Case report

Chronic progressive eosinophilic fasciitis: report of a 20-year failure to attain remission

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SUMMARY A retrospective diagnosis of eosinophilic fasciitis was made in a patient with disabling contractural disease of 20 years' duration. Chronic moderate-dose corticosteroid therapy had failed to halt either clinical or histological progression of the disease, but rapid worsening of skin thickening and contracture followed withdrawal of prednisone. Muscle wasting was severe in spite of normal serum creatine kinase levels; urinary excretion of creatinine was consistently elevated.

Because eosinophilic fasciitis is in its infancy as a diagnostic entity, the long-term course of this disease is uncertain. Considerable variability of the short-term outcome has been reported in about 75 patients since 1974. Remission, usually steroid-induced, appears to be the rule. However, some patients in clinical 'remission' had stable skin thickening and contractures. An occasional patient did not improve, and at least one worsened in spite of steroid therapy. In some patients relapses occurred as late as 7 years after the initial onset. However, all reported cases with as much as 15 years of follow-up had unequivocal remission of fasciitis.

This is a report of a patient with chronic progressive eosinophilic fasciitis over at least a 20-year period. Serial myofascial biopsies and creatine excretion showed active disease over the entire span in spite of steroid therapy. The disease was uniquely extensive and the patient's functional outcome was poor.

Case report

Twenty-four years ago the patient, a white male then 28 years old, was admitted to hospital for diffuse giant urticaria of 2 months' duration. He reported several previous episodes of urticaria associated with fever, and was being treated by atopic desensitisation without benefit. The eosinophil count was 350 per mm$^3$ (0.35 × 10$^9$/l). He responded promptly to chlorpheniramine.

Twenty years ago he was admitted to hospital because of aching pain in all extremities for 3 months and recurrent urticaria for 3 weeks. All the muscles were tender, but their strength, motion, and mass were normal. Several urticarial patches marked the thorax and face as well as the limbs. The scrotum and perianal region showed vitiligo.

The peripheral eosinophil count was 3200 per mm$^3$ (3.2 × 10$^9$/l); the sedimentation rate 14 mm in 1 h; the globulin fraction 3.2 g/dl (32 g/l); the albumin 3.3 g/dl (33 g/l); rheumatoid factor and LE cell determinations negative; and the SGOT 44 units (normal 5–40 units). Muscle biopsy showed profound mononuclear and eosinophilic infiltrate of the fascial and subcutaneous layers. Muscular septa contained modest focal accumulations of eosinophils, more prominent in areas adjacent to the fascia. Myonal necrosis was absent. The epidermis was normal. The pathological diagnosis was 'anaphylactoid myositis.' The patient developed fevers, progressive weight loss, and stiff, swollen hands. Transient crops of urticaria recurred. All these symptoms improved on prednisone 5 mg t.i.d. and recurred when the steroid was tapered. He was discharged on prednisone 5 mg t.i.d.

Eighteen years ago he was readmitted to hospital because of aching in both shoulders and difficulty swallowing in spite of 20–30 mg prednisone daily. Muscle wasting and generalised thickening of the skin was noted in the limbs. Motion of the shoulders,
elbows, and fingers was limited. Routine laboratory investigations were normal. The urine creatine excretion was 140 mg in 24 hours (normal <50 mg). Barium swallow was normal. Repeat muscle biopsy showed greater fascial thickening with somewhat less intense mononuclear infiltrate and occasional eosinophils. He was discharged on prednisone 5 mg t.i.d. as a case of progressive systemic sclerosis.

Between 15 and 13 years ago, during a series of hospital evaluations for flank pain and peptic ulcer disease, physicians noted thickening of nearly the entire cutis. Movement of the mouth, trunk, and fingers became limited. Also noted were muscle wasting and weight loss. Routine laboratory and extensive radiographic examinations showed no abnormality except for duodenal ulcer and sedimentation rates averaging 35 mm/h. Changes seen on a third muscle biopsy resembled those on the previous biopsies. Prednisone was continued at 10–15 mg daily; para-amino benzoic acid 12 g daily was begun for a 2-year course terminated by gastrointestinal intolerance and with questionable effect.

Nine years ago the patient developed causalgia of the right leg 6 months after right iliofemoral bypass graft. Symptoms improved following lumbar sympathectomy. Prednisone dosage was changed to 30 mg q.i.d. Attempts to withdraw this drug led to increased muscle pain, so that he was continued at this dosage for the next 6 years.

Between 8 and 3 years ago the patient was admitted to hospital many times, at several university-affiliated government hospitals, because of intractable neuropathic pain in the feet. Extensive laboratory and radiographic investigations aimed at clarifying both his neurological and musculoskeletal symptoms revealed no new abnormalities. Serum muscle enzymes were repeatedly normal. The 24-hour urinary excretion of creatine averaged 156 mg. Sedimentation rates ranged between 15 and 57 mm/h. Gammaglobulins showed a polyclonal rise of 3.8 to 4.0 g/dl (38–40 g/l). Several electromyograms were normal.

A fourth muscle biopsy again showed profound inflammatory fascial thickening with mild, focal, non-necrotising myositis. The clinical diagnosis was now dermatomyositis. Skin changes were regarded as insufficient for the diagnosis of scleroderma.

Three years ago prednisone was slowly withdrawn. Enteric-coated aspirin was given in therapeutic dosage for arthralgias. Contractures and muscle atrophy in all limbs and digits were evident, but the skin, while taut to palpation, visually appeared normal.

One year ago the patient was admitted to the hospital because of marked increase in skin thickening and contractures. The skin ranged from woody to rock-hard in consistency, with broad areas of lumpy surface; worsening of long-standing finger deformities was apparent, though hand films showed no bony changes. Muscle biopsy revealed severe fasciitis with substantially greater infiltrate than seen in previous biopsies. The dermis was normal. The Westergren ESR was 12 mm/h, the globulins 3.7 g/dl (37 g/l). The urinary excretion of creatine was 305 mg in 24 hours (urinary creatine:creatinine = 0.28). After 40 days on 60 mg prednisone it increased to 402 mg (urinary creatine:creatinine = 0.36).

Reinstitution of prednisone 40 mg. q.o.d. was attended by improved pain and objectively diminished skin tightening and contractures. Urinary creatine excretion gradually declined over a 6-month period to 110 mg/24 hours. Nevertheless the patient, now 51, remains bound to a powered wheelchair and dependent on others for much of his care.

Discussion

Eosinophilic fasciitis of this extent and chronicity is unprecedented in medical literature. Indeed, the sustained severity of this man’s illness impeded the recognition of the correct diagnosis for several years after eosinophilic fasciitis became widely known. The eosinophilic nature of the onset was buried in thousands of pages of medical charting, and the classic skin changes became prominent only when prednisone was stopped.

This patient, as an extreme example of the disease process, appears to confirm further the concept of eosinophilic fasciitis as a disease chiefly of the body surface, with incidental involvement of muscles and joints. Only 10% of reported patients have associated disease outside these tissues. In this patient pulmonary, cardiovascular, hepatic, renal, and intestinal problems either did not occur or were clearly attributable to intercurrent processes. Suppression of haematopoiesis, reported by others in eosinophilic fasciitis, did not occur. The causalgia of the feet was never clearly attributed, but may have been diseases-related by virtue of chronic peripheral nerve irritation in inflamed fascia. Another compressive neuropathy, the carpal tunnel syndrome, occurred in one-third of one series of patients. No other clinical finding, no laboratory test, and no biopsy specimen suggested vasculitis.

This case clearly makes the point that eosinophilic fasciitis can be extensive, chronic, and irreversibly disabling. It also focuses attention on the difficulty of evaluating disease activity. We recognise 4 general areas in the assessment of disease activity: acute phase (eosinophilia, elevated acute phase reactants, hypergammaglobulinaemia); skin thickening and contracture; muscle atrophy; and histological changes.
Acute phase changes usually subside in the first year or two of illness, whether or not the skin changes resolve completely. In this patient eosinophilia disappeared within 6 months of onset. The ESR varied widely thereafter but was not clearly related to disease activity. It was normal at the onset of the disease and during most of the last 3 years of the case record, times at which muscle biopsies showed marked fasciitis. Moderate polyclonal hypergammaglobulinaemia persisted throughout the illness, almost as a fixed serological abnormality. Episodes of depressed cryoglobulins and complement were absent.

Fascial thickening is the hallmark of the disease, but no objective measurement of it has been proposed. The weight of 7 mm skin thickness cores, as is used to evaluate scleroderma, was increased in 5 of 8 patients with eosinophilic fasciitis in spite of the relative sparing of the dermis in the infiltrative process. Serial skin determinations have not yet been reported. The thickening might also be indirectly followed by range of motion measurements, as is frequently done in scleroderma. Perhaps such measurements would have detected the late intensification of this patient's disease following steroid withdrawal, but they were not recorded.

Muscle atrophy has not been emphasised in other case reports. In this patient muscle atrophy was substantial within 5 years of the disease's onset. Over 20 years it became profound in spite of continuously normal muscle enzyme levels and evidence of modest focal muscle involvement on biopsy. Urinary creatine excretion was increased on the several occasions it was tested, but was not responsive to steroid therapy except over a course of many months. Unlike most myositis patients, this patient's strength has been proportional to observed muscle mass. He has been more limited by contracture than by weakness, suggesting the former might be responsible for the latter.

Repeat myofascial biopsies in 2 reported cases 18 months after initiation of steroid therapy revealed persistent fasciitis. In both patients reduced skin thickening persisted as an apparently non-progressive, 'stable' lesion. This observation suggests that biopsy is a sensitive method for detecting active fasciitis. In the patient presented here, biopsy results did appear to parallel disease activity. Whether biopsy information is unique and useful in therapeutic decisions await a study of careful serial observations in patients with chronic eosinophilic fasciitis.

References

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