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Appearance of ANCA – associated vasculitis under Tumor necrosis factor-alpha inhibitors treatment

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Summary

Background: Tumor necrosis factor-alpha inhibitors treatment is accosiated with several side effects. The most common are injection side reactions, headache, nausea and infections. The more rare are development of systemic autoimmune diseases.

Case Report: We describe two patients, who developed ANCA associated vasculitis during Tumor necrosis factor alpha inhibitors treatment. The diagnosis was confirmed by appropriate tissue picture, CT scan and laboratory findings.

Conclusions: Our case series are unique, because vasculitis appeared after many years of the treatment and during complete patient's remission of there main illness.

key words: **psoriatic arthritis • rheumatoid arthritis • systemic vasculitis • tumor necrosing factor alpha inhibitors**

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Background

Tumor necrosis factor alpha inhibitors (TNF-i) drugs have changed dramatically the management of Rheumatoid arthritis (RA), Psoriatic arthritis (PsA) and other inflammatory arthridities. This treatment is usually well tolerated. The most common side effects are injection side reactions, headache, nausea and infections [1]. With the continues use of this medicine and a longer follow up period, there is a growing number of reports describing a side effect of emergence of new autoimmune processes. Although rare, there are reports of anti-TNF-i induced systemic lupus erythematosus [2], cutaneous leukocytoclastic vasculitis[3], and antineutrophil cytoplasmic antibody (ANCA) associated systemic vasculitis (AASV) [4].

Herein, we report of two cases of AASV, developed in two patients – one with RA and the other with PsA, who have been treated with TNF-i.

Case Report

Case 1

A 58 years old woman has suffered from Rheumatoid Factor (RF) positive Rheumatoid Arthritis (RA) 13 years. During the last 7 years she has been treated with Methotrexate 15 mg/week and Etanercept 25mg twice a week. She has been in remission during the last 6 years. One year ago she presented with high C-reactive protein (CRP) and high Erythrocyte sedimentation rate (ESR), and without complains on joint pain. Her physical examination at this time was unremarkable. There was no active sinovitis in her joints, and no tenderness. Blood pressure was 130/81, blood tests revealed normal renal function, no anemia, negative ANA. Test for ANCA at this time was not done. Two months later she was hospitalized with clinical picture of acute renal failure, with creatinine level of 7.3 mg/dl. Blood serology revealed positive C-ANCA with high titer of proteinase 3 antibody, negative ANA and normal complement. Kidney biopsy showed segmental necrotizing glomerulonephritis, compatible with Granulomatosis with polyangiitis (Wegener's Vasculitis). The diagnosis of C-ANCA associated vasculitis was made. Etancercept treatment was discontinued and high dose prednisone therapy was initiated. Following treatment, her acute phase reactants normalized and ANCA titer decreased, but the patient developed end stage renal failure. The patient now treats with hemodyalisis and small doses of Prednisolone.

Case 2

A 52 years old man has suffered from Psoriatic Arthritis (PsA) for 10 years. He has been treated with Infliximab 5 mg/kg during the last 5 years. Two years ago he developed Bronchial asthma with nasal polyposis following later. Nine months ago he was hospitalized with clinical picture of pneumonia with palpable purpura on his lower extremities. Blood tests showed hypereosonophilia, and positive P-ANCA with high titer of myeloperoxidase antibody. Chest CT revealed infiltrates in both lungs. Skin biopsy revealed signs of leukocytoclastic vasculitis. Churg Strauss vasculitis diagnosis was made. Infliximab therapy was stopped and high dose Prednisolone treatment was introduced. After improvement in clinical, laboratory and radiological assessment, slow tapering of prednisone dose was initiated. Now, the patient receives only Methotrexate 15 mg per week as treatment for PsA.

Discussion

In our series, the first patient, with a history of RF positive RA, developed AASV with renal involvement. Rheumatoid vasculitis is a well known entity, and clinically manifests in 2–5% of patient with long standing Rheumatoid factor positive active RA. A renal disease, such as amyloidosis, glomerulonephritis, or vasculitis, also may be a complication of RA [5]. With the introduction of TNF-i treatment, other forms of vasculitis were noticed as well. There were several reported cases of biopsy proven renal vasculitis after TNF-i therapy. Thus, Stokes et al. [6] described 5 RA patients with vasculitis, of whom 2 patients treated with etanercept and infliximab developed pauci-immune necrotising crescentic glomerulonephritis. In 2006 Saint Marcoux and De Bandt [7] reported 10 cases of TNF-i induced systemic vasculitis. Seven patients in this group had necrotising vasculitis and 3 had glomerulonephritis.

Our second patient, with a history of PsA, had a clinical picture of Churg Strauss vasculitis and p-ANCA positivity. Systemic vasculitis among patients with PsA rarely occurs. There are only sporadic case reports describing patients with PsA and ANCA positive vasculitis in the literature [8]. Most cases are associated with pustular psoriasis, even though drugs are most common etiology [9]. Development of autoantibodies without any vasculitic manifestations is quite common phenomenon among Psoriasis patients, while positive ANCA is described in 8% of patients affected by psoriasis [10]. Whereas it seems, that patients with PsA, treated with TNF-i are more prone to develop systemic vasculitis, then patient on convencional treatment. In their interesting review, Ramos-Casals et al. report occurence of vasculitis triggered by TNF-i treatment among patients with immune mediated diseases. They describe 233 patients with TNF-i related vasculitis, of whom only 3 suffering from PsA [11].

New biological therapies have been developed to treat chronic inflammatory diseases, such as RA, ankylosing spondylitis, inflammatory bowel disease, PsA, and psoriasis. Their increasing use and efficacy can be confirmed by different national registries[12].

A few cases of vasculitis in patients receiving treatment with TNF-i have been published in the literature[13,14], mostly leukocytoclastic vasculitis. The mechanisms involved in putative TNF-i-induced vasculitis are uncertain. Guillevin et al. [15] suggest that TNF-i may form immune complexes, activate complement, and mediate inflammation by switching T helper cytokine response from type 1 to type 2. This new response may up regulate antibodies production, which is characteristic for vasculitis.

The diagnosis of drug induced AASV can be challenging, particularly in our case series because of long period of TNF-i therapy before the appearance of vasculitis. On the other hand, the rarity of AASV among patients with RA and PsA before the era of TNF-i treatment, and the increasing number of reports of this group of vasculitis with TNF-i treatment,

mean that causal relationship may be considered. In our patients, the clinical presentations, strongly positive ANCA and characteristic biopsy pictures, along with the exclusion of other possible causes, all support the diagnosis of AASV due to TNF-i treatment. Like in other drug induced vasculitis, cessation of TNF-i therapy can lead to improvement. Unfortunately, our patients' diseases required additional immunosuppressive treatment by high doses of steroids.

Conclusions

We have described here two patients with a rare complication of TNF-i treatment. Although the implication of vasculitis is serious, the risk of its development is very low. So, in our opinion, it should not influence the decisions to initiate TNF-i treatment in patients with inflammatory joints diseases. If vasculitis develops, the cessation of treatment is recommended, as in the other drug induced diseases, but may be insufficient to insure the resolution of vasculitis.

Competing interests

There were no competing interests and nothing to disclose.

Reference:

1. Alonso-Ruiz A, Pijoan JI, Ansuategui E et al: Tumor necrosis factor alpha drugs in rheumatoid arthritis: systematic review and metaanalysis of efficacy and safety. BMC Musculoskelet Disord, 2008; 9: 52
2. Williams VL, Cohen PR: TNF alpha antagonist-induced lupus-like syndrome: report and review of the literature with implications for treatment with alternative TNF alpha antagonists. Int J Dermatol, 2011; 50(5): 619–25
3. Fujikawa K, Kawakami A, Hayashi T et al: Cutaneous vasculitis induced by TNF inhibitors: a report of three cases. Mod Rheumatol, 2010; 20(1): 86–89
4. Simms R, Kipgen D, Dahill S et al: ANCA-associated renal vasculitis following anti-tumor necrosis factor alpha therapy. Am J Kidney Dis, 2008; 51(3): e11–14
5. Nakano M, Ueno M, Nishi S et al: Analysis of renal pathology and drug history in 158 Japanese patients with rheumatoid arthritis. Clin Nephrol, 1998; 50(3): 154–60
6. Stokes MB, Foster K, Markowitz GS et al: Development of glomerulonephritis during anti-TNF-alpha therapy for rheumatoid arthritis. Nephrol Dial Transplant, 2005; 20(7): 1400–6
7. De Bandt M, Saint-Marcoux B: Tumour necrosis factor alpha blockade and the risk of vasculitis. Ann Rheum Dis, 2006; 65(11): 1534–35
8. Chewoolkar V, Bichile LS, Jain N, Raj P: Psoriatic arthritis with ANCA-positive vasculitis: a rare association. Int J Rheum Dis, 2008; 11(2): 192–94
9. Wong SS, Marks R: Cutaneous vasculitis in psoriasis. Acta Derm Venerrol, 1994; 74: 57–60
10. De Bandt M, Meyer O, Haim T, Kahn MF: Antineutrophilic cytoplasmic antibody in Rheumatoid arthritis. Br J Rheumatol, 1996; 35: 38–43
11. Ramos-Casals M, Brito-Zeron P, Minoz S et al: Autoimmune Diseases Induced by TNF-Targeted Therapies. Analysis of 233 Cases. Medicine, 2007; 86: 242–51
12. Curtis JR, Jain A, Askling J et al: A comparison of patient characteristics and outcomes in selected European and U.S. rheumatoid arthritis registries. Semin Arthritis Rheum, 2010; 40(1): 2–14.e1
13. Mcilwain L, Carter JD, Bin-Sagheer S et al: Hypersensetivity vasculitis with leukocytoclastic vasculitis secondary to ifliximab. J Clin Gastroenterol, 2003; 36: 411–13
14. Jarreff SJ, Cunnane G, Canaghan PG et al: Anti-tumor necrosis factor-alpha therapy-induced vasculitis: case series. J Rheumatol, 2003; 30: 2287–91
15. Guillevin L, Mouthon L: Tumor necrosis factor-alpha blocade and the risk of vasculitis. J Rheumatol, 2004; 31: 1885–87