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Original Research Paper

Pathology

HISTOPATHOLOGICAL STUDY OF THE CASES OF VASCULITIS AT A TERTIARY HOSPITAL DURING A PERIOD OF 1MONTH

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ABSTRACT

Background: Clinically vasculitis can present with a wide array of morphologies which include urticaria, purpura, hemorrhagic vesicles, ulcers, nodules, livedo, infarcts, and/ or digital gangrene. The classification of cutaneous vasculitis is best approached morphologically by determining vessel size and principal inflammatory response. These histological findings when coupled with direct immunofluorescence examination, Antineutrophilic Cytoplasmic Antibodies (ANCA) status and findings from work-up for systemic disease, allow for specific diagnosis, and ultimately, more effective therapy. A prospective observational study was conducted which included 5 patients for a duration of 1 month. The demographic data like age, sex and detailed clinical history like site, size, morphology, duration of lesion, significant medical history, investigations and clinical diagnosis were noted. The histopathological examination of skin biopsy was done on Hematoxylin and Eosin (H and E) stains and Periodic acid-Schiff (PAS) stain in a few cases. Out of 6 cases, majority of the patients were in the age group of 21-30 .Most common site of lesion was lower extremities . On histopathological examination, most common type of vasculitis found was leukocytoclastic vasculitis and eosinophilic vasculitis . The histopathologic examination of skin biopsy plays a valuable role in the process of arriving at the final diagnosis, knowing the severity of the lesion and confirming the clinical diagnosis of vasculitis.

KEYWORDS : Skin biopsy, Histopathological examination, vasculitis.

INTRODUCTION:

Vasculitis refers to inflammation of the blood vessels leading to tissue destruction with or without organ damage. Vasculitis is classified as small vessel, medium vessel or large vessel vasculitis[1] and maybe either idiopathic or associated with an underlying pathology/disease. Small vessel vasculitis can be seen secondary to systemic vasculitides such as Anti-neutrophil Cytoplasmic Antibody (ANCA) associated vasculitis (Microscopic polyangiitis, Granulomatosis with polyangiitis or Eosinophilic granulomatosis with polyangiitis), Behçet's disease, and Cogan's syndrome. Immune complex-mediated small vessel vasculitis can be seen in rheumatoid arthritis, systemic lupus erythematosus, Sjogren syndrome, Henoch-Schönlein purpura, cryoglobulinemic vasculitis, Hypocomplementemic urticarial vasculitis, and cutaneous leukocytoclastic angiitis, formerly known as hypersensitivity vasculitis. Other causes of small vessel vasculitis or leukocytoclastic vasculitis include drug-induced vasculitis, paraneoplastic vasculitis, and infection associated vasculitis (hepatitis B, hepatitis C, syphilis).

Leukocytoclastic vasculitis is a small vessel vasculitis characterized histopathologically by immune complex-mediated vasculitis of the dermal capillaries and venules. Cutaneous leukocytoclastic vasculitis is usually confined to skin with rare extracutaneous manifestations in less than 30% of the cases. Key clinical features of cutaneous leukocytoclastic angiitis include palpable purpura, lower extremity location, small vessel involvement.[2][3][4] If leukocytoclastic vasculitis is suspected, a punch biopsy should be performed with direct immunofluorescence studies. If no systemic symptoms are present, laboratory testing including C-reactive protein, complete blood count (CBC), basic metabolic panel, liver function tests, and urinalysis should be done as well. If there is a concern for systemic involvement, a more extensive workup needs to be performed. Most cases of idiopathic cutaneous small-vessel vasculitis cases are self-limited with 90% resolving in weeks to months of onset. In persistent vasculitis, treatment depends on the severity of disease and can range from oral corticosteroids to various steroid-sparing agents.[5][6]

On discovering the etiology it is found to be idiopathic up to 50% of the cases. Infections and drugs are the most common triggers for secondary leukocytoclastic vasculitis.[7] It can be seen secondary to underlying systemic autoimmune diseases, chronic infections, and malignancies as well. Post-infectious leukocytoclastic vasculitis is most commonly seen after upper respiratory tract infection caused by streptococcus. Other infectious triggers include a variety , but are not limited to, *Mycobacterium*, *Staphylococcus aureus*, *Chlamydia*, *Neisseria*, and HIV. Some of the chronic infections such as hepatitis B, hepatitis C, and syphilis can be associated with leukocytoclastic vasculitis as well. Several drugs have been associated with leukocytoclastic vasculitis where the onset is typically noted 1 to 3 weeks after drug initiation. These include, but are not limited to, beta-lactams, erythromycin, clindamycin, vancomycin, sulfonamides, furosemide, allopurinol, NSAIDs, amiodarone, gold, thiazides, phenytoin, beta-blockers, TNF-alpha inhibitors, selective serotonin reuptake inhibitors, metformin, warfarin, valproic acid, among many others. Neoplastic or hematologic triggers of leukocytoclastic vasculitis include, but are not limited to lymphomas, leukemias, visceral tumors such as intestinal adenocarcinoma and lung cancer. Systemic diseases including connective tissue diseases (systemic lupus erythematosus, Sjogren syndrome), inflammatory bowel disease, Behcet disease, and rheumatoid arthritis cryoglobulinemic vasculitis, Henoch-Schönlein purpura (HSP), Hypocomplementemic urticarial vasculitis are also associated with leukocytoclastic vasculitis.[8]

The annual incidence of biopsy-proven leukocytoclastic vasculitis is approximately 45 per million individuals. The epidemiology of leukocytoclastic vasculitis varies with the underlying etiology. Leukocytoclastic vasculitis occurs in all ages and both genders; however, it typically presents in adults. However, HSP which is also a type of vasculitis is usually seen in children and young adults with an incidence of up to 270 cases per million children per year with a slight male predominance.

Pathophysiology:

The pathogenesis of leukocytoclastic vasculitis involves immune complex deposition in small vessel walls in addition to activation of the complement system. Neutrophils are

recruited, and injury to vessel walls ensues with secondary exudation of erythrocytes, fibrin, and serum. Fibrinoid necrosis of small vessel walls will be noted secondary to lysosomal enzymes such as collagenases and elastases as well as reactive oxygen species. Lymphokines aid in the evolution of the clinical findings as well. IL-1, IL-6, IL-8, and tumor necrosis factor are increased in circulation. Turbulence and increased venous pressure present in the lower extremities can elucidate why leukocytoclastic vasculitis commonly tends to occur on the legs.[9]

Histopathological Findings:

The histopathologic features of leukocytoclastic vasculitis will vary based on the time frame of the vasculitis. Fresh lesions biopsied within the 1st 18-24 hours of onset, from a nonulcerated site have the highest yield with most diagnostic findings. On light microscopy, findings of vessel wall destruction by the infiltration of inflammatory cells within and around the vessel wall can be seen. Classically leukocytoclastic vasculitis demonstrates neutrophil infiltration in the small vessel walls. The neutrophils undergo degeneration, known as leukocytoclasis with nuclear dust (karyorrhexis). Fibrinoid necrosis of the vessel walls can be apparent around the vasculature. Extravasation of red blood cells can be present in the dermis as well. In drug-related cases, eosinophils are often noted in the dermis. Older lesions especially those more than 48 hours old can demonstrate lymphocytic infiltration.

MATERIALS AND METHODS:

A prospective study was conducted to assess histomorphological features of cutaneous vasculitis. In a period of 1 month of the study total 35 skin biopsy specimens were received of which 5 were of cutaneous vasculitis. Detailed clinical history like age, sex, site, duration of the lesions, size of the lesions, significant medical history and clinical diagnosis were noted from histopathology requisition forms and medical records. Histopathological examination of skin biopsies was done on Hematoxylin and Eosin stains and Periodic acid-Schiff stain in a few cases. The study had inclusion and exclusion criteria as follows- Inclusion criteria :All skin biopsy specimens with clinical suspicion or diagnosis of cutaneous vasculitis and patients of all age groups and either gender. Exclusion criteria- Skin biopsy specimens with clinical diagnosis other than cutaneous vasculitis and inadequate / inappropriately preserved biopsy specimens.

OBSERVATION AND RESULTS:

Case 1:

A punch biopsy from the palm of 38 year old male was received with clinical impression of ? Secondary syphilis or erythema multiforme. The tissue on gross examination was 0.3x0.2x0.1 cm, greyish white and soft to firm in consistency.
Histopathology revealed multiple and serial sections studied from totally submitted specimen labeled as punch biopsy from palm reveal full thickness skin biopsy comprising of epidermis, dermis and sub cutis. Epidermis shows hyperkeratotic parakeratosis, spongiosis. Papillary dermis shows focal dermal edema with dense perivascular and periadnexal lymphocytic inflammatory infiltrate along with proliferating capillary sized blood vessels and focal destruction of vessel walls.

No evidence of granuloma/bacterial colonies/regular acanthosis/alternating zones of hyper and hypogranulosis. Histomorphological features suggestive of Small vessel vasculitis

Case2:

A skin biopsy of 37 year old male who had urticarial vasculitis on his back in a known case of pityriasis rosea. The tissue on gross examination was 0.6x0.5x0.4 cm, greyish white and soft to firm in consistency.
Histopathology revealed full thickness skin biopsy showing epidermis, dermis and subcutaneous tissue. Epidermis comprising of stratified squamous epithelium with focal follicular plugging. Dermis reveal mild dermal edema along with perivascular and interstitial mixed cell inflammatory infiltrate comprising of lymphocytes, plasma cells, few eosinophils and occasional neutrophils. There is lymphocytic vasculitis and dilatation of blood vessels lined by plump endothelial cells and reveals chronic cell inflammatory infiltrate comprising of lymphocytes in and around the vessel wall.

No evidence of mounds of parakeratosis/ spongiosis as seen in pityriasis rosea in totally submitted tissue.

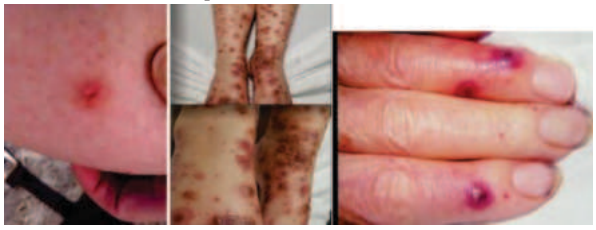
Case 3:

A skin biopsy from the leg of 28 year old female where the dermatologists suspected ?Atypical erythema multiformis or urticarial vasculitis secondary to infection. The tissue on gross examination was 0.7x0.3x0.1 cm, greyish white and soft to firm in consistency.

Histopathology reveal full thickness skin biopsy comprising of epidermis, dermis and subcutis. The epidermis shows mild hyperkeratosis, focal spongiosis, focal flattening and basal layer vacuolar degeneration. The dermis shows mild edema, perivascular inflammatory infiltrate composed of lymphocytes, eosinophils and few neutrophils. Periadnexal sparse lymphocytic infiltrate seen. Subcutis is unremarkable.

No evidence of granuloma/subepidermal vesiculations /atypia/malignancy in the sections studied.

Histomorphological features were suggestive of Urticarial vasculitis with eosinophils



Case 4:

A 38 year old female had complaints of red raised lesion over the body - B/L lower limbs,upper limbs Probable clinical diagnosis- ?Maculopapular rash - to rule out ? type 1 reaction in BTH ; to rule out EM minor ? Sweets syndrome .

The tissue on gross measured 0.1x0.1x0.1 cm each, grayish brown, soft to firm. Totally submitted.Histopathology reveals full thickness skin biopsy composed of epidermis, dermis and subcutis. Epidermis shows hyperkeratosis, spongiosis and focal acanthosis. The dermis shows perivascular lymphoplasmacytic inflammatory infiltrate and destruction of the small capillaries with occasional neutrophilic infiltration of the vessel wall with extravasation of RBCs. The deeper dermis and subcutis is unremarkable.

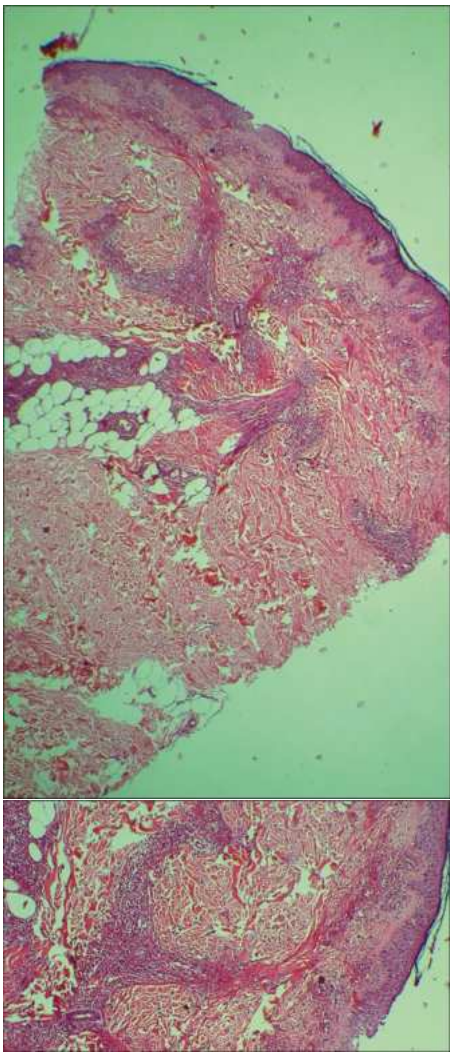
No evidence of epithelioid cell granuloma/ necrosis/ atypia/ malignancy in present sections studied. Histomorphologic features are suggestive of Drug induced vasculitis.

Case 5:

The tissue on gross measured 0.3x0.3x0.2cm, greyish white, soft. Histopathology revealed epidermis, dermis and subcutaneous tissue. Epidermis is keratinised stratified squamous epithelium showing thinning of epidermis, flattening of rete ridges and vacuolar degeneration of basal layer with neutrophilic infiltrates in the epidermis. Dermis shows extravasation of RBCs and perivascular inflammatory

infiltrate composing of lymphocytes, histiocytes and few neutrophils along with endothelial swelling, karyorrhexis. Capillaries also showing karyorrhexis and endothelial swelling. No evidence of granuloma/atypia/malignancy in the present sections studied.

Histomorphological features are suggestive of cutaneous vasculitis.



CONCLUSION:

Cutaneous vasculitis is a poorly understood entity, because of its variable clinical manifestations and its overlap with various infections, connective tissue disorders and malignancies. Hence immunoflorescence with histopathological correlation remains the gold standard.

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