Expanding the clinicopathological spectrum of late cutaneous Lyme borreliosis (acrodermatitis chronica atrophicans [ACA]): A prospective study of 20 culture- and/or polymerase chain reaction (PCR)-documented cases

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Background: The diagnosis of acrodermatitis chronica atrophicans (ACA), the late cutaneous manifestation of Lyme borreliosis, can be challenging. Histologic changes in ACA have been described in a few studies from endemic countries, relying on cases documented by serology only.

Objectives: We sought to reassess the clinicopathological spectrum of ACA in a series of thoroughly documented cases.

Methods: Patients prospectively included in a national prospective study were selected on the basis of positive culture and/or polymerase chain reaction of a skin biopsy sample. The diagnosis of ACA was confirmed by reviewing the clinical and serologic data. Histopathological samples were carefully reviewed.

Results: Twenty patients were included. Unusual clinical features (ie, numerous small violaceous patches and equidistant small spinous papules with background faint erythema) were observed in 2 patients. Histopathological examination revealed a classic plasma cell–rich perivascular and interstitial pattern with telangiectases in 16 of 25 samples, whereas strikingly prominent granuloma annulare–like or lichenoid features were observed in 4 and 2 of 25 cases, respectively, and discrete nonspecific minor changes in 3 of 25 cases.

Limitations: The small number of patients was a limitation.

Conclusions: Genuine culture- and/or polymerase chain reaction–proven ACA can rarely present as numerous violaceous patches or cluster of spinous papules clinically, and as a granuloma annulare–like or lichenoid dermatosis histologically. (J Am Acad Dermatol 2016;74:685-92.)

Key words: acrodermatitis chronica atrophicans; *Borrelia burgdorferi*; borreliosis; granuloma annulare; lichenoid dermatitis; plasma cells.

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Supported by a Société Française de Dermatologie grant.
Conflicts of interest: None declared.
Accepted for publication October 22, 2015.

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Published online January 9, 2016.
0190-9622/$36.00

http://dx.doi.org/10.1016/j.jaad.2015.10.046

Acrodermatitis chronica atrophicans (ACA), the late stage of cutaneous Lyme borreliosis, is mainly caused by *Borrelia afzelii*.[1] ACA is suspected clinically and high titers of specific serum IgG anti-*Borrelia* antibodies strongly support this diagnosis.[2] A biopsy is sometimes performed either because clinicians are not familiar with the entity or to rule out differential diagnoses. Skin biopsy specimen is of particular importance in patients with atypical lesions, because a positive serologic result does not systematically reflect an active borrelial infection.[3]

The histopathological findings of ACA have been thoroughly studied in a few series of patients mainly from Northern Europe, concerning approximately 200 serologically documented cases in total.[4-9] A lymphocytic perivascular and interstitial infiltrate, with an admixture of plasma cells and histiocytes, almost invariably associated with the presence of telangiectases, is typical. Variable features are the presence of fibrotic and/or sclerotic changes. This latter finding is observed in 25% of patients, especially in biopsy specimens from fibrous nodules/bands or sclerodermatous lesions.[8] More rarely, focal lichenoid changes,[8] lichen sclerosus et atrophicus–like changes,[4,5] granuloma annulare (GA)-like changes,[6] or pseudolymphomatous changes[9] have been described. When such changes occur, histopathological diagnosis becomes challenging.

The objective of this study was to reassess the spectrum of clinicopathological changes in ACA in unequivocal cases confirmed by a positive polymerase chain reaction (PCR), culture from skin samples, or both.

CAPSULE SUMMARY

- The clinicopathological spectrum of acrodermatitis chronica atrophicans was established from serologically documented cases only.
- Culture- and/or polymerase chain reaction–proven acrodermatitis chronica atrophicans can rarely present as numerous small violaceous patches or spinous papules on erythematous background clinically, and as a granuloma annulare–like or lichenoid dermatosis histologically.
- Both pathologists and clinicians should be aware of such unusual clinicopathological presentations.

METHODS

Patients were prospectively included between 1998 and 2013 in a still-running national prospective study, the aim of which is establishing the diversity of *B burgdorferi* strains involved in the skin manifestations of borreliosis in France (https://clinicaltrials.gov/ct2/show/NCT00576082). The study was approved by our local Comité de Protection des Personnes. Patients were selected on the basis of a positive *Borrelia* PCR and/or culture on skin samples and a compatible clinical presentation, as defined by the European Union Concerted Action on Lyme Borreliosis Advisory Board.[2] The diagnosis of ACA was confirmed by reviewing the prospectively collected clinical data. Presence of specific anti-*Borrelia* serum IgG antibodies was mandatory. Every patient who also had a skin biopsy specimen for histopathologic examination was considered for inclusion. The histopathologic slides were then obtained from local laboratories and carefully re-examined.

In all the cases, detection of borrelial DNA in skin samples was made in the French national reference center for *Borrelia* (Strasbourg) by specific real-time PCR using a probe (LightCycler FastStart DNA Master Plus HybProbe, ROCHE Diagnostics, Meylan, France) targeting a highly conserved zone of the flagellin gene (*fla*) of the *B burgdorferi* sensu lato complex.[10] *B burgdorferi* species identification was made by further real-time DNA amplification using hybridizing probes targeting species-specific zones of the *fla* gene.[11] When quality of samples allowed it, culture was also performed as described.[12]

RESULTS

Clinical findings

Twenty patients with ACA (12 woman and 8 men, age 33-86 years) were included. High-quality photographs were available in 17 of 20 cases. Clinical characteristics of the 20 patients are summarized in Table I. At the time of diagnosis, the lesions had been noticed for a duration ranging from 2 months to 10 years (mean, 2 years). A tick bite was remembered by the patients in 4 cases, whereas the presence of a prior episode of erythema migrans was noted in 5 cases. The lesions were typical of ACA in all but 1 case. Fibrous nodule, ulnar bands, or both were present in 6 patients (30%), whereas a sclerotic lesion was present in only 1 case. Violaceous dactylitis of a toe was found in 2 cases (case 14, already published[13]; and case 20). One patient had unusual nonconfluent violaceous macules and patches on his thigh, conferring a pseudoreticulated pattern (case 7) (Fig 1, *A*). Another patient had multiple equidistant small keratotic (spinous)