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Relapsing Hepatitis B (HBV)-Associated Vasculitis with Features of Polyarteritis Nodosa (PAN) and cANCA-Associated Vasculitis

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Abstract

HBV-associated vasculitis typically manifests as the medium vessel vasculitis, PAN. HBV-associated PAN (HBV-PAN) is ANCA (-), without glomerulonephritis (GN) or pulmonary involvement; relapse does not occur after successful HBV seroconversion. We describe a unique case of HBV-associated vasculitis with features of a small and medium sized overlap vasculitis and atypical long-term course.

The patient is a 60-year-old male with hypertension and HBV who initially presented with abdominal pain and scrotal swelling. Abdominal angiogram revealed beaded morphology and aneurysms involving mesenteric, hepatic, and intraparenchymal renal arteries. Hepatitis B core antibody, cANCA, PR3, and rheumatoid factor were (+). He received pulse steroids and Cytoxan for treatment of PAN and Entecavir for HBV, resulting in resolution of symptoms. Serum Cr rose from 0.8mg/dL to 2.0mg/dL during the first 2 months of treatment, and then remained stable. Multiple urinalysis (UA) measurements were negative. Two years later, the patient developed abdominal pain, orchitis, hemoptysis, and acute kidney injury (serum Cr of 11mg/dL). HBV viral load was negative. UA showed 3+ blood and 3+ protein. Renal biopsy displayed pauci-immune crescentic GN with active crescents involving ~ 50% of the glomeruli (Figure 1, Jones stain). Two arteries had evidence of past arteritis with elastic lamina disruption (Figure 2, EVG stain); acute necrotizing arteritis was not present. The patient recovered renal function (most recent serum Cr=3.2mg/dL) after therapy with pulse steroids, plasma exchange, Rituxan, and Cytoxan.

Our patient with HBV-associated vasculitis initially presented with manifestations of medium vessel involvement, but with an unusual feature of cANCA/PR3 seropositivity. Relapse occurred 2 years later with PAN symptoms (orchitis, severe abdominal pain) and evidence of ANCA-associated small vessel vasculitis (GN, hemoptysis). While the initial trigger may have been HBV, the vasculitis later became self-perpetuating as it recurred during a time when there was no HBV viremia. Patients with HBV-PAN who are ANCA+, should be closely followed because they could be at higher risk of vasculitis relapse.

Keywords: HBV viremia; Vasculitis; Microscopic polyangiitis; Hepatitis-B; Abdominal angiogram; Granulomatous

Abbreviations: PAN: Polyarteritis Nodosa; MPA: Microscopic Polyangiitis; ANCA: Anticytoplasmic Antibodies; Anti GBM: Anti-glomerular Basement Membrane

Introduction

Chapel Hill Classification has classified vasculitis on basis of size of vessels which differentiated many vasculitis entities from Polyarteritis Nodosa (PAN) including Microscopic polyangiitis (MPA) [1]. PAN is necrotizing medium vessel vasculitis involving medium to small sized arteries that can involve any organ of body characteristically sparing lungs. MPA involves small vessels -arterioles, venules and capillaries which can also involve lungs. MPA is anticytoplasmic antibodies (ANCA) associated vasculitis; however, 10-20 % cases of PAN can have positive ANCA [2]. In the literature, there have been no reported cases of simultaneous occurrence of the two vasculitis. Interestingly, there have been increasing reports of ANCA associated vasculitis involving larger arteries challenging the size-based classification of vasculitis [3]. Typically some reported cases the large vessel symptoms preceded the small vessel symptoms. We report a case of simultaneous occurrence of c-ANCA associated vasculitis in a hepatitis-B patient already with diagnosed with PAN which can be viewed as primarily as ANCA associated vasculitis manifesting first as a large vessel vasculitis followed by involvement of small vessels. Moreover, none of the case has been reported with hepatitis B involving PAN and MPA; although there is one case report of Wagner's and PAN in a patient with hepatitis B infection.

Case

A 60-year-old male with hypertension and HBV who initially presented with abdominal pain and scrotal swelling. Abdominal

angiogram revealed beaded morphology and aneurysms involving mesenteric, hepatic, and intraparenchymal renal arteries. Hepatitis B core antibody, c-ANCA, PR3, and rheumatoid factor were (+). He received pulse steroids and Cytoxan for treatment of PAN and Entecavir for HBV, resulting in resolution of symptoms. Serum Cr rose from 0.8mg/dL to 2.0mg/dL during the first 2 months of treatment, and then stabilized at new baseline 1.7-1.9mg/dl. Two years later, the patient developed generalized fatigue, malaise, abdominal pain, orchitis, hemoptysis, uncontrolled hypertension and acute kidney injury (serum Cr of 11mg/dL). On presentation he was hemodynamically stable, blood pressure 160/88mmHg. Laboratory workup significant for elevated inflammatory markers ESR (erythrocyte sedimentation rate) and CRP (c-reactive protein); drop in hemoglobin from 15gm/dl to 10.5g/dl. Urinalysis with hematuria-(3+, >100 BCs); new onset proteinuria>3gm/day; fractional excretion of sodium (FeNa) 2.2% consistent with intrinsic renal disease. HBV viral load was negative. Positive c-ANCA > 1:640 titer; however, immunoglobulin levels, p-ANCA, complement levels, albumin was within normal limits; with negative ANA, anti-glomerular basement membrane antibody (anti GBM) and M-spike. Nasal biopsy was negative for granulomatous polyangiitis. Renal biopsy displayed pauci-immune crescentic glomerulonephritis with active crescents involving ~ 50% of the glomeruli - consistent with ANCA vasculitis (Figure 1, Jones stain). Two arteries had evidence of past arteritis with elastic lamina disruption-consistent with PAN (Figure 2, EVG stain); acute necrotizing arteritis was not present. He was started on intravenous pulsed dose of steroid for 3 days along with plasma exchange for 5 days; later transitioned to oral prednisone 60mg daily along with rituximab. Tenofovir was restarted because of the of hepatitis B virus reactivation risk. Renal function recovered with aggressive induction regimen and never required hemodialysis. Later, he was placed on cyclophosphamide for maintenance therapy for ANCA vasculitis.

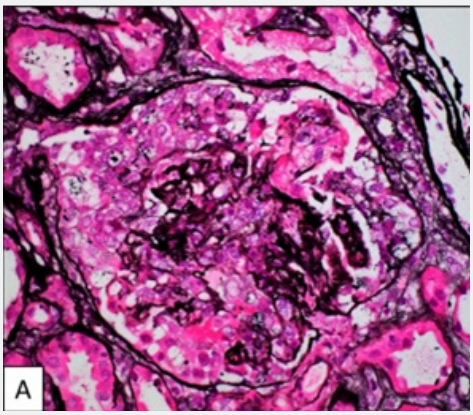

Figure 1: (Jones stain) Crescentic glomerulonephritis - consistent with ANCA vasculitis.

Discussion

Polyarteritis Nodosa (PAN) encompassed many vasculitis presentations previously including Microscopic polyangiitis, until formal classification by Chapel Hill Consensus Conference [1]. PAN is a systemic necrotizing vasculitis involving the medium sized muscular arteries and categorically does not involve small vessels like arterioles, venules and capillaries; hence no glomerulonephritis. MPA is differentiated from the PAN by involvement of small vessels, usually characterized by non- granulomatous crescenteric glomerulonephritis, pauci-immune in nature. Within reported literature, there is no report of simultaneous occurrence of the two vasculitis. We report a case of de-novo diagnosis of MPA in a patient with PAN who had been previously treated and on remission maintenance. It is debatable though that whether these two are separate vasculitis entities or continual spectrum of ANCA associated vasculitis.

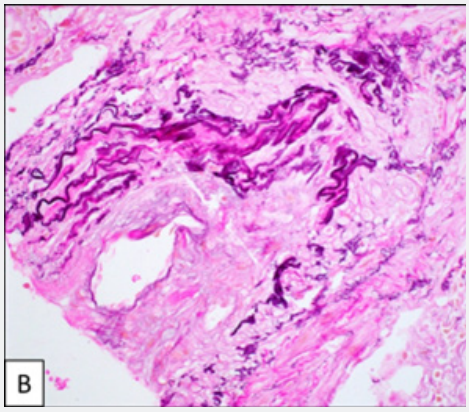

Figure 2: (EVG stain) Elastic lamina disruption- consistent with PAN- Absent acute necrotizing arteritis.

Polyarteritis nodosa can manifest as systemic PAN involving multiple organs or isolated PAN, however, interestingly spares the lungs. It has a well-established association with chronic hepatitis B infection. It involves trans-mural inflammation of artery sparing small vessels, with lesions at variant stages, leucocytoclasis, lacking granulomas and eventually leading to fibrinoid necrosis along with aneurysm formation. Therefore, involvement of small vessels with a glomerulonephritis like picture points to a coexistent disease process as in our case. The involvement of kidney by PAN leads to reno-vascular hypertension, acute renal failure and mildly active urinary sediment [2,4].

ANCA associated vasculitis involving both small and large vessels is an emerging entity of vasculitis which have patients with different demographic characteristics as compare to traditional large vessel vasculitis patients. Large vessel symptoms can precede the small vasculitis symptoms. The treatment outcomes and prognostic factors for these entities need to be established yet. Chirinos et al. [3] in their literature review of ANCA associated with large vessel involvement have enlisted carotid and aortic vasculitis with high ANCA titers with normalization of antibody titers on treatment [3]. Similarly, there have been case reports with ANCA associated vasculitis involving large and medium sized arteries such as the superior and inferior mesenteric arteries with aneurysm formation

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[5]; gastroduodenal and iliac arteries along with small vessels (glomerulonephritis and pulmonary capillaritis) in the same patient. Interestingly there seems to be a correlation between ANCA titers and disease activity with lowering of ANCA levels post treatment advocating direct role of ANCA in pathogenesis of the vasculitis [6].

HBV infection has been associated with PAN and immune complex associated vasculitis. However, interestingly our case points out an association of HBV infection immune mediated process with ANCA associated vasculitis. There has been a case report of HBV mediated c-ANCA vasculitis leading to subarachnoid hemorrhage, myelitis and membranous neuropathy [7]. In a study involving patients with chronic hepatitis B infection, c-ANCA levels were found to be significantly elevated pointing to a potential role of the antibody in vasculitis manifestations associated with the chronic viral infection [8]. Therefore, there is possibility with hepatitis B infection being the driving factor in systemic vasculitis which can manifest both as PAN and ANCA vasculitis associated features. Likewise, there has been a case report of Wagner's granulomatosis and PAN in a patient with hepatitis B infection which supports our notion of coexistence of these two vasculitis entities, however, either these are a continuous spectrum of hepatitis B mediated vasculitis or separate vasculitis entities with co-occurrence can be debated [9].

MPA is classified as small vessel ANCA associated vasculitis [1]. It can manifest as generalized symptoms of fatigue, malaise, weight loss and decreased appetite. The most common manifestation is palpable purpura [10]. In severe cases, it may have renal-pulmonary picture. The typical presentation is of nephritis like picture with urinalysis showing hematuria with dysmorphic red blood cells, proteinuria <3g/day and biopsy with pauci-immune crescenteric non-granulomatous glomerulonephritis with lesions at different stages. ANCA can be positive in 10-20 % cases of PAN as well, which adds to the importance of biopsy for definite diagnosis [2]. So, in our case the diagnosis of MPA was made in concurrence with PAN because of pulmonary symptoms; presence of proteinuria, hematuria, active urine sediments; pauci-immune glomerulonephritis on kidney biopsy (consistent with MPA) coupled with fibrosis and some active inflammation involving arcuate artery (consistent with PAN).

Remission can be achieved with steroids alone or in combination with cyclophosphamide- for severe disease presentation [10]. In cases with severe renal vasculitis defined as serum creatinine >5.8mg/dL, the addition of plasmapheresis improved the renal recovery as compared to intravenous steroids, thus decreasing the progression to ESRD [11,12]. This approach was utilized in our case. In ANCA vasculitis resistant to remission with cyclophosphamide, rituximab has been reported to successfully induce remission [13]. However, it must be used with caution in patients with history of hepatitis B infection as in our case. Once the remission is achieved, patient can be transitioned to azathioprine or methotrexate for maintenance therapy usually for 18 months in total of immunosuppression including cyclophosphamide duration [14]. Renal recovery depends on the serum Creatinine at presentation and degree of arterial sclerosis on renal biopsy [15].

PAN can have relapse, although less frequent as compared to small vessel vasculitis. The relapse has mainly been reported in cases of non-HBV PAN (5-year relapse rate 24%) and cutaneous PAN [16]. The relapse or recurrence may manifest in previously affected organ or may involve a new one. However, in our case the new onset rapidly progressive glomerulonephritis cannot be explained by the relapse of PAN so a renal biopsy was done which showed a histopathology picture consistent with MPA which is a rare concomitant occurrence. Therefore, in cases of new onset renal insufficiency in PAN, along with relapse and the renal insufficiency secondary to vascular compromise, the differential of a new onset vasculitis should be kept in mind.

References

1. Jennette JC, Falk RJ, Andrassy K, Bacon PA, Churg J, et al. (1994) Nomenclature of systemic vasculitides. Proposal of an international consensus conference. Arthritis Rheum 37(2): 187-192.
2. Sakaguchi Y, Uehata T, Kawabata H, Niihata K, Shimomura A, et al. (2011) An autopsy-proven case of myeloperoxidase-antineutrophil cytoplasmic antibody-positive polyarteritis nodosa with acute renal failure and alveolar hemorrhage. Clin Exp Nephrol 15(2): 281-284.
3. Chirinos JA, Tamariz LJ, Lopes G, Del Carpio F, Zhang X, et al. (2004) Large vessel involvement in ANCA-associated vasculitides: report of a case and review of the literature. Clin Rheumatol 23(2): 152-159.
4. Branagan NM, Higgins SP, Halim SA, Le TH (2009) Systemic polyarteritis nodosa mimicking pyoderma gangrenosum in a rare association with small lymphocytic leukaemia/chronic lymphocytic leukaemia. Clin Exp Dermatol 34(5): e127-e129.
5. Abissegue Y, Lyazidi Y, Arache W, Ouldsalek E, Chtata HT, et al. (2016) Multiple visceral artery aneurysms: an uncommon manifestation of antineutrophil cytoplasmic antibody vasculitis. Ann Vasc Surg 34: 271. e9-271.e13.
6. Villacorta J, Crespo FD, Stanescu R, Juarez GM (2016) Large and Small vessel Severe Involvement in ANCA-Associated Vasculiitis. Journal of Vasculitis 2: 105.
7. Joshi U, Subedi R, Gajurel BP (2017) Hepatitis B virus induced cytoplasmic antineutrophil cytoplasmic antibody-mediated vasculitis causing subarachnoid hemorrhage, acute transverse myelitis, and nephropathy: a case report. J Med Case Rep 11(1): 91.
8. Calhan T, Sahin A, Kahraman R, Altunoz ME, Ozbakir F, et al. (2014) Antineutrophil cytoplasmic antibody frequency in chronic hepatitis B patients. Dis Markers 2014: 982150.
9. Gil E, Lutalo P, D'Cruz D (2011) Systemic vasculitis: a dual diagnosis? BMJ Case Rep 2011.
10. Kluger N, Pagnoux C, Guillevin L, Frances C, French Vasculitis Study G (2008) Comparison of cutaneous manifestations in systemic polyarteritis nodosa and microscopic polyangiitis. Br J Dermatol 159(3): 615-620.
11. de Groot K, Harper L, Jayne DR, Flores Suarez LF, Gregorini G, et al. (2009) Pulse versus daily oral cyclophosphamide for induction of remission in antineutrophil cytoplasmic antibody-associated vasculitis: a randomized trial. Ann Intern Med 150(10): 670-680.

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12. Jayne DR, Gaskin G, Rasmussen N, Abramowicz D, Ferrario F, et al. (2007) Randomized trial of plasma exchange or high-dosage methylprednisolone as adjunctive therapy for severe renal vasculitis. J Am Soc Nephrol 18(7): 2180-2188.

13. da Silva LS, de Campos KV, de Melo AK, de Brito DC, Braz AS, et al. (2015) Rituximab as an alternative for patients with severe systemic vasculitis refractory to conventional therapy: report of seven cases and literature review. Rev Bras Reumatol 55(6): 531-535.

14. Jayne D, Rasmussen N, Andrassy K, Bacon P, Tervaert JW, et al. (2003) A randomized trial of maintenance therapy for vasculitis associated with antineutrophil cytoplasmic autoantibodies. N Engl J Med 349(1): 36-44.

15. Hogan SL, Nachman PH, Wilkman AS, Jennette JC, Falk RJ (1996) Prognostic markers in patients with antineutrophil cytoplasmic autoantibody-associated microscopic polyangiitis and glomerulonephritis. J Am Soc Nephrol 7(1): 23-32.

16. Pagnoux C, Seror R, Henegar C, Mahr A, Cohen P, et al. (2010) Clinical features and outcomes in 348 patients with polyarteritis nodosa: a systematic retrospective study of patients diagnosed between 1963 and 2005 and entered into the French Vasculitis Study Group Database. Arthritis Rheum 62(2): 616-626.

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