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Clinicio-Patho-Etiological Study of Cutaneous Vasculitis

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Abstract : *Cutaneousvasculitisis a reactiveclinical pattern and increasing incidence maybe due to idiopathic or associatedwith a spectrum of conditions such as infections,drugs ,autoimmunediseases etc. The aim of the presentstudywas to evaluate the etiologicalfactorscausingcutaneousvasculitis and to studycommonclinical pattern of vasculitis..A cohort study was conducted on 25 clinically suspected cases of cutaneous vasculitis attending the out patient department of dermatology, Osmania general hospital, Hyderabad,India for a period of 12 months . Drugs turned out be commonest causative agent in present study, particularly NSAIDs. .Infections seem to be an important etiological factor of allergic vasculitis in this study.Streptococcal infection in allergic vasculitis and tuberculosis in erythema nodosum turned out to be major etiological agents.Connective tissue disease seem to be ananother important etiological factor of allergic vasculitis in present study. Clinically palpablepurpura was the predominant morphological pattern seen here, and.Histo pathologicallyleukocytoclastic variant accounts most types of vasculitis followed by lymphocytic variant.*

Keywords: *Allergic vasculitis,Cutaneous vasculitis, erythema nodosum,NSAIDs,Palpablepurpura.*

I. Introduction

Cutaneous vasculitis is inflammation of cutaneous vessels with variety of clinical manifestations. The appropriate way of diagnosis is histological examination, but can be done with clinical presentation in some cases.[1]vasculitismay be idiopathic or associated with a spectrum of conditions such as infections , drugs , etc.vasculitis manifest with various clinical pictures, such as palpable purpura, nodules, urticarial lesions, ulcerations and necrosis.In this study, patients who came with classical manifestations of vasculitis where evaluated through diagnostic approaches, that helps to elucidate the most frequent causative factor, and at the same time we studied the common clinical patterns, and the most frequent histopathologicalvarients in vasculitis.

II. Materials And Methods

A cohort study was conducted on 25 clinically suspected cases of cutaneous vasculitis attending the out patient department of dermatology, Osmania general hospital, Hyderabadfrom January 2013 to December 2013.

Aim of the study : To study the etiological factors of cutaneous vasculitis, in patients, who came with classical manifestations and evaluatingthem through diagnostic approachesto elucidate most possible frequent causative agents, and to study various clinical patterns, with most common histopathological patterns in vasculitis.

Procedure: Clinically suspected cases of patients with evidence of cutaneous vasculitis irrespective of age ,sex, duration of disease, were enrolled in the study. Informed consent was taken from all patents, involved in this study.The cases were presented with symptomatic palpablepurpura, ,vesicles, bullae,pustules, ulcers and other cutaneous findings like urticaria. Cases presenting with palpable purpura in association with jointpains, pain abdomen,hematuria and malena recorded as Henoch-schonlein purpura. Patients presenting withurticarial wheals which lasted for more than 24hours associated with purpuric lesions along with constitutional symptoms like fever , joint pains were taken up as urticarial vasculitis.

Painful erythematous tender nodules on lower legs were recorded as erythema nodosum.cases presenting with ulcers and atrophy and scarring taken up as pyodermagangreonosum. patients with history of medication at disease onset were also taken in the study. Patients with thrombocytopenia and disorders of coagulation are not taken in the study. Erythema nodosumleprosumwas not included in the study. The enrolled patients were enquired about the history relevant to vasculitis . data was obtained according to following questionnaire.

1. Name,age,sex,religion,socialstrata,occupation,address
2. Complaints ,duration, evolution, progress
3. Detailed history regarding the clinical features

3.1 joint pains,myalgia
3.2 abdominal pain,malena
3.3 hematuria,fever
3.4 upper respiratory tract infection

3.5 chest pain, dyspnea
3.6 headache , seizures
4. Detailed history regarding etiology

Infections : History of sore throat regarding streptococcal infections, history of tuberculosis, history of leprosy, recent flu like illness, cystitis, sinusitis, tonsillitis, dental diseases or vaccination.

Food and drugs: NSAIDs, antibiotics, oral contraceptives, thiazide diuretics, ayurvedic and homeopathic medicines. Any medicine given for any specific illness.

Soft drinks especially high colored and intake of food and drugs to which patient is known to be allergic. History of any known chronic illness like diabetes mellitus, hypertension, rheumatoid arthritis ,other form of collagen diseases like SLE, blood disorders, chronic respiratory disease ,disorder of bowel, liver and malignant disease. Recent surgery or pregnancy, history of recurrent episodes in the past, personal and family history in relation to vasculitis

A detailed cutaneous examination was carried out in all cases and morphological details and precise distribution patern were noted. A provisional diagnosis was made and the cases were investigated to establish cause and frequency of occurrence. Routine investigations like CBP, ESR, BT, CT, CUE, Platelet count, stool examination were carried out. LFT and serum proteins were also done. Radiological investigations like chest x ray, ultrasound abdomen were done and results are noted. specific investigations like mantoux test, ASO titres, C reactive protein, VDRL, HIV, HBsAg were done and results noted.

specific immunological investigations like ANA, and Anti ds DNA antibodies, cryoglobulins, and RA factor were carried out and results noted.

specific investigations like C-ANCA, P-ANCA were done and results noted.

Procedure of skin biopsy: skin biopsy was done in all cases under local anaesthesia with xylocaine 2%. Before injecting local anaestheticXylocaine sensitivity was tested.an early lesion was chosen ,local infiltration with 2% xylocaine was given . an incisional biopsy with sufficient depth to include the subcutaneous tissue was done. The sample was collected in a bottle containing 10% formalin and specimen was sent to department of pathology, OGH.

Direct immunofluorescence:perilesional skinbiopsy is done in all cases under local anesthesia. Samples are collected in normal saline and kept in ice box and transported to Apollo hospital within 24 hours. Four micron thick sections are cut on acryostat at -20 degree centigrade and each section is stained with one of antisera (flouresecein conjugated antibodies) against a series of immunoreactants such as IgA, IgM, C3 and fibrin. They are observed under a fluorescent microscope and results are noted.

Results

A total of 25 clinically suspected cases of cutaneous vasculitis were studied and the results were recorded.

Incidence: Cutaneous vasculitis accounted for 0.2% of total out patient cases attending the department of a Dermatology, Osmania general hospital, Hyderabad during the period of January 2013 to December 2013.

Figures and Tables

Table -1 Sex distribution of the patients

S.NO	Sex	No. of patients	Percentage
1	Male	9	36%
2	Female	16	64%

Of the total patients 09 were males accounting for 36% and 16 were females accounting for 64% with afemale to male ratio of 1.8:1

Table IIAge distribution of the patient

s.no	Age group	Males (n=9)	Females (n=16)	Total
1	1-10	2 (22.22%)	---	2 (8%)
2	11-20	2 (22.22%)	3 (18.75%)	5 (20%)
3	21-30	3 (33.33%)	7 (43.75%)	10 (40%)
4	31-40	2 (22.22%)	4 (25%)	6 (24%)
5	41-50	---	2 (12.5%)	2 (8%)

In the present study age distribution ranged from 1-50 years. The maximun number of cases belonged to the age group of 21-30 with a total of 10 patients and accounted to 40%. Among the males maximum number of cases were recorded among the patients of age group 21-30 with 33.33% and females were also recorded with same age group contributing to 43.75%

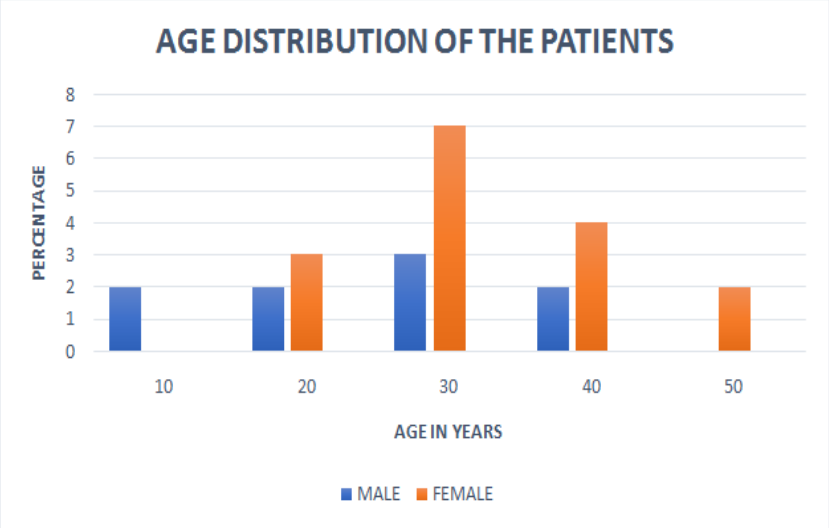


Table III Shows the predominant morphological type of lesions presenting as vasculitis

s.no	Type of lesions	Total (25)
1	Palpable purpura	18 (72%)
2	Nodules	6 (24%)
3	Urticarial wheals	1 (4%)

In the present study palpable purpura was the most common presentation of vasculitis contributing to 72% was also the main presenting feature of allergic vasculitis and Henoch-schonleinpurpura. Nodules accounted for 24% and urticarial wheals accounted for 4%.

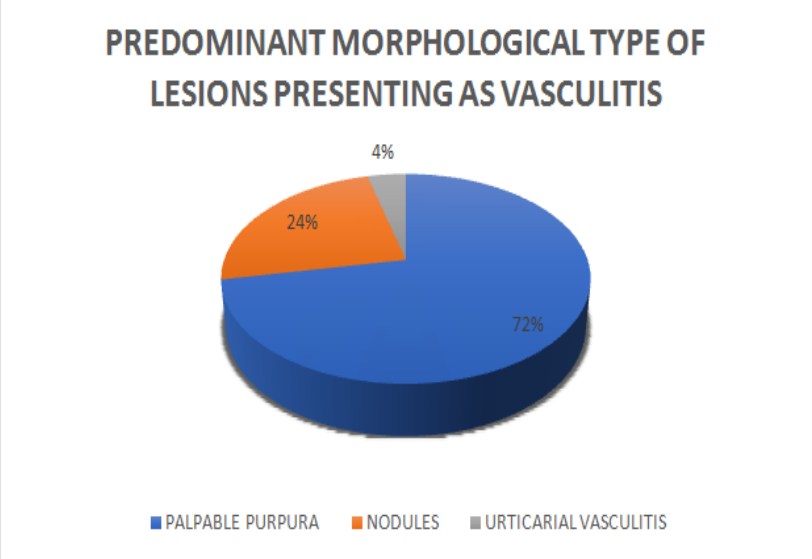
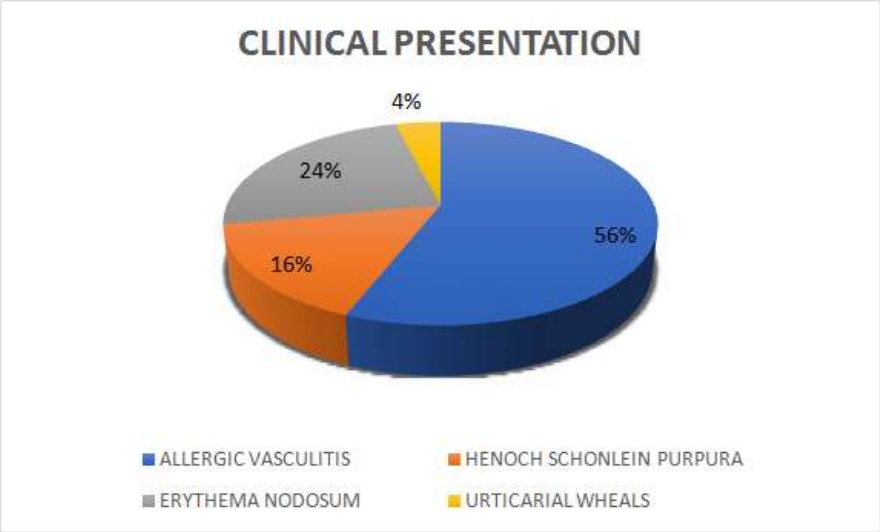


Table IVShows the various types of presentation of cutaneous vasculitis

s.no	Type of presentation	Males (n=9)	Females (n=16)	Total
1	Allergic vasculitis	5 (55.55%)	9(56.25%)	14(56%)
2	Henoch-schnoleinpurpura	2(22.22%)	2(12.5%)	4(!6%)
3	Erythema nodosum	1(11.11%)	5(31.25%)	6(24%)
4	Urticarial vasculitis	1(11.11%)	---	1(4%)

In the present study maximum number of cases 56% presented with features of allergic vasculitis was the common presentation among males and females accounted for 55.55% in females. Next common presentations were erythema nodosum 24%, Henoch-schnoleinpurpura 16% and urticarial vasculitis 4%



Laboratory findings:

CBP was found to be normal in all casesESR was raised in 14 out of 25 cases which accounted to 56% Bleeding time, clotting time and platelet count was found normal in all casesComplete urine examination – out of 25 cases ,4 cases found abnormal i.e 2 allergic vasculitis cases presented with pus cells in urine and hematuria in Henoch-schnoleinpurpura, 1 case of SLE had proteinuria and granular casts.

Liver function tests: was found raised in 1 patient with complaints of allergic vasculitisBlood sugar: normal in all cases except in 1 case of allergic vasculitis with fasting blood sugar 135mg/dlStool examination: normal in all casesVDRL Test: non reactive in all casesHIV test: reactive in 1 case of allergic vasculitisHBsAg : negative in all casesChest x-ray pa view: clear in all casesUltra sound abdomen: one case of allergic vasculitis had splenomegalyColourdoppler: normal in all casesSpecific investigations:

Mantoux test : it was done in all cases , only in cases it was found to be positive C-reactive protein: Found to be positive in 3 cases out of 2 cases of allergic vasculitis and 1 case of HSPASO titres: raised in 5 cases out of which 2 cases of allergic vasculitis , 2 cases of HSP and 1 case of erythema nodosumRA factor:found to be positive in 1 case of allergic vasculitisANA :positive in 2 cases of allergic vasculitisP-ANCA:normal in all casesC-ANCA:normal in all casesSkin biopsy: leukocytoclasticvasculitis accounted moreDIF Report: 12 cases of allergic vasculitis shown IgM, C3 deposits and 4 cases of HSP shown IgA, C3 deposits. 2cases of idiopathic allergic vasculitis shown IgM and C3 deposits. 1 case of urticarial vasculitis is shown with IgM & C3 deposits.

Table VAbnormal laboratory findings

Investigations	**Allergic vasculitis**	**HSP**	**Erythema nodosum**	**Urticarial vasculitis**
ESR	6	3	4	1
ASO titre	2	2	1	-
Blood sugar	1	-	-	-
LFT	1	-	-	-
CUE	2	2	-	-
Mantoux test	-	-	3	-
RA factor	1	-	-	-
C reactive protein	2	1	-	-
ANA	2	-	-	-
HIV	1	-	-	-

TableVIPossible causative factors

Causative factors	Allergivvasculitis (n=14)	HSP (n=4)	Erythema nodosum (n=6)	Urticarial vasculitis (n=1)
Drugs	5 (35.71%)	-	-	-
Infections	3 (21.42%)	3 (75%)	3 (50%)	-
Connective tissue diseases	2 (14.28%)	-	-	-
Idiopathic	2 (14.28%)	-	2 (33.33%)	-
Others (diabetes)	1 (7.14%)	1 (25%)	1 (16.66%)	-

In present study drugs found to be the most common etiological factor accounting for 35.71% in allergic vasculitis . infections accounted for next common etiological factor followed by connective tissue diseases and idiopathic causes.

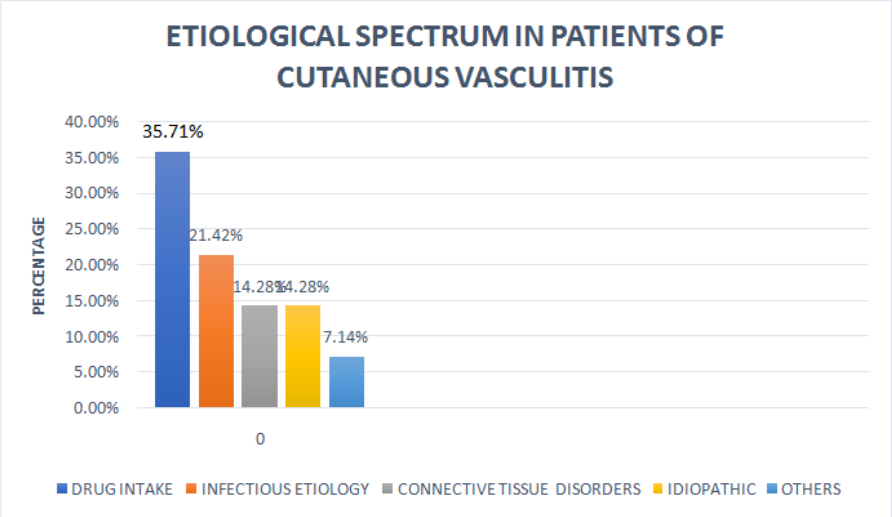
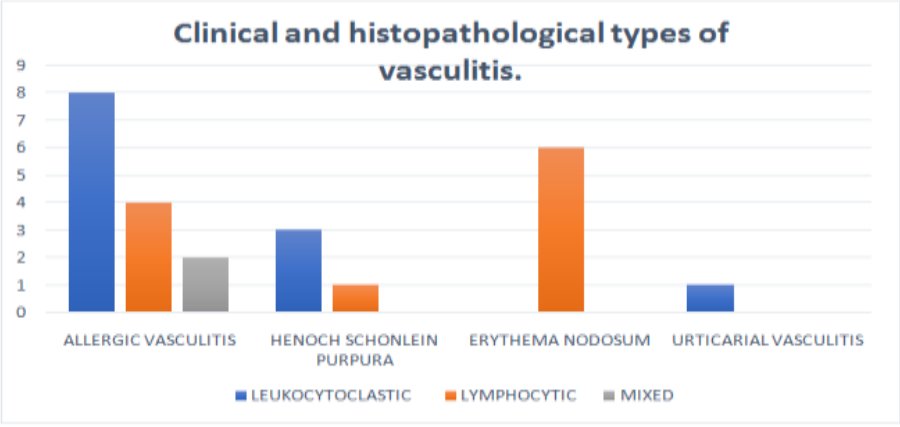


Table VIIIHistopathological findings

Histopathologicallyleukocytoclasticvariant accounted for 57.14% in allergic vasculitis ,75% in HSP and 100% in urticarial vasculitis. Lymphocytic variant accounted for 28.57% in allergic vasculitis,25% in HSP and 100% in urticarial vasculitis

Clinical diagnosis	No. of cases	Histopathological type of vasculitis		
		Leukocytoclastic	Lymphocytic	Mixed
Allergic vasculitis	14	8 (57.14%)	4(28.57%)	2(14.28%)
HSP	4	3 (75%)	1(25%)	-
Erythema nodosum	6	-	6(100%)	-
Urticarial vasculitis	1	1 (100%)	-	-



V. Discussion

In view of observation made in present study,the following points are discussed and compared with othe reports on subject.Incidence:25 clinically suspected cases of cutaneous vasculitis were taken up in present study which spread over 12 months .during this period cutaneous vasculitis accounted for 0.2% of total tpatient attendance at Dept of Dermatology,Osmania General Hospital Hyderabad.Females accounted for an incidence of 64% and males accounted for an incidence of 36%with a female to male ratio of 1.8:1 in present study. The female preponderance in present study correlates With that of Chua et al(1999)[2], who reported a female to male ratio of 2:1 I their study of 47 cases.In the subgroup of allergic vasculitis ,there is higher incidence among females(56.25%),than males(55.55%)in the present study.Marques et al(1995)[3],in their study of 51 cases of cutaneous necrotizing vasculitis reported 64.7%of females and 35.29% are males . the female preponderance in allergic vasculitis in present study correlates with that of marques et al .Henochshonleinpurpuraaccounted for

16%(4 cases)of cutaneous vasculitis in present study with equal incidence in both sexes.Most HSP cases occurs in child hood, with palpable purpura[4]. In this study 3 cases were child hood age group and one case of HSPwas present in 45year old female. the incidence of HSPin relation to age group, present study correlated with Blanco R et al (1997)[5], in which he studied 162 cases among which 116 were children and 46 were adults .Erythema nodosum accounted for 24%(6 cases)in present study out of which males accounted for 11.11%(1 case)and females 31.25% (5 cases).in present study the female incidence of Erythema nodosum is compared with Sarveswari et al[6], in which females accounted for 53.3%out of total 15 cases.

Urticarial vasculitis accounted for 11.11%of cutaneous vasculitis .Age incidence:in present study age distribution of cutaneous vasculitis range from 1-50 yrs.Maximum no cases belongs to age group of 21-30years and mean age is 25.5.All cases of Henoch –schonleinpurpura were upto age of 15years except one case of female at the age of 45 years..Presentation of cutaneous vasculitis:patients presented with various morphological lesions which include palpable purpura,nodules,urticariallesions,most common presentation is palpable purpura accounting for 72%.this can be correlated with Sais et al[7], andEkenstam et al[8], studies on incidence of palpable purpura accounting for 89.2%nd 62% of cases respectively.

The causes for cutaneous vasculitis are numerous , which include drugs,infections,connective tissue disorders,malignancies and idiopathicvasculitis. In present study out of 25 casesthe causative factors were found in 21cases, which accounted for 84%based on history and investigations .Taking each type of vasculitis into consideration in allergic vasculitis, drugs are accounted for 35.71% of cases included those who developed the lesions secondary to intake of NSAIDS(Ibuprofen,paracetamol,diclofenac). Drug induced vasculitis is common cause of leukocytoclasticvasculitis, and penicillins, sulfonamides, allopurinol, followed by NSAIDS are responsible forleukocytoclastic vasculitis[9].Relevant drug history is reported in 10%of patients inEkenstam et al[8] study.Infections :based on positive history of sorethroat and raised ASO titres streptococcal infections considered to be the possible causative agent in allergic vasculitis accounted for 21.42%.this can be correlated with Marques et al [3](1995)in which infection has a causative factor accounted for 6%cases..14.28%(2 cases) of allergic vasculitis found to be idiopathic and can be correlated with Gupta et al[10], 2009 in which 26% of cases were found to be idiopathic, cause could not be ruledout.The Henoch –schonleinpurpura contributed to 16%(4 cases) of cutaneous vasculitis .75%of cases were associated with infection with preceding history of sore throat and raised ASO titres.The Erythema nodosum contributed to 24%(6 cases)of cutaneous vasculitis.50% of cases found to have infective etiology of tuberculosis,based on raised ESR and positive Mantoux test (>10mm of induration).the present study is correlated with Sarveswari et al[6],in which tuberculosis is infective etioliogy contributed to 46%of cases in erythema nodosum. In 33.33% of cases of erythema nodosum cause could not be known.Connective tissue disease, in present study we found 14.28%of allergic vasculitis patients had SLE, .Ekenstan and Callen (1984)[6]have also reported connective tissue diseases in 20.75% of allergic vasculitis patients, 17 out of 82[8]. In present study morphological pattern of urticarial vasculitis contributed to 11.11%, but cause could not be found out, as in normocomplementamic urticarial vasculitis[12].

Clinicopathological correlation :in present study out of 14 cases of allergic vasculitis (8cases)showed leukocytoclasticvasculitis of 57.14%.this study is compard with Gupta et al (2009)in which 75%cases of allergic vasculitis showed leukocytoclasticvasculitis .In present study 28.57%of allergic vasculitis showed lymphocytic infiltrate.this study compared with Gupta et al(2009)in which 12%cases showed lymphocytic vasculitis.

In present study 14.28%cases of allergic vasculitis showed mixed type of infiltrate with neutrophils and lymphocytes .In present study 75%cases of Henoch-schonleinpurpura had leukocytoclastic vasculitis and 25%cases had lymphocytic vasculitis .Mittal et al[11](1996)have reported 22%cases of leukocytoclasticvasculitis and 33%of lymphocytic vasculitis.In present study a single case of urticarial vasculitis had leukocytoclasticvasculitis picture.The higher incidence of leukocytoclasticvasculitis picture is seen in allergic vasculitis,Henoch-schonleinpurpura and in urticarial vasculitis.In present study 6 cases (100%)of erythema nodosum had lymphocytic vasculitis.Mittal et al 1996,85.7%cases of Erythema nodosum had lymphocytic infiltration.

VI.summary

1. In present study the incidence of cutaneous vasculitis was 0.2% of total out patient of dermatology .
2. There was higher incidence in females than males with a ratio 1.8:1
3. Palpable purpura was most common morphological presentation 72%
4. Allergic vasculitis was most common clinical presentation 56% followed by henoch-schonleinpurpura, erythema nodosum,urticarial vasculitis
5. Drugs were common etiological agents accounting for 31.7% in allergic vasculitis
6. In henoch-schonleinpurpura 75%cases shown infectious etiology
7. In erythema nodosum , tuberculosis was the major etiological agent accounting for 50% cases
8. Connective tissue disease accounted for 14.28% in present study causing cutaneous vasculitis

9. Idiopathic cases in allergic vasculitis accounted for 14.28%, and 33.3% in erythema nodosum
10. Urticarial vasculitis accounted for 11.11% cause could not be found
11. Histopathological examination of all cases shown leukocytoclasticvasculitis in majority followed by lymphocytoclasticvasculitis

VII.Conclusions

The following conclusions can be drawn from the clinico-patho- etiological study of cutaneous vasculitis

1. Drugs turned out be commonest causative agent in present study particularly NSAIDs like paracetamol, ibuprofen,diclofenac.patch test with offending drug may be helpful in knowing the causative drug.
2. hence avoiding the offending drug can prevent the vasculitis
3. Infections seem to be an important etiological factor of allergic vasculitis in present study
4. Streptococcal infection in allergic vasculitis and tuberculosis in erythema nodosum turned out to be major etiological agents
5. All cases of allergic vasculitis and erythema nodosum screened for evidence of streptococcal and tuberculosis infection
6. Connective tissue disease seem to be an another important etiological factor of allergic vasculitis in present study . hence all patients should be screened thoroughly for evidence of connective tissue disease.
7. histopathologically, leukocytoclasticvasculitis accounts majority of cases.

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