Case Report

Treatment of cystic fibrosis associated cutaneous vasculitis with chloroquine

Ian D. Molyneux a,⁎, Tanya Moon a, A. Kevin Webb b, Alyn H. Morice c

a Respiratory Medicine, Castle Hill Hospital, Castle Road, Cottingham, HU16 5JQ, UK
b Manchester Adult Cystic Fibrosis Centre, University Hospital South Manchester, Southmoor Rd, Manchester, M23 9LT, UK
c Cardiovascular and Respiratory Studies, Hull York Medical School, University of Hull, Castle Hill Hospital, Castle Road, Cottingham, HU16 5JQ, UK

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Abstract

Vasculitis is a well recognised complication of Cystic Fibrosis. Corticosteroids are the mainstay of treatment but some cases can be resistant and may require additional disease modifying agents.

We describe a case of steroid resistant cutaneous vasculitis which was successfully treated with chloroquine in addition to corticosteroids and a subsequent relapse with chloroquine alone.

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1. Case history

The patient is a 28 year old male ΔF508 homozygote with well controlled lung disease prior to the vasculitic episodes (FEV1 3.2L; 75% predicted). He has insulin treated diabetes and a long standing history of seronegative inflammatory arthritis primarily affecting the small joints of the hands and feet. His joint disease was stable on sulphasalazine for more than 10 years. Antinuclear factor was negative.

He initially developed a purpuric rash on the lower limbs in association with an exacerbation of his lung disease which resolved over a period of 5 weeks. A course of intravenous antibiotics was given but no active treatment was necessary for the purpura.

He was subsequently admitted to hospital with a putative diagnosis of Distal Intestinal Obstruction Syndrome. Imaging was consistent with obstruction secondary to ileocolic intussusception and he underwent a right hemicolectomy after the failure of conservative treatment with gastrografin. A polypoid lesion found at the apex of the intussusception post-resection consisted of inflamed and oedematous ileal mucosa.

Six weeks later, he was readmitted with a recurrence of the purpura on both lower limbs (Fig. 1) and on the posterior aspects of both arms. On this occasion there was no deterioration in respiratory symptoms. Renal function was normal throughout.

Sulphasalazine was withdrawn as a drug reaction was suspected and treatment was commenced with oral prednisolone 60 mg daily. Skin biopsy was performed during incidental surgical insertion of a totally implantable venous access device which showed abundant neutrophils within the dermis with evidence of leucocytoclasis. No eosinophilic infiltrate was seen in the biopsy. Antineutrophil cytoplasmic antibody (ANCA) screen was reported as atypical with negative MPO and PR3 antibodies.

He was discharged from the hospital after 5 days. There was no noticeable improvement after 7 days of steroid therapy (Figs. 2 and 3). Chloroquine was suggested as a potential...
additional therapy and treatment was commenced at a dose of 250 mg b.d. for 1 week. Oral prednisolone was continued at the same dose. The rash improved rapidly after initiation of chloroquine and had resolved completely at 3 weeks after presentation. Fig. 4 is an image taken on day 3 of combined treatment.

The patient had a further relapse of cutaneous vasculitis after 4 months which was successfully treated with chloroquine alone using the same regimen. On this occasion, chloroquine was commenced 4 days after the appearance of the rash and complete resolution was achieved within 2 weeks of starting treatment. He was not taking sulphasalazine at the time of the second relapse and it has since been re-introduced in response to a deterioration in his joint disease with no adverse effects.

2. Discussion

Vasculitis is a well documented complication of CF [1]. Suggested mechanisms include systemic response to bacterial colonization and immune complex deposition secondary to chronic airway inflammation [2–4]. There is also an association between joint disease in CF and vasculitis [5,6]. Typical presentation is with a purpuric rash affecting the lower limbs with classical histological findings of a leucocytoclastic vasculitis [2,7].

ANCA positivity is common in CF and although MPO and PR3 specificity can be found, antibodies are often directed against bactericidal/permeability increasing protein (BPI), a neutrophil product which has antimicrobial action against Pseudomonas aeruginosa [8,9]. The presence of anti-BPI is associated with pseudomonal colonisation and increased severity of lung disease [10,11]. Although it was not specifically identified in the patient described, anti-BPI is a
common finding in ANCA positive but MPO/PR3 negative vasculitis and has a higher prevalence in CF patients with vasculitis than those without [12,13].

Cutaneous vasculitis can be associated with sulphasalazine therapy however the clinical features in this case do not support a drug-induced aetiology [14,15]. There was no eosinophilic infiltrate seen in the skin biopsy, the second relapse occurred several months after stopping treatment and the agent was later re-introduced without complication.

The colonic intussusception was not confirmed histologically to have a vasculitic origin as the changes seen were felt to be reactive rather than causal, although the temporal association of the events could suggest that the two were related. Ileocaecal intussusception is a recognised complication of CF and an association with henoch–schönlein purpura (HSP) has also previously been reported [16,17]. HSP was initially considered as an alternative diagnosis as it can also manifest with an IgA mediated leucocytoclastic vasculitis. Immunofluorescence was not performed but the age of the patient and the absence of renal involvement and arthralgia meant that he did not meet the diagnostic criteria [18,19].

CF associated vasculitis can resolve spontaneously however where there is a need for treatment, corticosteroids have been used and there has been a previous case reported of successful treatment using methotrexate [1,2,20]. Chloroquine is used as an antimalarial and as a disease modifying agent in rheumatoid arthritis and lupus erythematosus [21,22]. Its mechanism of action is not clearly understood but may involve reduced eicosanoid production via inhibition of phospholipase A2 or interference with proinflammatory cytokines [23]. It was chosen on the basis of clinical experience of its use and minimal side effect profile. We found no previous reports in the literature of cases where chloroquine has been successfully used to treat CF associated vasculitis. In this case, there was a dramatic improvement in the appearance of the rash when chloroquine was added to corticosteroids. Resolution occurred more quickly in the relapses treated with combination therapy and with chloroquine alone than in the initial self-limiting episode. The patient suffered no adverse effects from either treatment.

There is insufficient evidence to advocate the routine use of chloroquine monotherapy in CF associated vasculitis. Corticosteroids remain the first choice but chloroquine may be useful as an adjunct in steroid resistant cases.

References