using the Kruskal-Wallis test and Spearman rank correlation coefficients. All tests were 2 sided, and P < .05 was considered statistically significant.

PATIENT DEMOGRAPHIC CHARACTERISTICS

Table 1 summarizes the age at onset and the sex of the 78 study patients by underlying ACTD. The mean patient age at the onset of calcinosis cutis was 40.1 years (range, 4-75 years). Sixty-four patients (82%) were female and 14 (18%) were male. Table 1 also provides the mean time to development of calcinosis cutis by underlying ACTD. The duration of ACTD until the onset of calcinosis cutis varied among the underlying diseases.

CALCINOSIS CUTIS LOCATIONS

Locations of calcinosis cutis were classified as the head, extremity (including the buttocks but excluding the hands and feet), trunk, and hands or feet (Figure 1). The location of calcinosis cutis differed on the basis of the underlying ACTD in which the calcinosis occurred (Table 2). Forty-three patients (53%) had ulcer formation in the context of calcinosis cutis, and 54 patients (69%) had pain associated with calcinosis cutis. For 20 patients, the diagnosis was confirmed by skin biopsy; for 38 patients (49%), calcinosis cutis was confirmed using 1 or more imaging studies (radiography, computed tomography, magnetic resonance imaging, or ultrasonography).
TREATMENT OF CALCINOSIS CUTIS

Table 3 summarizes the treatment categories of the patients in the study and the best response to treatment that each patient achieved.

Specific Treatments

Calcium channel blockers were the most frequently used medical treatment; of 18 patients who received a calcium channel blocker, 17 received diltiazem (≤480 mg/d). Eight patients received colchicine (≤1.2 g/d), 6 each received intravenous immunoglobulin or minocycline hydrochloride (≤200 mg/d), 5 received bisphosphonates, and 4 were treated with warfarin sodium. Only 1 patient treated with medical therapy alone had a complete response: the patient received methotrexate (20 mg by mouth once weekly) combined with colchicine. Other treatments were given to 3 or fewer patients each and are reported in Table 4.

Treatment Based on Calcinosis Cutis Severity

For a surrogate to judge the severity of calcinosis cutis, we enumerated the number of locations involved per patient, reasoning that more severely affected patients would have more calcinosis over more areas of their body. Patients were scored as having 1, 2, or 3 or more areas of the body affected (hands or feet, trunk, extremities, and head). We compared the number of body locations affected by calcinosis cutis with the number of calcinosis cutis treatments that each patient received by using a Kruskal-Wallis test (P = .07) (Figure 2).
Treatment Based on the Severity of the Underlying ACTD

For a surrogate measure of the severity of ACTD, we enumerated the number of treatments administered to each patient for their underlying ACTD, reasoning that the more treatments administered, the more severe the disease. We compared this treatment number with the number of treatments administered for calcinosis cutis and with the number of locations affected by calcinosis cutis (ie, 1, 2, or ≥3) (Figure 3). No significant relationship was present between the severity of the ACTD and the number of treatments administered for calcinosis cutis based on a Spearman rank correlation coefficient of 0.19 (P = .10). In addition, Figure 3 shows that no significant correlation existed between the severity of ACTD and the number of locations affected by calcinosis cutis based on the P value from a Kruskal-Wallis test (P = .24).

Treatment With Warfarin

To investigate whether warfarin use may have affected the treatment response of the 19 patients who received medical therapy alone, we compared the best treatment result achieved in the 4 patients treated with warfarin for conditions other than calcinosis cutis while receiving treatment for calcinosis cutis with that in the 13 patients who did not receive warfarin during medical therapy for calcinosis cutis. There was no obvious difference in the response to treatment between these 2 groups: of those who received warfarin, 2 had a partial response, 1 had no response, and 1 had an unknown response, and of those who did not receive warfarin, 1 had a complete response, 3 had a partial response, 3 had no response, and 6 had an unknown response.

SURVIVAL

Three patients had no follow-up. For the other 75 patients, mean follow-up after diagnosis of calcinosis cutis was 104 months (median, 60 months; range, 1-696 months). Seven patients died, at a mean of 101 months after calcinosis cutis diagnosis (median, 120 months; range, 3-228 months). Cause of death was metastatic breast carcinoma and adenocarcinoma of unknown primary in 2 patients and unknown in the other 5. Among the 68 patients who were still alive at the last follow-up,
Rothe et al\textsuperscript{10} reviewed 23 previously described cases of calcinosis cutis vs 20\%).\textsuperscript{1} We observed that the onset of calcinosis cutis in juvenile- vs adult-onset dermatomyositis (44\%-70\% vs 20\%).

The present findings corroborate this observation. We discuss briefly the present findings and what has been reported in the medical literature previously. Reiter et al\textsuperscript{6,7} recently reviewed the diagnostic pathway and treatment options for calcinosis cutis.

**UNDERLYING ACTD**

**Systemic Sclerosis**

Calcinosis cutis has been reported to most frequently occur 10 to 12 years after the onset of systemic sclerosis.\textsuperscript{1,8} The present results suggest that the mean time to the onset of calcinosis cutis after diagnosis of systemic sclerosis is 7.5 years. Investigators\textsuperscript{1} have reported that the most frequently involved body site of calcinosis cutis in systemic sclerosis is the hands and feet, particularly the fingers; the present findings concur with these reports.

**Dermatomyositis**

Calcinosis cutis has been reported to be more common in juvenile- vs adult-onset dermatomyositis (44\%-70\% vs 20\%).\textsuperscript{1} We observed that the onset of calcinosis cutis (after the diagnosis of dermatomyositis) in juvenile dermatomyositis was much earlier than in classic dermatomyositis (2.9 years vs 7.8 years), which agrees with previous studies.\textsuperscript{4} We also found that in juvenile and classic dermatomyositis, the location of the calcinosis tended to involve the extremities, a finding that agrees with previous studies.\textsuperscript{9} Involvement of the head, although rare, was much more likely in juvenile dermatomyositis than in any other ACTD.\textsuperscript{7}

**Systemic Lupus Erythematosus and Lupus Panniculitis**

Rothe et al\textsuperscript{10} reviewed 23 previously described cases of calcinosis cutis associated with systemic lupus erythematosus (SLE) and remarked that the disease was clinically silent in many of these patients. Of the 78 patients in the present case series, we observed that only 2 had calcinosis cutis and an underlying diagnosis of SLE. The time to diagnosis of calcinosis cutis has been reported to occur after long-standing systemic disease.\textsuperscript{10} We confirmed this finding because the mean time to diagnosis of calcinosis cutis in the 2 patients was more than 20 years after the diagnosis of SLE. Lupus panniculitis occurs in 2\% to 3\% of patients with SLE.\textsuperscript{11} and calcinosis cutis has been reported to occur in association with it.\textsuperscript{1,11} The present case series also had 4 patients with lupus panniculitis. The mean time between the diagnosis of ACTD and the onset of calcinosis cutis was much shorter in lupus panniculitis (4.8 years) than in SLE (21.5 years).

**Overlap CTD**

Overlap CTD rarely has been reported in association with calcinosis cutis. Chan et al\textsuperscript{12} described 2 patients with overlap CTD (1 with dermatomyositis and SLE overlap and the other with systemic sclerosis and SLE overlap) who both had calcinosis cutis on their left buttock 5 and 3 years after presentation of their underlying ACTDs. We describe 6 patients with overlap CTD and calcinosis cutis. Given the small size of this patient population and the heterogeneous presentations of the ACTD, it is difficult to draw conclusions about the clinical behavior of calcinosis cutis in overlap CTD.

**Undifferentiated CTD**

Calcinosis cutis has been reported rarely as being associated with underlying undifferentiated CTD. Herein, we describe 6 such patients. Torralba et al\textsuperscript{13} described a patient who 4 years after diagnosis of undifferentiated CTD had calcinosis involving the upper and lower extremities and the submandibular areas.

**Mixed CTD**

We found only 4 patients with mixed CTD and calcinosis cutis. The location of the calcinosis cutis differed. There have been rare reports of dystrophic calcinosis cutis associated with underlying mixed CTD.\textsuperscript{14,15} Itoh et al\textsuperscript{14} described 1 patient with dystrophic calcinosis and mixed CTD. In this patient, the onset of calcinosis occurred only 3 months after the diagnosis of mixed CTD. The calcinosis diffusely involved the legs and buttocks. The patient died of pulmonary fibrosis, thought to be a sequel of the CTD.

**Polymyositis and Rheumatoid Arthritis**

We describe calcinosis cutis in 1 patient with polymyositis and 1 patient with rheumatoid arthritis. In both patients, calcinosis cutis involved the extremities alone. Rarely, polymyositis has been described in association with calcinosis cutis.\textsuperscript{16,17} More recently, a case was reported of dystrophic calcinosis cutis of the buttocks and elbow in a patient with rheumatoid arthritis.\textsuperscript{18}

**TREATMENTS**

We discuss the most frequently used and most efficacious treatments in this case series, and we discuss the findings and compare them with those in the literature.
Calcium Channel Blockers

The mechanism by which this class of medications treats calcinosis cutis is unclear. It has been suggested to occur through a decrease in the influx of calcium ions into cells and, thus, correction of an abnormal imbalance of intracellular calcium concentration that may lead to crystal formation. Calcium channel blockers were the most frequently used medical treatment for calcinosis cutis in the present study. Of the medical therapies, this class of medications was the most efficacious, with 10 of the 18 patients responding favorably to treatment and showing improvement in their cutaneous lesions. Only 5 patients did not respond to treatment or their cutaneous lesions worsened.

Colchicine

Colchicine has been reported to have positive effects in reducing calcinosis and to have no effect on calcinosis but rather on inflammation secondary to calcinosis. In the present case series, 3 of 8 patients treated with colchicine responded favorably, with 1 patient having a complete response (this was the only patient treated with medical therapy alone who had a complete response).

Minocycline

Robertson et al described a series of 9 patients with systemic sclerosis and calcinosis cutis who were treated with low-dose minocycline. Of the 9 patients, 8 were reported to achieve improvement in their calcinosis, as measured through clinical examination and radiologic studies. The mechanism by which minocycline treats calcinosis cutis is unknown; however, investigators have postulated that it is a combination of anti-inflammatory effects, inhibition of collagenolytic enzymes (particularly, matrix metalloproteinase), and chelation of calcium. It is unclear why patients in the present case series did not respond as favorably to this treatment as previously reported. Of note, we did not monitor response using imaging studies; rather, the responses that we could abstract were those described clinically in the patient’s medical record. This detail may explain the discrepancy between the present retrospective review and the prospective trial of Robertson et al.

Intravenous Immunoglobulin

Intravenous immunoglobulin has been tried as a therapy for dystrophic calcinosis cutis, with positive and negative results. When intravenous immunoglobulin has worked, investigators have postulated that its effectiveness occurs through decreased inflammation, possibly through inhibition of macrophage function. In the present series, 6 patients received treatment with intravenous immunoglobulin; however, the results of the treatment in all 6 patients were unclear because of either the lack of follow-up data or incomplete information in the medical records.

Bisphosphonates

Bisphosphonates inhibit calcium turnover and, thus, have been tried as therapies for calcinosis cutis. Their use has been investigated for a long time, with positive and negative results. One case of calcinosis cutis in the clinical setting of juvenile dermatomyositis showed improvement with alendronate therapy despite preceding failure with probenecid and diltiazem. In the present case series, 5 patients received treatment with this class of medications. Only 1 patient had a partial response, and 3 had no response (1 response was unknown).

Warfarin

Lesions of calcinosis cutis have been found to contain elevated levels of γ-carboxyglutamic acid. Carboxylated glutamine can bind calcium and, thus, was postulated to be part of a mechanism promoting cutaneous calcification. Because the generation of γ-carboxyglutamic acid is vitamin K dependent, warfarin was suggested as a possible treatment option for calcinosis cutis through its inhibition of γ-carboxyglutamic acid generation. Since the study by Berger et al, there have been conflicting reports about the efficacy of warfarin therapy for calcinosis cutis. These conflicting data have led to the hypothesis that the response of calcinosis cutis to warfarin treatment depends on the size of the lesions and the time lapse since lesion formation, with larger and older lesions being resistant to the treatment.

In the present case series, 4 patients were treated with warfarin directly for their calcinosis cutis. Among them, only 1 patient partially responded to treatment. Of the patients receiving medical therapy alone, an additional 4 had received warfarin. The best response to treatment achieved for calcinosis cutis in this patient set did not differ from that of patients who never received warfarin for any reason.

Surgical Excision

Minami et al described widespread calcinosis cutis in 2 patients with SLE. Surgical excision was used to remove the calcification of the forearm in these patients because of the pain elicited in that region. In both patients, calcification did not return to the excised areas. In 2 separate patients, Saddic et al and Wu and Metz reported excellent results from incision and drainage of painful calcific lesions on the fingers of patients with systemic sclerosis, found that 13 of these reports were for treatment of calcinosis cutis. Most of the studies reviewed were reported to have resulted in “relief of pain” and “improved function.” Risks were noted of slower wound healing and a possible reduction in range of motion.

In the present study, 11 patients received surgical excision alone, and all 11 responded, with 8 having a complete response. In cases with either discrete calcification or widespread calcification with discrete symptomatic lesions, surgical excision of these areas may provide benefit for patients.
et al recently reviewed additional treatment options for ACTD is unclear, consider ruling out metastatic, idiopathic, and iatrogenic subtypes of calcinosis cutis; selected circumstances may require analysis of serum calcium, phosphorus, creatinine, parathyroid hormone, vitamin D, angiotensin-converting enzyme, and serum protein electrophoresis.

- Imaging studies may be helpful in selected cases to evaluate for soft-tissue calcification (eg, radiography, computed tomography, magnetic resonance imaging, and ultrasonography)
- For patients with ulcerated lesions, consider a swab culture for bacteria to rule out secondary infection

### Table 5. Recommendations for the Management of Calcinosis Cutis Associated With ACTD Based on the Findings From the Present Study

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| • For cases in which the diagnosis of dystrophic calcification due to ACTD is unclear, consider ruling out metastatic, idiopathic, and iatrogenic subtypes of calcinosis cutis; selected circumstances may require analysis of serum calcium, phosphorus, creatinine, parathyroid hormone, vitamin D, angiotensin-converting enzyme, and serum protein electrophoresis. | • There is no universally effective treatment for calcinosis cutis or an accepted therapeutic algorithm  
• Treatment should be centered on reducing the pain, disability, and morbidity associated with calcinosis cutis rather than on attempting to “cure” the calcinosis  
• Therapies may be used singly or in combination  
• It has been suggested that aggressive treatment of the underlying ACTD (eg, with immunosuppressive agents) may help decrease the development of calcinosis cutis. |
| • If the diagnosis is unclear, skin biopsy can help confirm the presence of calcium and rule out disorders of ossification. | • Surgical therapy: surgical excision of large, discrete, and symptomatic lesions can be beneficial  
• Medical therapy: treatment duration varies; typically, it is months to years  
• Calcium channel blockers (eg, diltiazem [120-480 mg/d]): our recommended first-line approach (often in conjunction with surgical excision of discrete, symptomatic lesions)  
• Colchicine (0.6-1.8 mg/d) |
| • Imaging studies may be helpful in selected cases to evaluate for soft-tissue calcification (eg, radiography, computed tomography, magnetic resonance imaging, and ultrasonography) | 4. Wound care: treatment of overlying infection with antiseptic wet dressings (eg, acetic acid) and possibly with oral antibiotics (guided by antimicrobial susceptibilities of swab culture)  
5. Physical therapy: to prevent joint contractures when calcinosis cutis involves joints and affects range of motion or mobility |

#### Abbreviation: ACTD, autoimmune connective tissue disease.

### Treatment of Calcinosis Cutis Based on Underlying ACTD

We could not determine whether a specific calcinosis cutis treatment benefitted patients on the basis of their underlying ACTD. There did not seem to be a predilection for a treatment type based on the underlying ACTD.

**CALCINOSIS CUTIS SEVERITY NOT PREDICTED BY ACTD SEVERITY**

Some investigators have suggested that the severity of calcinosis cutis in the clinical setting of underlying ACTD is related to the severity of the underlying ACTD and the duration of disease activity. We examined this hypothesis using a surrogate marker for disease severity—the number of treatments used. We asked whether a greater number of treatments used for the underlying ACTD correlated with worse calcinosis cutis. Using this evaluation method, we did not detect a significant correlation.

**RECOMMENDATIONS**

On the basis of the results of the present study, we propose an approach to managing calcinosis cutis in the clinical setting of ACTD, as summarized in Table 5. Reiter et al recently reviewed additional treatment options for calcinosis cutis that were either not beneficial or not used in the present cohort of 78 patients; these additional treatment options include warfarin (1 mg/d), bisphosphonates (eg, alendronate [10 mg/d]), minocycline (50-100 mg/d), ceftriaxone (2 g/d for 20 days), aluminum hydroxide (1.8-2.4 g/d), probenecid (1.5 g/d), intravenous immunoglobulin (2 g/kg/mo), intralesional corticosteroids, extracorporeal shock wave lithotripsy, and carbon dioxide laser.

**CONCLUSIONS**

We report a case series of 78 patients with calcinosis cutis occurring in association with underlying ACTD. We acknowledge the study’s limitations: its retrospective design, lack of certain clinical data for some patients, inability to determine in all patients whether the ACTD was active at the time of calcinosis onset, and incomplete follow-up for some patients. The study design did not allow us to determine whether the sex distribution of calcinosis cutis observed was different from the sex distribution of the underlying ACTDs. Moreover, this study was not population-based and, therefore, could not determine the incidence and prevalence of calcinosis cutis in each particular ACTD.

Nonetheless, clinical features of calcinosis cutis in this study differed on the basis of underlying disease. Thus, this study may help guide physicians in the education of their patients’ expectations for the development of lesions over time as the respective ACTD progresses. We recommend that surgical excision be considered for patients with discrete lesions or particularly symptomatic lesions. In patients for whom surgical excision was contraindicated and medical therapy was desired, the best results were achieved with diltiazem therapy, although reproducibility from patient to patient was variable in this study. Prospective controlled trials are needed to further determine whether specific treatments for calcinosis cutis are more effective for patients with certain ACTDs,
thus allowing therapeutic measures to be tailored rationally to each patient depending on his or her underlying ACTD.

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Author Contributions: All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Balin, Wetter, and Davis.

Acquisition of data: Balin, Wetter, and Andersen. Analysis and interpretation of data: Balin, Wetter, and Davis. Drafting of the manuscript: Balin and Wetter. Critical revision of the manuscript for important intellectual content: Balin, Wetter, Andersen, and Davis. Administrative, technical, and material support: Balin. Study supervision: Wetter and Davis.

Financial Disclosure: None reported.

Additional Contributions: Christine M. Lohse, MS, assisted with the statistical analysis of the data.

REFERENCES


