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Clinicopathological and morbidity profile of childhood polyarteritis nodosa in a tertiary referral center

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ABSTRACT

Background: Polyarteritis nodosa (PAN) is a primary systemic necrotizing vasculitis predominantly targeting medium-sized arteries defined as the main visceral arteries and their branches. The objective of this study was to analyze the epidemiology, clinico-pathological and point outcome of PAN in children at a tertiary care centre in Karnataka.

Methods: This prospective observational study was conducted among eighteen children diagnosed with PAN from December 2015 to May 2017. All the children fulfilling EULAR/PRES/PRINTO classification criteria for childhood PAN were included in this study. Clinico-pathological profile of these patients was studied and documented.

Results: This study had shown that there are two peaks of age at onset of symptoms at 5 to 7 years and from 11 to 13 years. No sex predilection was noted. Most children present with nonspecific symptoms like myalgia (94%), fever (84%), weight loss (50%) and joint pain (50%). Skin manifestations were seen in all the children. Neurological involvement (61%) in the form of mononeuritis multiplex (38.8%), hypertensive encephalopathy (11%) and stroke (11%) was observed. Four children (22%) presented with pain abdomen while two boys had testicular pain. Only one child had renal manifestation in the form of glomerulonephritis. Most children had neutrophilic leukocytosis, elevated ESR and thrombocytosis. Skin biopsy was performed in ten children and out of these, 9 reports were suggestive of PAN. Angiography was done in four children revealing multiple aneurysms or stenosis in the systemic arteries. All the children received corticosteroids. Cyclophosphamide was used as an induction agent in about 50% of the patients. Corticosteroid treatment alone was sufficient in only one patient. Steroid sparing agent like azathioprine (38%), mycophenolate mofetil (33%) and hydroxychloroquine (5%) were used with low dose steroids as maintenance therapy. Seven children (39%) achieved remission off drugs while 8 children are still on treatment, one child relapsed and three children were lost to follow up.

Conclusions: Childhood vasculitis leads to considerable delay in diagnosis the initiation of treatment. High index of suspicion and early referral is required in all cases of vasculitis to reduce morbidity and mortality.

Keywords: Aneurysms, Inflammation, Multisystem disease, Vasculitis

INTRODUCTION

Vasculitis is defined as the presence of inflammation in a blood vessel that may occur as a primary process or secondary to an underlying disease. Primary vasculitides are rare in children. These are classified according by both the size of vessels involved and the type of inflammatory response (Figure 1, Table 1).^{1,2}

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Table 1: Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides.¹⁹

	Type of vasculitis			
I I I'd AMD	Takayasu arteritis (TA)			
Large-vessel vasculitis (LVV)	Giant cell arteritis (GCA)			
M P 1 12 0 0 0 0 0	Polyarteritis nodosa (PAN)			
Medium-vessel vasculitis (MVV)	Kawasaki disease (KD)			
	Anti-neutrophil cytoplasmic antibody (ANCA)- associated vasculitis (AAV)			
	Microscopic polyangiitis (MPA)			
	Granulomatosis with polyangiitis (Wegener granulomatosis) (GPA (WG))			
G 11 1 1'-' (GYAY)	Eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome)			
Small-vessel vasculitis (SVV) B	Immune complex SVV			
D	Anti-glomerular basement membrane disease			
	Cryoglobulinemic vasculitis			
	IgA vasculitis (Henoch-Schönlein) (HSP)			
	Hypocomplementemic urticarial vasculitis (anti-C1q vasculitis)			
Westelle acceptance with	Behçet's disease			
Variable vessel vasculitis	Cogan's syndrome			
	Cutaneous leukocytoclasticangiitis			
	Cutaneous arteritis			
Single-organ vasculitis	Primary central nervous system vasculitis			
	Isolated aortitis			
	Others			
	Lupus vasculitis			
Vasculitis associated with systemic	Rheumatoid vasculitis			
disease	Sarcoid vasculitis			
	Others			
	Hepatitis C virus-associated cryoglobulinemic vasculitis			
	Hepatitis B virus-associated vasculitis			
37 192 27 1 24 1 11	Syphilis-associated aortitis			
Vasculitis associated with probable	Drug-associated immune complex vasculitis			
etiology	Drug-associated ANCA-associated vasculitis			
	Cancer-associated vasculitis			
	Others			

Table 2: ACR criteria for diagnosis of PAN.9

Vasculitis	ACR criteria
	≥3 of the following 10 criteria:
	Granulocyte or mixed leukocyte infiltrate in an arterial wall on biopsy
	Arteriographic abnormalities
	Livedoreticularis
Polyarteritis	Myalgia
nodosa	Diastolic blood pressure >90 mmHg
	Mono- or polyneuropathy
	Elevated blood urea nitrogen or
	creatinine
	Testicular pain/tenderness
	Hepatitis B reactants
	Weight loss >4 kg

Polyarteritis nodosa (PAN) is a rare vasculitis in childhood, which is characterized and defined by necrotizing arteritis of predominantly medium sized vessels leading to micro-aneurysms, rupture and

hemorrhages manifesting as multi-system disease.^{3,4} The characteristic histopathologic changes of PAN are fibrinoid necrosis of the walls of medium or small arteries, with a marked inflammatory response within or surrounding the vessel wall.³ PAN is diagnosed based on ACR criteria (Table 2) and PRINTO/PReS 2008 criteria (Table 3).

In contrast to anti neutrophil cytoplasm antibodies associated vasculitis, lung and glomerular involvement are distinctly uncommon in PAN. PAN is serologically bland without any signature autoantibodies. Despite some overlap with smaller vessel disease, PAN is a distinct entity and has an estimated annual incidence of 2.0-9.0/million in adults.⁵ Peak age of onset in childhood is 7-11 years, with often a male preponderance.⁶

Notably, the disease varies in its presentation from a relatively benign cutaneous form, which may resolve without treatment, to a severe systemic form. ^{7,8} This study is aimed to study the epidemiology, clinical profile

of childhood PAN and to understand the point outcome of this rare disease.

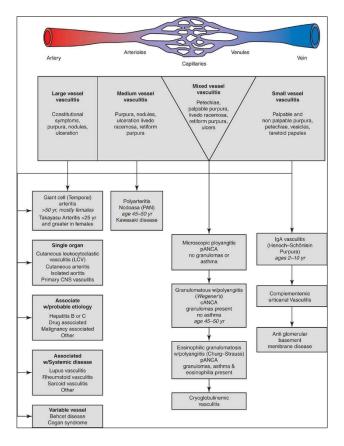


Figure 1: Vessel size, morphology, and related conditions.

Table 3: Ankara 2008 criteria for diagnosis of PAN. 10-13

Vasculitis	Criteria
Polyarteritis	Histopathology or angiographic abnormalities (mandatory) plus one of five:
	Skin involvement
	Myalgia/muscle tenderness
	Hypertension
	Peripheral neuropathy
	Renal involvement

METHODS

A prospective study was conducted in the Pediatric Rheumatology Clinic of Indira Gandhi Institute of Child Health (IGICH), Bengaluru, from December 2015 to May 2017. Out of all the children presenting to the outpatient department of IGICH. those fulfilling classification EULAR/PRES/PRINTO criteria childhood PAN were included in this study. Consent was taken from the parents/legal guardian before they were recruited for the study. Detailed information was recorded in a preformed structured proforma. The

demographic profile, which includes age, sex and address with contact numbers, was recorded. The presenting complaints and the organ involvement were noted down with treatment history with significant past medical events along with clinical findings. Investigations included complete blood count, erythrocyte sedimentation rate (ESR), serum C-reactive protein (CRP) level, anti-streptolysin O (ASLO) titers, hepatitis B surface antigen (HBsAg) by enzyme linked immunosorbent assay (ELISA). Experienced pathologist in the field performed histopathologic examination from the skin biopsy. Statistical analysis was done by generating univariate frequency tables for the parameters. Treatment history was recorded which included response to first line treatment, medications, remission or relapse. The adverse effects of the medications were recorded on each follow up. Angiography was performed either by MRI/CT.

RESULTS

Eighteen children were diagnosed as childhood PAN based on EULAR/PRES/PRINTO criteria. All the children in this study had skin involvement while, 11 out (61.1%) had neurological manifestation. Arthralgia/arthritis was present in 9 children (50%) and only one child had renal manifestation. Acute abdominal pain was reported in four (22%) children, 2/4 patients underwent exploratory laparotomy; appendicectomy was performed in both the children. Pain abdomen in these two can be explained by the vasculitis nature of the disease involving the vessels of the abdomen. One child underwent CECT of the abdomen, which showed transient intussusception, which might be the manifestation of the disease similar in nature to HSP. Two out of 9 boys (22.2%) had presented with scrotal pain (Table 4).

Table 4: System involvement in childhood PAN.

Systems	Numbers	Percentage(%)
Skin	18	100
Neurological	11	61.1
Gastrointestinal	4	22.2
Renal	1	5.5
Genitourinary	2	22.2

The study showed that all the children had skin manifestations in various forms (Table 5). Painful subcutaneous nodule was present in 12 children (66.6%) while livedo reticularis and Raynaud's phenomenon was present in 5 children (27.7%) and 2 children (11.1%) respectively. Ischemic changes were seen in 11 patients, 7 children (38.8%) had gangrenous changes in the toes, fingers, tongue and lips while 4 children (22.2%) had ulcers in the elbow, knees, shin and digits. Autoamputation was seen in 5 children in the fingers and, toes with one child having a severe disease involving tongue and lips.

Table 5: Skin manifestations in childhood PAN.

Skin manifestations		Number	Percentage (%)
Subcutaneous Nodule		12	66.6
Livedo reticularis		5	27.7
Purpura		15	83.3
Raynaud's Phenomenon		2	11.1
Ulceration Gangrene		4	22.2
Ischemia	(digital)	7	38.8
	Autoamputation	5	27.7

Neurological manifestation (Table 6) was noted in 11 children (61.1%). Mononeuritis multiplex was the most common feature affecting 7 patients (38.8%) presenting with foot drop, wrist drop, bulbar palsy, transient facial palsy, hypoesthesia and paresthesia. Two children presented as hypertensive encephalopathy with convulsion and altered sensorium while 2 children (11.1%) had stroke in the young

Table 6: Different neurological manifestations in the study.

Neurological Features	Number	Percentage (%)
Mononeuritis multiplex	7	38.8
Hypertensive encephalopathy	2	11.1
Stroke	2	11.1

Selective angiography was performed in 4 children, which showed aneurysms in the brain, intra-renal artery aneurysm, stenosis at the junction of hepatic and splenic artery, and multiple abdominal artery aneurysms.

Table 7: Treatment received for childhood PAN.

Medication	Number of children	Percentage (%)
Steroid	18	100
Oral prednisolone	11	61.1
With Pulse therapy	7	38.8
Cyclophosphamide	9	50
Azathioprine	7	38.8
Mycophenolate Mofetil	6	33.3
Hydroxychloroquine	1	5.5
Penicillin Prophylaxis	3	16.6

The treatment received by the children in our study is summarized in (Table 7). The most common induction agents were corticosteroid (oral or pulse therapy) with IV cyclophosphamide. Nine (50%) children received combination therapy with cyclophosphamide and steroid. Injection cyclophosphamide was given at a dose of 500-750 mg/m² monthly doses for 6 months. Seven (38.8%) children were given pulse methylprednisolone at a dose of 30 mg/kg/day for 3 consecutive days. Three children (16.6%) received combination therapy of steroid with

mycophenolate mofetil for induction of remission, and 3 children (16.6%) were treated with corticosteroids alone. For maintenance therapy, tapering doses of oral steroids and steroid sparing agents were used, which include azathioprine in 7 children (38.8%), mycophenolate mofetil in 6 children (33.3%) and hydroxychloroquine in 1 child. Penicillin prophylaxis was given in those 3 children with elevated ASO titers.

Out of 18 children, 7 children achieved remission and are off medications. One child had relapse of the disease on stopping azathioprine. Eight (43.3%) children are on medications with regular follow up and are doing well but not yet achieved remission while 3 children (16.6%) were lost to follow up (Table 8).

Table 8: Current treatment profile of childhood PAN patients.

Profile	Numbers	Percentage (%)
On treatment	8	43.3
Complete remission off drugs	7	38.3
Relapse	1	5.5
Lost for follow up	3	16.6

DISCUSSION

This descriptive observational study was conducted in the Pediatric Rheumatology Clinic of IGICH over a period of eighteen months. The objective of the study was to assess the clinico-epidemiological profile and the point outcome of children presenting with PAN. Eighteen children diagnosed as childhood PAN on the basis of EULAR/PRES/PRINTO criteria were included in the study and were followed up prospectively in the rheumatological clinic. There are very few reported case series of childhood PAN. The largest and most notable multicentric study was by Ozen et al, which included 110 children among which 63 children had systemic PAN.14 There are two reported case series from India, one by Kumar et al, (8 children) in 1996 and the other one Mondal et al, (15 children) in 2014. 15,16 The other case series include Maeda et al, Blau et al, Jelusic et al, Ettlinger et al, and Eleftheriou et al. 17-21

In the present study the mean±SD age of presentation was 8.7±3.0 years. Earlier two studies from India (Kumar et al and Mondalet al) had similar age of presentation to that of the present study. 15,16 Ozen et al, among Turkish population had reported higher mean (range) age of presentation of 15.45 years among Turkish population. 22 We observed that there are two-peak age of onset of symptoms at 5-7 years and 11 to 13 years, although this has not been documented in previous literature. Variability in age of presentation can be attributed to the differences in populations being. Equal numbers of male and female children were affected in the present study. Although childhood PAN don't have gender predilection, in all previous studies except Mondal et al, and Ozen et

al, males were affected more compared to females.¹⁶ Mean (range) duration of follow up was 30.7 (5-60) months.²² Longer duration of follow up had been reported by the three large studies Ozen et al, and Eleftheriou et al.^{3,21,22} The duration of follow up may not be accurate as for this study purpose children were followed up to one year.

Fever is the most common constitutional symptom in childhood PAN. In the present study 15 (83.3%) children presented with fever, which was similar to the findings of earlier studies. In various studies (Mondal et al, Kumar et al, Maeda et al, Ettlinger et al, fever was a presenting feature in all children. 15-17,20 Articular involvement in terms of arthralgia and or arthritis had been reported among 43-80% of childhood PAN. One child had bilateral sacroiliac joint involvement; one child had

painful elbow and wrist joints and two children presented with painful swelling of ankle and knee joint. Five out of seven children (71.4 %) with higher ASLO titers and four out of eight (50%) had articular manifestation. But previous literatures did not show any correlation between ASLO titer and articular manifestation in childhood PAN. Myalgia had been reported variably in 33-100% children. Seventeen children (94%) had presented with myalgia. Hypertension, which was defined as systolic or diastolic more than the 95th centile for age and height, was observed in 4 (22.2%) children similar to the findings of Ozen et al (14.5%), Eleftheriou et al (16%) and Talukder et al (23%).^{2,21,23} But earlier studies from India had reported hypertension in 100% Kumar et al. and 93% Mondal et al, of children diagnosed with childhood PAN (Table 9), 15,16

Table 9: Comparison of clinical profile of present study with the earlier studies.

	Fever	Articular symptom	Myalgia	Hypertension
Present study, n=18(%)	15(83)	9(50)	17 (94)	4 (22)
Mondalet al, n=15(%)	15 (100)	12 (80)	15 (100)	14 (93)
Kumar et al, n=8 (%)	8 (100)	5 (62)	5 (62)	8 (100)
Talukderet al, n =13 (%)	13 (100)	9 (69)	7 (54)	3 (23)
Arabian study [80], n=11(%)	8 (72)	-	-	-
Maeda et al, n =14(%)	12(86)	7(50)	7(50)	5(36)
Jelusicet al, $n = 7(\%)$	6 (85)	4 (60)	-	-
Blauet al, n=11(%)	10(90)	8(73)	7(64)	11(100)
Ettlingeret al, n=7(%)	7(100)	3(43)	0(0)	4(57)
Eleftheriou et al, n=69(%)	60(87)	52(75)	57(83)	11(16)
Ozenet al, n= 60(%)	-	34 (57.6)	-	-
Iudici et al, n= 21 (%)	10 (48)	12 (57)	11 (52)	-
Ozenet al, n =110(%)	56 (50.9)	13 (57)	37 (33.6)	16 (14.5)

Skin manifestations of childhood PAN are: tender subcutaneous nodules, purpuric skin rashes, livedo reticularis (reticular purplish pattern, usually distributed around subcutaneous fat lobules, which becomes more prominent with cooling), skin infarctions, nail bed infarctions, splinter hemorrhages, necrosis and or gangrene of distal phalanx and or other peripheral tissues (nose and ear tips). Earlier studies had variable skin manifestations involving 45-100% of children diagnosed with childhood PAN. But, detailed manifestation of the skin involvement was rarely being published except very few studies. In our patients, tender subcutaneous nodule was found in 12 (66%) children similar to the findings of Talukder et al, (10, 77%).²³ Eleftheriou et al, (16, 33%) and Iudici et al (10, 48%) have reported lesser number of cases with tender subcutaneous nodules. 21,24 Author found purpuric rashes in 15 children (83%), which were similar to the findings of Maeda et al, Ettlinger et al, Talukder et al. 17,20,23 Four (22%) children had ulceration, out of which three had non-healing ulcers and one had healed ulcers. Ulcers were located mostly in the lower extremities involving toes, malleoli, dorsum of the feet and lower end of leg. Seven (38%) children had gangrene involving toes and fingers except in one child where gangrenous involvement of lips, tongue was reported. Mondal et al, had reported ulceration in 9 (60%) out of 15 children, but site of involvement were not available. ¹⁶ Talukder et al, (4, 31%) and Eleftheriou et al, (3, 4%) had reported lesser incidence of ulceration and gangrene. ^{21,32} Though previous studies had no mention about the incidence of autoamputation, we had observed autoamputation involving the distal phalynges of fingers and or toes in five (27.7%) children and autoamputation of lips and tongue in one child (Table 10).

In this study authors have observed higher incidence of testicular involvement as compared to the existing literature. Many of our children presented with gangrenous changes with auto amputation, non-healing ulcer, hypertension with encephalopathy either due to late referral, non-compliance to treatment or inadequate medications resulted in increased relapse rate. The

adverse effects of the immunosuppressants need to be monitored as we have observed growth failure, hyperglycemia, osteoporosis and cystitis in our children, most probably due to steroids; other adverse effects should also be looked for during follow up. Finally, larger studies with longer duration and regular follow up are needed to establish the long-term complications and the outcome of the disease in these children.

Table 10: Comparison of skin manifestation of present study with earlier studies.

	Skin involvement	Tender nodules	Rash	Livedo reticularis	Ulceration	Gangrene	Raynaud's phenomenon
Present study n=18(%)	18 (100)	11 (66)	15 (83)	5 (27)	4 (22)	7 (38)	2 (11)
Mondal et al, n= 15(%)	15 (100)	-	6 (40)	-	9 (60)	9 (60)	-
Kumar et al, n =8(%)	6 (75)	-	7 (50)	-	1 (12)	1 (12)	-
Talukder et al, n=13(%)	9 (69)	10 (77)	9 (69)	-	4 (31)	4 (31)	-
Maeda et al, n=14(%)	10 (71)	-	7 (50)	-	-	-	-
Ettlinger et al, n=7(%)	6 (86)	-	6 (86)	-	-	-	-
Eleftheriou et al, n=69(%)	61 (81)	16 (33)	28 (41)	34 (49)	3 (4)	3 (4)	16 (23)
Iudici et al, n= 21 (%)	17 (81)	10 (48)	-	-	-	-	-

Table 11: Comparison of clinical profile of present study with the earlier studies.

	Neurological	Renal	Testicular	Gastrointestinal	Pulmonary
Present study, n=18(%)	11(61)	1(5)	2(22)	4(22)	0(0)
Mondal et al, $n = 15(\%)$	7 (46)	0(0)	-	2 (13)	-
Kumar et al, n =8 (%)	6(75)	5(62)	-	5(62)	-
Talukder et al, n =13 (%)	-	-	-	12(92)	-
Maeda et al, n =14(%)	2(14)	-	-	6(43)	-
Jelusic et al, $n = 7(\%)$	3 (42)	-	-	-	-
Blau et al, n=11(%)	12 (20)	-	-	7(64)	-
Ettlinger et al, n=7(%)	8 (38)	5 (24)	-	6(86)	0(0)
Eleftheriou et al, n=69(%)	7(10)	13(19)	4(6)	28(41)	2(3)
Ozen et al, $n = 60(\%)$	-	32(53)	-	20 (33)	3 (5)
Iudici et al, n= 21 (%)	8 (38)	5 (24)	-	4 (19)	0(0)
Ozen et al, n=110(%)	16 (14)	13(12)	4 (6)	19 (17)	6(5)

Study by Ozen et al, Mondal et al and Eleftheriou had reported pain abdomen in 13%, 41% and 33% children respectively. 16,21,22 In the present study, four (22%) children had acute abdominal pain at the time of presentation. Out of which, two children underwent laparotomy and third child had transient intussusception. The pain abdomen can be explained by the inflammatory changes in the small and medium vessel of the gastrointestinal circulation. Eleftheriou et al, found that severe gastrointestinal tract involvement was associated with increased rate of relapse. 21 Earlier studies had reported variable renal involvement from nil (Mondal et

al, and Talukder et al, to 62% Kumar et al. 15,16,23 It was observed that only one (5.5%) child had renal involvement with features of acute glomerulonephritis while earlier studies like Eleftheriou et al, and Ozen et al and 2006 had reported in 19%, 12% and 53% respectively. 3,21,22

Variation in nervous system involvement had been reported by various earlier studies. Eleven (61.1%) children were noted to have nervous system involvement, out of these, 44% children had mononeuritis multiplex, 11% children had presented with hypertensive encephalopathy and stroke respectively. Kumar et al, had

reported 75% of children having neurological manifestations while Mondal et al, had reported involvement of only peripheral nervous system in 41% children. The two largest case series by Ozen et al, and Eleftheriou et al, also had reported nervous system involvement in 14% and 10% respectively. However nervous system involvement was absent in Talukder et al, Blau et al, and Ettlinger et al. However have all and Ettlinger et al. However persons presented with testicular pain while Ozen et al and Eleftheriou et al, had observed testicular involvement in 6.3% and 6% children respectively (Table 11). Later than the present study 2 (Table 11).

All children diagnosed with childhood PAN were managed based on the available treatment recommendation in various literatures. The most common induction agents were steroids (100%) with pulse methylprednisolone in seven (38.8%) children and intravenous cyclophosphamide in nine children (50%). For maintenance therapy, low dose of oral steroids and steroid sparing drugs like azathioprine, mycophenolate mofetil or hydroxychloroquine were used. Eleftheriou et al, used biologic agents like infliximab, etanercept or rituximab or plasma exchange therapy for the management of unresponsive disease.²¹ Due to the high cost and non-availability of these agents, it was not used in our patients. Eight patients are on regular therapy on maintenance therapy with tapering doses of steroid and steroid sparing drug either with azathioprine or mycophenolate mofetil. Seven children are in remission and off medication and are on follow up in the clinic. Three children were lost for follow up due to geographical differences (one from Syria, two from West Bengal).

CONCLUSION

Childhood vasculitis is a challenging and complex group of conditions that have protean clinical manifestation ranging from isolated cutaneous disease to multisystem involvement. Childhood polyarteritis nodosa though very rare in children may be under diagnosed because of many nonspecific-presenting features of PAN mimicking infectious causes and chronic inflammatory condition. This leads to considerable delay in diagnosis the initiation of treatment. High index of suspicion and early referral is required in all cases of vasculitis to reduce morbidity and mortality.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

REFERENCES

1. Khubchandani RP, Viswanathan V. Pediatric vasculitides: a generalists approach. Ind J Pediatr. 2010 Oct 1;77(10):1165-71.

- Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, Flores-Suarez LF, Gross WL, Guillevin L, Hagen EC, Hoffman GS. 2012 revised international chapel hill consensus conference nomenclature of vasculitides. Arthr Rheumat. 2013 Jan;65(1):1-1.
- 3. Ozen S, Anton J, Arisoy N, Bakkaloglu A, Besbas N, Brogan P, et al. Juvenile polyarteritis: results of a multicenter survey of 110 children. J Pediatr. 2004 Oct 31;145(4):517-22.
- 4. Mogale KD, Shrivastava A. Childhood polyarteritis nodosa: a clinical diagnosis. Ind Pediatr. 2006;43(10): 911-3.
- 5. Watts RA, Scott DG. Epidemiology of vasculitis. In: Ball GV, Bridges SL, editors. Vasculitis. 2nd ed. Oxford: Oxford University Press; 2008:7-21.
- 6. Dillon MJ, Eleftheriou D, Brogan PA. Mediumsize-vessel vasculitis. Pediatr Nephrol. 2010;25:1641-52.
- Ettlinger RE, Nelson AM, Burke EC, Lie JT. Polyarteritis nodosa in childhood: a clinical pathologic study. Arthritis Rheum. 1979;22:820-5.
- 8. Besbas N, Ozen S, Saatci U, Topalogclu R, Tinaztepe K, Bakkaloglu A. Renal involvement in polyarteritis nodosa: evaluation of 26 Turkish children. Pediatr Nephrol. 2000;14:325-7.
- 9. Jennette JC, Falk RJ, Andrassy K, Bacon PA, Churg J, Gross WL, et al. Nomenclature of systemic vasculitides. Arthr Rheumat: Official J Am Coll Rheumatol. 1994 Feb;37(2):187-92.
- Arend WP, Michel BA, Bloch DA, Hunder GG, Calabrese LH, Edworthy SM, et al. The American College of Rheu¬matology 1990 criteria for the classification of Takayasu arteritis. Arthr Rheum 1990;33:1129-34.
- 11. Leavitt RY, Fauci AS, Bloch DA, Michel BA, Hunder GG, Arend WP, et al. The American College of Rheumatology 1990 criteria for the classification of Wegener's granulomatosis. Arthritis Rheum. 1990;33:1101-7.
- 12. Lightfoot RW, Jr., Michel BA, Bloch DA, Hunder GG, Zvaifler NJ, McShane DJ, et al. The American College of Rheumatology 1990 criteria for the classification of polyarteritis nodosa. Arthritis Rheum. 1990;33:1088-93.
- 13. Mills JA, Michel BA, Bloch DA, Calabrese LH, Hunder GG, Arend WP, et al. The American College of Rheumatology 1990 criteria for the classification of Henoch- Schonlein purpura. Arthritis Rheum. 1990;33:1114-21.
- 14. Ozen S, Pistorio A, Iusan SM, Bakkaloglu A, Herlin T, Brik R, et al. EULAR/PRINTO/PRES criteria for Henoch–Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: final classification criteria. Ann Rheum Dis. 2010 May 1;69(5):798-806.
- 15. Kumar L, Sarkar B, Singh S, Bajwa RP, Joshi K, Malik N. Polyarteritis nodosa-a few unusual findings. Indian Pediatr. 1996 Jun 1;33:459-64.

- Mondal R, Sarkar S, Pal P, Nandi M, Hazra A, Sabui TK. Childhood polyarteritis nodosa: a prospective multicentre study from eastern India. Ind J Ped. 2014 Apr 1;81(4):371-4.
- Maeda M, Kobayashi M, Okamoto S, Fuse T, Matsuyama T, Watanabe N, et al. Clinical observation of 14 cases of childhood polyarteritis nodosa in Japan. Pediatr Inter. 1997 Apr 1;39(2):277-9.
- 18. Blau EB, Morris RF, Yunis EJ. Polyarteritis nodosa in older children. Pediatr. 1977 Aug 1;60(2):227-34.
- 19. Jelusic M, Batinic D, Milosevic D, Malenica B, Malcic I. Polyarteritis nodosa in Croatian children: a retrospective study over the last 20 years. Rheumatol Inter. 2013 Dec 1;33(12):3087-90.
- 20. Ettlinger RE, Nelson AM, Burke EC, Lie JT. Polyarteritis nodosa in childhood. Arthr Rheumatol. 1979 Aug 1;22(8):820-5.
- 21. Eleftheriou D, Dillon MJ, Tullus K, Marks SD, Pilkington CA, Roebuck DJ, et al. Systemic Polyarteritis Nodosa in the Young: A Single-Center Experience Over Thirty-Two Years. Arthr Rheumat. 2013;65(9):2476-85.

- 22. Ozen S, Bakkaloglu A, Dusunsel R, Soylemezoglu O, Ozaltin F, Poyrazoglu H, et al. Childhood vasculitides in Turkey: a nationwide survey. Clini Rheumatol. 2007 Feb 1;26(2):196-200.
- 23. Talukder MK, Islam MI, Rahman SA. Clinical and laboratory profile of childhood polyarteritis nodosa in a Bangladeshi tertiary hospital. Inter J Rheumat Dis. 2014 Mar 1;17(3):313-6.
- 24. Iudici M, Puéchal X, Pagnoux C, Quartier P, Agard C, Aouba A, et al. Brief Report: Childhood-Onset Systemic Necrotizing Vasculitides: Long-Term Data From the French Vasculitis Study Group Registry. Arthr Rheumatol. 2015 Jul 1;67(7):1959-65.

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