

Skin Involvement in AAV

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ANCA Associated Vasculitis (AAV) are classified as granulomatous polyangitis (GPA), microscopic polyangitis (MPA) ve and eosinophilic granulomatosis with polyangitis (EGPA). This group of vasculitits is quite rare, they involve various organ systems and cause severe systemic vasculitis. Skin involvement is a common finding in AAV, it is approximately found in %47 of GPA, %44 of MPA and %40 in EGPA [1-3].

Unlike immune complex vasculitis, vascular damage develops directly in AAVs. Vascular damage is mediated by neutrophils, therefore AAVs are also called “pauci-immune” vasculitis. The formation of ANCA in this group of vasculitis also causes impairment in neutrophil apoptosis resulting in a long-term opportunity for autoantibody development.

The type and size of the vessels involved are taken into consideration in the classification of vasculitis, Small and medium sized vessels are involved in AAV and also small and medium-sized arterioles in the upper layers of the skin and in the deeper subcutaneous tissues are involved in AAVs. Therefore the clinical examination spectrum includes findings related to vasculitic involvement of these vessels [4].

Skin involvement rarely develops in large vessel vasculitis and is seen as diffuse necrosis of the skin. Livedo reticularis, retiform purpura, nodules, ulcers, infarcts and necrosis are observed in medium sized vessel vasculitis. Palpable purpura, macular purpura and urticarial papules are most commonly observed in small vessel vasculitis. Palpable purpura is the most common cause of clinical signs of small and medium vessel involvement in AAV. When evaluating a case with a suspicion of vasculitis for the presence of palpable purpura, the patient should be assessed systemically, laboratory tests and ANCA tests should be performed, biopsy and histopathological examination is required and additional skin sample should also be taken for direct immune fluorescence analysis method that determines the accumulation of immune reactant /deposits. Additional studies should be conducted for classification [5-6].

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The most common vasculitic skin findings in MPA are palpable purpura, erythematous macules, urticarial or purpuric papules, livedo racemosa, ulcers and splinter hemorrhages. Small vessel vasculitis is observed in histopathological samples, no granuloma is observed.

The most common vasculitic skin findings in GPA are palpable purpura, sensitive micropapular gingiva (strawberry gingiva), oral ulcers, palisaded neutrophilic granulomatous dermatitis, subcutaneous nodules and pyoderma gangrenosum-like ulcers. Perivascular granulomas and leukocytoclastic vasculitis are observed in histopathological examination. Oral mucosa lesions may predominantly occur in GPA. In some cases, oral mucosal lesions can constitute 50-60% of skin lesions, oral mucosal involvement may be the first symptom in 5-6% of GPA. Hyperplastic gingivitis, mature strawberry like appearance of the hyperplastic anterior gingiva, painful ulcers in the palate or gingiva, mobility of the teeth, non-healing wounds after tooth extraction, cranial nerve paralysis and parotid gland swelling are important oral mucosal findings of GPA that should be kept in mind [7].

The most common vasculitic skin findings in EGPA are palpable purpura, palisaded neutrophilic granulomatous dermatitis, subcutaneous nodules, urticarial plaques, livedo racemosa, retiform purpura and ulcers. Extravascular eosinophils and granulomatous inflammation are observed in histopathology besides small-medium vessel vasculitis. In addition to vasculitic skin findings, non-vasculitic skin findings are frequently observed in EGPA. These include severe pruritus, blisters, erythema multiforme-like skin lesions, urticaria and angiodem-like lesions; infiltrating edematous areas can be observed [8].

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In a recent review on cutaneous involvement in AAVs, 1184 AAV cases were evaluated and 35% (N = 414) were found to have skin findings. While the rate of cutaneous symptoms in EGPA was 47%, it was 34% in GPA and 28% in MPA. Skin findings were observed more frequently in AAVs with cANCA (+) and ANCA (-) than pANCA (+) AAVs [9].

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While the most common skin finding in all AAVs is petechiae-purpura, additional skin findings frequently observed in EGPA are pruritus, urticaria, maculopapular rash which were significantly higher than other AAVs.

Livedo reticularis and livedo racemosa were observed more frequently in MPA than other AAVs. While painful skin lesions and ulceration were at similar rates in EGPA and GPA, these findings were observed less in MPA. In the same study, comparison of AAV patients with and without skin lesions revealed significant differences. Findings such as pulmonary, renal, neurological, musculoskeletal system, gastrointestinal (GIS) involvement, mononeuritis multiplex, > 1g / lt proteinuria in 24-hour urine were observed to occur more frequently in the presence of skin lesions in GPA. In the presence of skin lesions in EGPA, findings such as renal, neurological, musculoskeletal involvement, >30% increase in creatinine, >25% decrease in creatine clearance, mononeuritis multiplex, sensory neuropathy were observed to occur more frequently. Interestingly, in the presence of skin lesions in MPA, it has been shown that pulmonary involvement, increased creatine, decreased creatine clearance and glomerulonephritis were less likely to develop. Similarly, patients with (+) pANCA and skin lesions have been shown to less likely develop pulmonary and renal disease. Patients with (+) cANCA and skin lesions were followed up with more renal, pulmonary, neurological, GIS and musculoskeletal system involvement. It has been determined that patients with AAV with skin lesions and (-) ANCA have more pulmonary, neuromuscular, musculoskeletal and GIS involvement. When patients with AAV with and without skin involvement are compared in terms of severe systemic involvement criteria such as scleritis, sensorineural hearing loss, mesenteric ischemia, alveolar hemorrhage, and creatinine increase above 30%, these rates were higher in cases accompanied by skin findings: 70% -55% in GPA, 71% -58% in EGPA 56% -38% in ANCA (-) patients and 75% -62% in cANCA (+) patients. Based on these findings, it was concluded that the presence of skin involvement symptoms such as petechiae-purpura are associated with severe systemic involvement [9].

As a result, the skin is an organ frequently involved in AAVs; approximately 35% of the cases have skin involvement. Cutaneous symptoms are common and variable in GPA, EGPA and MPA and 50% of the cases with skin involvement have more than 1 cutaneous symptom. The most important and common cutaneous finding is petechiae and purpura and should be considered a sign of systemic vasculitis. Cutaneous involvement is observed more frequently in EGPA and GPA than MPA and there is a significant relationship between skin involvement and systemic involvement severity in these diseases. Skin involvement increases the risk of systemic involvement of the disease. In EGPA and ANCA (-) patients, non-vasculitic skin findings such as itching, urticaria, maculopapular rash can be observed.

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