LONG-TERM FOLLOW-UP OF JUVENILE-ONSET CUTANEOUS POLYARTERITIS NODOSA ASSOCIATED WITH STREPTOCOCCAL INFECTION

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SUMMARY

Polyarteritis nodosa (PAN) is a multisystem inflammatory disease associated with necrotizing vasculitis of small and medium arteries. Although predominantly an adult disease, PAN is well described in children. It can occur in a systemic form with manifestations in skin, joints, heart, nervous system, gastrointestinal tract, lungs and kidneys, and a limited form in which disease is confined to the skin, muscles, joints and peripheral nerves. In either case, streptococcal infection has been implicated by a positive throat swab or a significant increase in either antistreptolysin O (ASOT) or antihyaluronidase titres. The limited form is thought to run a benign course, but little has been written about its long-term outcome. We describe two patients who developed a cutaneous vasculitis following a probable streptococcal infection. Both have run a relapsing and remitting course with significant elevations of ASOT and in one, at least, prophylactic penicillin has had a strikingly beneficial effect. In both patients, the disease seems to have reed during childhood, only to recur, retaining its original form, in adult life. Their current ages are 22 and 19 yr, respectively.

KEY WORDS: Polyarteritis nodosa, Streptococcal infection, Cutaneous vasculitis.

CASE REPORT

Patient 1

A 7-yr-old girl was admitted urgently with pain in her left hip and right wrist. Two days earlier, she had developed a sore throat, fever and lethargy. There was no other relevant past medical history. On examination, she had synovitis in her right wrist and proximal interphalangeal joints, a painful, restricted left hip and a 1 cm erythematous nodule at the distal end of the right forearm. Investigations revealed Hb 11.9 g/dl, WBC 13.2 × 10^9/l (90% neutrophils, 7% lymphocytes, eosinophils 1%), platelets 800 × 10^9/l, ESR 106 mm/h, antistreptolysin O titre (ASOT) 600 rising to 800 Todd units (U), throat, blood and left hip synovial fluid cultures negative, X-rays normal, and RF and ANA negative. She remained unwell and developed panniculitis of both arms with an increasing neutrophilia despite i.v. antibiotics. Six weeks after presentation, she developed widespread multiple subcutaneous, erythematous, indurated nodules. A biopsy confirmed a deep dermal arteritis without evidence of giant cells or granulomata. Her condition improved following the introduction of a non-steroidal anti-inflammatory drug (NSAID) and prophylactic penicillin V. Her symptoms recurred on each of two occasions when penicillin withdrawal was attempted.

Fifteen months later, having stopped all her treatment for 6 months, she presented with tonsilitis, polyarthritis and a recurrent vasculitis. Her ESR had increased to 123 with an ASOT of 1200 U. Penicillin V, NSAID and prednisolone (1 mg/kg) were required to control her symptoms. The dose of prednisolone was successfully reduced and stopped over a period of 3 months. Unfortunately, she continued to experience recurrent symptoms at the time of presumed streptococcal infections (increasing ASOT, negative cultures) and although she was encouraged to remain on penicillin prophylaxis, we suspect her compliance was poor.

At the age of 16, she was admitted with a 3 week history of a sore throat, fever, polyarthritis, abdominal pain and a vasculitis rash. Blood and throat swab cultures were again negative, ASOT 3200 U and ESR 58. Her symptoms improved with an increase in her steroid dose.

Despite prophylactic penicillin and low-dose prednisolone (2.5–5 mg/day), she continues to have minor flares. She has never demonstrated any evidence of major organ involvement.

Patient 2

An 11-yr-old boy was seen in a general paediatric clinic with a 7 month history of polyarthritis and a skin rash. His symptoms had started after an episode of alleged scarlet fever. At that time, he was noted to have tender purple annular lumps over his abdomen. The rash had spread to involve his back with synovitis in his wrists. His ESR was 68 with an ASOT of > 1200 U. RF and ANA were negative. Penicillin V was started for a presumed hypersensitivity reaction following a streptococcal infection.

Three months later, he was seen with a recurrence of his rash. Biopsy confirmed a necrotizing vasculitis affecting the vessels of the deep dermis without granulomata or giant cells. At 16, his penicillin was stopped pending an application to join the navy.

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Unfortunately, he experienced recurrent sore throats which necessitated the reintroduction of penicillin.

He stopped his penicillin again at the age of 21. Six months later, he developed a polyarthritis following a sore throat, his rash did not recur. A post-antibiotic throat swab was negative, but his ASOT, initially 800 U, rose to 1600 U. His ESR was 43. He was treated with penicillin and on this occasion required a course of oral steroids. At present, he remains well on prophylactic penicillin. He has demonstrated no evidence of major organ involvement.

DISCUSSION

We have described two patients who developed arthritis and deep dermal arteritis shortly after a systemic illness characterized by a sore throat, fever and somnolence. An association with streptococcal infection was suggested by a significant rise in ASOT.

The association between vasculitis and streptococcal infection has been reported by several authors [1–4]. The possible relationship was first suggested by Fink [5] who described 6/7 children with polyarteritis nodosa (PAN) and a preceding sore throat or otitis media. Several other series [6–8] identified two subgroups of polyarteritis: a generalized disease with major organ involvement and a cutaneous disease with non-specific systemic manifestations including fever, myalgia and arthralgia, but no evidence of internal organ damage.

Our first patient presented classically [4] with high fever, arthritis, myalgia and painful erythematous vasculitis nodules. She had a neutrophilia with an elevated ESR and rising ASOT. The second patient presented with similar symptoms, although he was not diagnosed until 7 months after the start of his illness.

Both patients have now been followed up for more than 10 yr. The first has experienced a relapsing course with minor flares associated with presumed streptococcal upper respiratory tract infections (URTIs) and antibiotic withdrawal, and two major flares associated with streptococcal infection confirmed by a rising ASOT. The second patient has had flares on the two occasions when we know he stopped his penicillin, recurrent sore throats during the first and polyarthritis with a rising ASOT during the second. Both patients have required systemic steroid treatment to control their symptoms, neither has needed cytotoxic treatment.

There is limited experience of the long-term follow-up of patients with post-streptococcal cutaneous PAN. David et al. [1] described 12 children with a mean follow-up of 8 yr although five made a full recovery, seven patients had a relapsing course with recurrent vasculitis on steroid reduction. Two went on to develop major organ involvement. Kumar et al. [3] reported 10 patients with cutaneous PAN and a mean follow-up of 5.6 yr, although only two patients had evidence of a preceding streptococcal infection. Fink [4] has suggested that most cases of childhood PAN are associated with streptococcal infection. Magilvay et al. [9] suggest that cutaneous PAN may be the initial manifestation of an evolving systemic PAN. Of six patients who had no initial evidence of systemic involvement, three went on to develop documented heart or kidney disease. On the other hand, Moreland and Ball [10] found no evidence of visceral involvement in 15 patients after a mean of 15 yr follow-up. Chen [11] reported 18 patients with non-progressive cutaneous PAN over a 17 yr period. He did, however, describe two patients (both ANA and RF positive) who progressed to the systemic form after 18 and 19 yr, respectively. Neither of our patients had positive RF or ANA.

The association with streptococcal infection was suggested by a significant increase of ASOT. The major flares in both patients were accompanied by rising titres. The ASOT may, however, reflect a general anamnestic immunoglobulin response, although in neither patient did serial measurements of total immunoglobulin reflect disease progression as well as the ASOT. More specific tests of streptococcal infection, e.g. DNaseB, were not carried out in either of our patients. The negative throat swabs were not surprising as most patients will spontaneously clear their pharyngeal infection [11]. A positive throat swab can indeed be misleading as many normal children are asymptomatic streptococcal carriers. The clear response to penicillin prophylaxis and the resulting flares when treatment was stopped also support the role of streptococcal infection in our patients.

The role of penicillin prophylaxis has not been studied in relation to post-streptococcal vasculitis. David et al. [1] recommended long-term penicillin for their patients. Experience in rheumatic fever [12] and post-streptococcal arthritis [4] would also endorse this view.

We have presented the long-term follow up of two cases of post-streptococcal cutaneous PAN. Both cases illustrate the relapsing nature of the disease and the potential for recurrent streptococcal infections to precipitate serious disease exacerbations even after lengthy periods of remission. We recommend that penicillin prophylaxis be lifelong. We would also suggest that long-term follow-up is appropriate in view of the tendency to relapse that has been illustrated.

REFERENCES