

Benign cutaneous polyarteritis nodosa in children below 10 years of age—a clinical experience

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Abstract

Objective—To report 10 children younger than 10 years of age with benign cutaneous polyarteritis nodosa (BCPAN).

Methods—Ten children aged 1.25–10 years (mean 4.7 years; M:F = 7:3) were admitted with an unusual vasculitis. The clinical features, laboratory investigations, treatment and follow up data were analysed.

Results—Clinical features of these patients included: fever (10), peripheral gangrene (eight), livido reticularis (four), ulceration, nodules and vesiculobullous lesions alone or in combination (10), black necrotic patches over limbs and trunk (three), and arthralgia or swelling of large joints (seven). Cryoglobulinaemia was transient in three children, lasting for eight months in one of them. Histopathology of the skin lesions revealed vasculitis of small and occasionally medium sized blood vessels in nine of the 10 children. Possible association of BCPAN was noted with diphtheria-pertussis-tetanus immunisation (one), drugs (two), streptococcal infection (two), wasp sting (one), and falciparum malaria (one). The clinical course was interspersed with remissions and exacerbations. Response to corticosteroids alone occurred in seven patients, while three children needed cytotoxic drugs in addition. In a follow up of 5.6 years (mean) no evidence of systemic involvement was noted.

Conclusions—A rare form of vasculitis, BCPAN, is reported in children. The features that distinguished our patients from those reported earlier were onset in the first decade of life and higher incidence of peripheral gangrene.

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Vasculitis syndromes are the result of inflammation and necrosis of the blood vessel walls which may result from a primary involvement of the blood vessels or may occur as one of the features of other well defined diseases (systemic lupus erythematosus, rheumatoid arthritis).¹ The American College of Rheumatology (ACR) 1990 classification recognises seven distinct types of vasculitides.² However, all the manifestations may not be present in many instances and hence the ACR criteria may not help in categorisation of a particular individual patient.³ Furthermore, some of the less common vasculitides have been omitted from the ACR classification.

Most cases of necrotising vasculitis are the result of immunopathogenic mechanisms set in motion by hypersensitivity reactions to known or unknown antigens.^{1,4} Benign cutaneous polyarteritis nodosa (BCPAN) is a rare disease, involving mainly small vessels and some medium sized vessels of the skin, muscles, and joints. It runs a benign, chronic, relapsing course. There is no evidence of hypertension or organ dysfunction even on long follow up.^{5,6} More than 100 cases of the disease entity have been described, a majority of them in adults. Some authors doubt the very existence of this type of vasculitis.^{7,8}

We report our experience of 10 children aged less than 10 years, with BCPAN presenting with peripheral gangrene and autoamputation as a striking clinical feature.

Patients and methods

Ten children with vasculitis syndrome presented to the Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh, India, between August 1980 and December 1991. At presentation, the ages of these patients, seven of whom were male, were between 15 months and 10 years. Duration of illness at admission ranged from two days to four years. All were febrile. Three children had marked itching heralding the onset of fever. Clinical features were typical in almost all the cases. The diagnosis of BCPAN was based on the histopathology of skin biopsy, which was positive in nine of the 10 patients. We have prospectively followed up these children and analysed the outcome.

Results

The characteristic features of the disease were skin manifestations which included maculopapular rash, skin nodules (painful in only one child), vesiculobullous lesions, purpura, ulceration and livido reticularis. Livido reticularis may have been missed in some children because of the dark complexion of our subjects. Peripheral gangrene was present in eight children (figure). Two patients had black, necrotic patches of variable size on the extremities and the trunk. Arthralgia or swelling of the large joints were noted in seven children. Radiographs of the affected joints failed to reveal any abnormality of the bones.

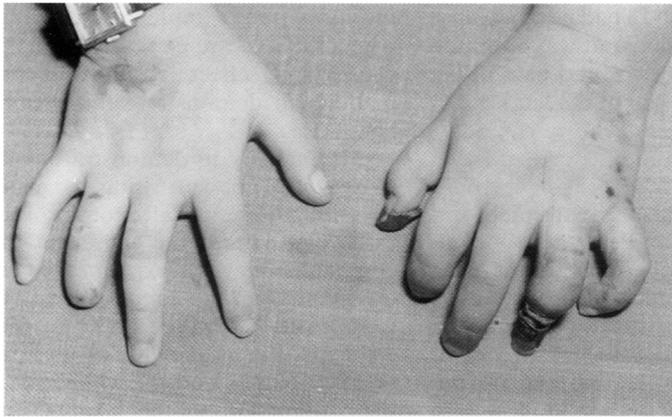
The possible factors (antigens) triggering the hypersensitivity were streptococcal infection in two children, *Plasmodium falciparum* malaria in one, diphtheria-pertussis-tetanus immunisation (DPT) in one, wasp sting in one, and upper

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Six year old female child (No 1 in the table). Autoamputation of distal phalanx of the fourth digit of right hand and gangrenous changes in distal phalanges of the other hand during course of the disease.

respiratory infection or the drug used to treat it in one. All children were normotensive except two who had transient hypertension initially. No involvement of central nervous system, heart, lungs, liver, or kidneys was evident from the history or clinical examination. The table summarises the clinical data. The diagnosis of BCPAN was made on the basis of predominant cutaneous involvement, absence of systemic involvement and skin biopsy showing vasculitis in nine of the ten subjects. A negative biopsy in one child was explicable on the basis of the well known segmental nature of disease.

Full blood count, liver function tests, and renal function tests were normal in all patients. Erythrocyte sedimentation rate (ESR) was uniformly increased during the acute phase of the disease. C reactive protein and anti-streptolysin O titres were increased only in two of the children. Serum complement concentrations, and tests for rheumatoid factor and LE cells did not contribute to the diagnosis. Antineutrophil cytoplasmic antibody (ANCA) testing became available to us only in the last few years of the study; the test was undertaken in two patients and was negative in both. Abdominal angiography was not done as there was no clinical or laboratory evidence of systemic involvement.

The children were followed up for periods of two to 13 years after the diagnosis was made (mean 5.6 years) (two for 13 years, seven for four years and one child for two years). All except three of the children responded to oral corticosteroid therapy. In addition, when the response to steroid therapy was inadequate, melphalan was given to one child and cyclophosphamide to two children. Three patients had two to five relapses during the follow up period, the majority during the first three to four years after the initial diagnosis. Three children remain on follow up: one is asymptomatic; one is receiving 5 mg/day of prednisolone because whenever attempts have been made to withdraw the drug she has complained of joint pain and of her hands and feet becoming cold (patient No 1 in the table);

Clinical profile of 10 children with benign cutaneous polyarteritis nodosa

Patient No	Age (yr) /Sex	Duration of illness at presentation (months)	Probable aggravating factors	Skin lesions		Peripheral gangrene	Joint pain and swelling	Skin biopsy	Therapy	Remarks
				Livido reticularis	Nodules vesicle ulcerations					
1	6/F	20	Tetracycline	+	+	+	+	Small vessel vasculitis showing fibrinoid necrosis, fibrin thrombi and infiltration with polymorphs and lymphocytes. No eosinophils seen	Prednisolone Melphalan	Remissions and relapses; autoamputation of finger and toe tips. Cryoglobulinaemia for eight months
2	2.5/M	1.5	Falciparum malaria	+	+	+	+	Two small vessels showing fibrinoid necrosis with perivascular infiltrates and RBC leakage. No immune complexes	Prednisolone Cyclophosphamide	Remissions and relapses; autoamputation of finger and toe tips
3	7/M	8	Streptococcal infection	-	+	-	+	Dermal vessels showing changes consistent with leucocytoclastic vasculitis	Pentoxifylline Prednisolone	For recent relapse Remission HbsAg negative
4	1.5/M	1	Penicillin	+	+	+	+	Fibrinoid necrosis of vessel wall with infiltration with polymorphs and lymphocytes. The lumen occluded by fibrin thrombus	Prednisolone	Remission, autoamputation of finger and toe tips. Transient cryoglobulinaemia
5	10/F	2/30	Streptococcal infection	-	+	-	-	Subcorneal bulla. Dermis showing blood vessels with oedema and infiltration with polymorphs and few eosinophils, IgG and C ₃ deposits +	Prednisolone	Remission
6	9/F	48	—	-	+	+	-		Prednisolone	Remission; autoamputation of finger and toe tips
7	1.25/M	1	DPT immunisation	+	+	+	+	Fibrinoid necrosis of venule with inflammatory cells, consistent with leucocytoclastic vasculitis	Prednisolone	Remission; amputation right foot, transient cryoglobulinaemia
8	1.5/M	7/30	—	-	+	+	-	Leucocytoclastic vasculitis with fibrin thrombi	Prednisolone	Remission; autoamputation of finger and toe tips
9	5/M	3	—	-	+	+	+	Fibrinoid necrosis of vessel wall with inflammatory cells occluding the lumen	Prednisolone Cyclophosphamide	Remission and relapses; autoamputation of finger toe tips
10	3/M	2	Wasp sting	-	+	+	+	Fibrinoid necrosis of vessel wall with occasional lymphomononuclear cell infiltration	Prednisolone	Remission

DTP = Diphtheria-pertussis-tetanus.

the third child (patient No 2) had a fifth relapse after nine years of remission and was admitted to hospital in April 1994, with red painful flat lesions over the shin and calf of the left leg.

Discussion

Benign polyarteritis nodosa is extremely uncommon in children. Diaz-Perez and Winkelmann were first to describe the condition, on the basis of histopathological features of nodular arteritis with polymorphonuclear infiltrates involving arteries in deep reticular dermis.⁶ These patients had a benign but chronic course and responded well to low dose corticosteroids. Only a few cases of BCPAN have been described in the paediatric literature.⁶⁻⁹ The major differences in our series of patients compared with those reported by Diaz-Perez and Winkelmann are: all our subjects were in their first decade of life; all had skin lesions in both upper and lower limbs; eight had peripheral gangrene in both upper and lower limbs, leading to autoamputation in seven of them (table); and seven had joint swelling in both upper and lower limbs. Peripheral gangrene has been described in a three day old baby girl born to a mother who had developed BCPAN in the second month of her pregnancy.⁹ This child had livido reticularis and gangrene of the upper and lower limbs similar to that seen in our patients.

Peripheral gangrene of this severity resulting in autoamputation is uncommon in the earlier reports of BCPAN.⁸ None of our patients had evidence of other disorders that could cause peripheral gangrene.¹⁰ All the children who had gangrene came to us late (one to 48 months after onset of symptoms). They already had clear demarcation of the affected area and therapy did not prevent further progress of gangrene and eventual autoamputation. However, in subsequent relapses during follow up, therapy was initiated as soon as blue discoloration or cold peripheral digital areas were noted; this rapid action prevented further morbidity in most of the patients. The extent of gangrene and autoamputation could probably have been minimised had these children received appropriate therapy at an early stage of their illness. Arteriography of the foot and hand may be useful, revealing distal arteriopathy with narrowing of vessel lumens or the absence of filling, thus identifying those patients suitable for an aggressive treatment regimen.⁸

Although some of our children fulfilled some of the ACR 1990 criteria for classification of hypersensitivity vasculitis, their clinical profiles—especially in relation to the age of onset and occurrence of peripheral gangrene in the majority of the patients and the chronic relapsing course of the disease—differentiated them from cases of hypersensitivity vasculitis.¹¹

There is no consensus of opinion as regards the aetiology of this disorder. The hypersensitivity mechanism could have been triggered by the various accompanying factors (drugs, falciparum malaria, streptococcal infection, wasp sting, or the second DPT

immunisation) (table). This must remain conjectural, as we could not establish a direct cause and effect relationship because of inability to demonstrate the specific immune complexes.

Our inability to demonstrate immune complexes was not surprising as many children presented quite late after onset of their illness, by which time the absence of immune complexes may be explained by their rapid clearance from the circulation.¹ Cryoglobulins were positive in three patients, persisting for eight months in one (No 1) and disappearing in two (Nos 4 and 7) within four weeks of their admission to the hospital (table). The possibility of a combination of cryoglobulinaemia with vasculitis was considered initially in patient No 1, but the age of the child, the response to prednisolone and melphalan, and the progressive decrease and disappearance of cryoglobulins from the circulation did not favour this diagnosis.

The usual therapy for BCPAN comprises low dose corticosteroids; a few patients may require cytotoxic drugs in addition.⁶ Other therapeutic modalities which have been used are NSAIDs, sulphapyridine (in BCPAN associated with Crohn's disease), pentoxifylline, and chloroquine, all of which have been reported to have a certain degree of success.^{7, 12}

This vasculitis was benign in that it was not life threatening, but six of eight children with peripheral gangrene suffered autoamputation of the toes and finger tips, while in one child a foot had to be sacrificed because dry gangrene extended up to the ankle. Recent literature has raised doubts about the benign nature of BCPAN. In a study by Minkowitz *et al*, seven of the nine adult patients had involvement of at least one organ other than the skin during a follow up period ranging from four months to 14 years (average 3.8 years).¹³ None of the patients in our series developed systemic involvement during the period of follow up.

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