

Association Between Churg Strauss Syndrome and Vitamin D Deficiency: A Myth or Truth? A Rare Case Report

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Received date: April 15, 2016; Accepted date: May 15, 2016; Published date: May 21, 2016

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Abstract

Churg-Strauss syndrome is a vasculitis of medium to small sized vessels. Diagnosis is mainly clinical with findings of asthma, eosinophilia, rhinosinusitis and signs of vasculitis in major organs.

Vitamin D is thought to be important for maintaining normal function of many non-skeletal tissues such as muscle (including heart muscle), immune function, and inflammation as well as cell proliferation and differentiation.

The authors are reporting a case of 56 yrs. old male, a known patient of reactive airway disease who was diagnosed to have Churg Strauss Syndrome associated with severe Vitamin D deficiency and degenerative bone disease. There is a deficiency of adequate documentation of this syndrome along with Vitamin D deficiency in the present medical literature available.

Keywords: Churg Strauss syndrome; Severe vitamin D deficiency; Degenerative bone disease

Introduction

Vitamin D refers to a group of fat soluble secosteroids whose deficiency causes decreased bone mineralisation, secondary hyperparathyroidism, increased cortical bone loss and has been associated with the pathogenesis of osteoporosis and hip fractures [1].

It can result in muscle weakness, and has been found to be the causative factor for a number of immune disorders and cancers. The evidence of a protective effect of ultraviolet ray (UVR) through the avoidance of vitamin D deficiency is proven.

Churg-Strauss Syndrome, also referred as Eosinophilic Granulomatosis and Polyangiitis (EGPA) is an uncommon disease with incidence of 1-3 per million. This is a multisystem disorder characterized by allergic rhinitis, asthma, and peripheral blood eosinophilia. The disease can occur at any age but not infants. The mean age of onset is 48 years with male to female ratio 1.2:1 [2].

In this case report we are one of the very few to report the occurrence of Churg Strauss syndrome with Vitamin D deficiency & degenerative bone disease. There is only one review article regarding environmental and genetic contributions to the anti-neutrophil cytoplasmic antibody (ANCA) associated systemic vasculitis, where vitamin D deficiency was strongly suggested [3].

Case Report

A 58year old male with history of reactive airway disease was admitted in Respiratory Care Unit with complaints of on & off fever for last one and half years, right sided weakness & paraesthesia of both the

lower limbs for last 4 months and bipedal oedema (R>L) for last 2 months.

He was a known case of reactive airway disease for last 16 years controlled with inhaled bronchodilators and steroids. Fever was low grade intermittent, not associated with chill and rigor and used to subside with medication.

Patient had a history of exacerbation for which he was admitted in hospital 6 months ago with respiratory distress and chest pain. There he was treated accordingly and discharged within 7 days. After almost a month of discharge he developed right sided weakness and tingling and numbness of both the lower limbs for which he was again admitted to nearby hospital.

There he was treated symptomatically. But instead of cure he developed severe burning pain over the both lower limbs and oedema. Then he was referred to this institution for better management.

The authors did not find any history of diabetes, hypertension, tuberculosis, ischaemic heart disease or any other chronic disease. There was history of nonspecific allergy and a family history of atopy. He had no history of addiction.

Physical Examination on admission revealed a well oriented, conscious patient with pallor and bilateral pedal oedema.

Vitals showed pulse-87/min, BP-132/76 mmHg, respiratory rate-26/min. Respiratory distress was present and on chest auscultation rhonchi was present in bilateral lung field. CNS examination showed → Tone B/L-↑, upper limb power-Right-4/5, Left-5/5, lower limb power-both 5/5, reflexes- brisk, right ankle jerk ↓, planter B/L flexor.

The following investigations were performed sequentially →

- Hb% -7.2 gm%, TLC- 25,700/cmm (N³⁰, L⁴⁰, E²⁸, M⁰²), Urea: 32 mg%, creatinine: 1.4 mg%, Na⁺: 136.9 mEq/L, K⁺: 3.7 mEq/L.
- Echocardiogram revealed normal study.
- Bilateral limb color Doppler- mild atherosclerotic changes with normal study.
- Pulmonary function test (PFT) showed obstructive features with bronchodilator reversibility.
- HRCT Thorax (Figure 1) -B/L centrilobar emphysema with ground glass haziness in irregular segments (post hemorrhagic).

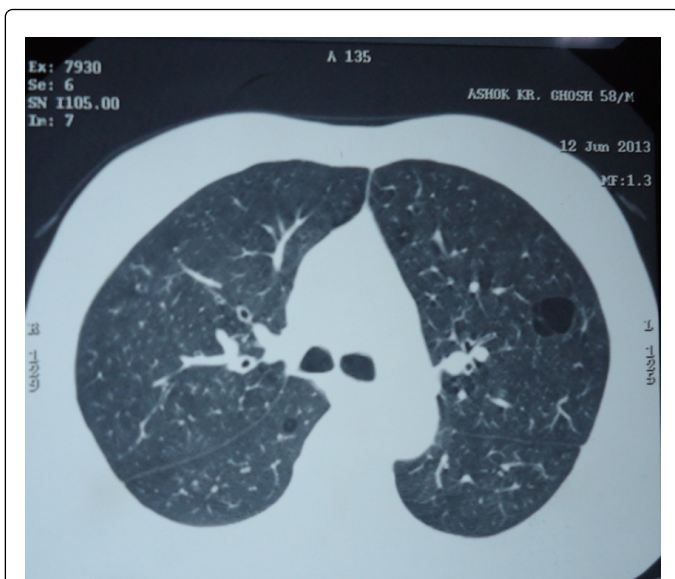


Figure 1: HRCT Thorax (Figure 1) -B/L centrilobar emphysema with ground glass haziness in irregular segments (post hemorrhagic).

- Electromyography and Nerve conduction study (EMG-NCV) revealed Chronic Axonal type of distal sensory motor polyneuropathy including both lower limbs>upper limbs which was provisionally diagnosed to be Mono-neuritis multiplex.
- MRI Brain- No obvious abnormality.
- MRI cervical Spine- Disc bulge revealed in C3-4, C4-5, C5-6. Discodegenerative disease of cervical spine, with left sided stenosis at C5-6 level (Figure 1).
- MRI lumbosacral spine (Figure 2)-suggestive of degenerative disease of spine mostly affecting L4-5, L5-S1, with B/L foraminal narrowing of the above level with secondary spinal canal stenosis of L5-S1.
- Antinuclear antibody (ANA) - negative, Perinuclear Anti-Neutrophil Cytoplasmic Antibodies (p-ANCA) - 83.16, Cytoplasmic antineutrophil cytoplasmic antibodies (c-ANCA)-1.58.
- Vit-D₃-11.63 ng/ml (<20 ng/ml-deficiency) [4-8].
- PTH-66 pg/ml (Normal 11-54 pg/ml) (Figure 2).



Figure 2: Bone marrow study- showed reactive bone marrow with normal myeloid: erythroid ratio. Normal iron store.

Treatment

The natural history of untreated ANCA Associated Vasculitis (AAV) is of a rapidly progressive, fatal disease [9]. The mainstay of treatment of Churg Strauss Syndrome are glucocorticoids where dose tapering is often limited due to presence of reactive airway disease. We started cyclosporine 2.5 mg/kg/day orally in 2 divided doses, prednisolone 60mg orally, vitamin D supplementation 50,000IU/week for 8 weeks followed by a maintenance dose of 800 IU/d (100 g/d) from food and supplements after achievement of normal plasma levels [10-12].

Symptoms including the right upper limb weakness gradually subsided and condition of the patient improved significantly during the time of discharge. Even after discharge we kept contact with the patient over telephone & OPD basis initially monthly for next 3 months and then 6 monthly.

The Response was assessed by-

- Symptomatic improvement.
- Decrease in eosinophil count
- Decrease of p-ANCA value.
- Repeat Serum Vit D₃-35 ng/ml (after 8 weeks).
- Repeat Serum PTH-42 pg/ml (after 8 weeks).

Discussion

In 1994 Chappel Hill Consensus conference (CHCC) presented the definition of ANCA associated vasculitis which were revised and updated in 2012 [13]. Churg strauss syndrome is thought of to be of unknown aetiology but generally considered to be an autoimmune disease due to allergic symptoms, immune complex mediation (48% are ANCA positive), increased T-cell mediated immunity, elevated immunoglobulin E (IgE) levels and Rheumatoid factor [14].

Environmental factors play an important role in the development and progression of autoimmune diseases along with susceptible genetic and hormonal factors. It has been suggested recently that vitamin D is an environmental factor that by modulating the immune system, affects the progression of autoimmune syndromes [15]. Thus, vitamin D deficiency may have a role in the pathogenesis of autoimmune vasculitis. Clinical diagnosis of Autoimmune vasculitis is as standardized by the American College of Rheumatology Criteria → presence of 4 or more of the following criteria: i) asthma, ii) eosinophilia >10%, iii) neuropathy, iv) migratory or transient pulmonary opacities, v) rhinosinusitis, vi) extra vascular eosinophils on biopsy. Presence of late onset asthma is the main differentiating feature from other vasculitis [11]. Histological diagnosis is by demonstration of vasculitis that is necrotizing, tissue infiltration with eosinophils and extra-vascular granulomas [12].

The differential diagnosis includes Wegener's granulomatosis, drug reaction, bronchogenic granulomatosis, fungal and parasitic infections and malignancy [14].

In case of our patient asthma was present for almost 16 years managed with inhaled bronchodilators and steroids. Blood investigations revealed ANCA Positive, ANA Negative type of picture. Nervous System involvement was established by clinical diagnosis and laboratory investigations. Patient presented with right sided weakness and parasthesia of both lower limbs for last 4 months. EMG-NCV revealed chronic axonal type of distal sensory motor polyneuropathy including both lower limbs. Pulmonary Function Tests and HRCT thorax both confirmed involvement of respiratory system.

Cardiac (<47%) and Renal involvement, though common in ANCA Positive Churg Strauss Syndrome, was not found in our patient [11]. The other striking feature was Vitamin-D deficiency which caused degenerative bone disease. MRI of spine revealed disc degenerative disease of cervical spine with disc bulge at C3-4, C4-5, C5-C6 levels. Cervical canal stenosis was present at C5-C6 level and lumbar canal stenosis at L5-S1 level.

Vitamin D has been shown to modulate the immune system and has anti-inflammatory properties [16]. The significant role of vitamin D compounds as selective immunosuppressants is illustrated by their ability to either prevent or markedly suppress animal models of autoimmune disease [17].

The net effect of the vitamin D on the immune response is an enhancement of the innate immunity coupled with regulation of adaptive immunity [18].

The administration of vitamin D in animals leads to improvement of immune-mediated symptoms [19].

Current studies have related vitamin D deficiency with several autoimmune disorders, including insulin-dependent diabetes mellitus (IDDM), multiple sclerosis (MS), inflammatory bowel disease (IBD), systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) [20,21].

In view of those associations, it has been suggested that vitamin D is an extrinsic factor capable of affecting the prevalence of autoimmune diseases [22].

Till now no case reports or trials are available which shows the link between Churg Strauss syndrome and Vitamin D deficiency. The

authors think that this case report will encourage others to find out and establish this association which the authors have presented in this unique case report.

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