

Case Report

Unusual Case of Pyoderma Gangrenosum, Leukoclastic Vasculitis and Bilateral Ear Changes and Its Differentiation from SLE Flare, Hepatitis C Caused Pyoderma Gangrenosum and Relapsing Polychondritis

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Abstract

The knowledge of skin as well as ear complications caused by cocaine with levamisole is evolving. We described a patient with primary autoimmune rheumatological disorder-Systemic Lupus Erythematosus/SLE/ as well as Chronic Hepatitis C and Pyoderma gangrenosum as well as ear changes which might be in differential diagnosis of Relapsing Polychondritis. Also the patient had positive P- ANCA and C- ANCA antibodies as well as elevated titers of ANA and decreased complement levels of C3, C4 and CH50. Although pyoderma gangrenosum is described in patients with SLE, hepatitis C etc. the time course of consumption of cocaine with levamisole as well antibody changes described were typical for drug induced ear changes and pyoderma gangrenosum. We think clinicians should always include the urine/ blood drug test when dealing with those disorders to exclude drug induced Pyoderma Gangrenosum and ear changes, before attributing those changes to primary rheumatological or infectious disorder.

Keywords: Pyoderma gangrenosum; Chronic hepatitis C; Leukoclastic vasculitis

Introduction

Levamisole has been considered an adulterant in cocaine and increasingly reported as the cause for many of the complications noted in cocaine users [1-3]. The main reason for intentionally adding this compound to street cocaine has been due to its effect to potentiate the sympathomimetic effects of cocaine. The exact mechanism by which this agent causes complications is unclear. We present a unique case of a cocaine user who presented with acute non-healing skin lesions, ear changes, inflammatory monoarthritis and other systemic signs with subsequent workup leading to the diagnosis

Case Presentation

A 55-year-old African American female with past medical history significant for Systemic Lupus Erythematosus/SLE/, Herpes simplex infection and recent history of right non-healing inguinal ulceration presented with increasing pain in the right non-healing inguinal ulceration site with some yellowish discharge. The size of the ulceration had progressively gotten worse. The patient also reported 1-2 day history of necrotic lesions on her bilateral forearms, left lower extremity below the knee and swelling, pain and necrotic lesion on

her tongue. She was a current every day smoker, denied alcohol and initially denied the use of recreational drugs. Right inguinal big ulceration had some pustular changes as well and also purulent drainage. It was very painful to touch. Discoloration and swelling of the cartilage of the both ears sparing the pinna was observed. Edema in the left ankle with warmth, erythema was observed with pain on active and passive motions suggestive of monoarthritis of the left ankle which was proved to be inflammatory and noninfectious on diagnostic tap of the left ankle. Also a round necrotic lesion on the left lower extremity below the knee was observed with raised edges which were well demarcated and painful.

The SLE was diagnosed 7-years ago based on positive ANA, Double strand DNA, Non erosive inflammatory arthritis of the hands, Pancytopenia and serositis- pleural effusion and small pericardial effusion. The SLE was treated with Plaquenil and steroids successfully with resolution of the painful arthritis of the hands, resolution of the serositis and improvement of the pancytopenia with resolution of the thrombocytopenia. Since the SLE was treated with Plaquenil on and off based on the patient's poor compliance.

Labs on admission showed low WBC count, neutropenia, microcytic anemia – Anemia work up was suggestive of anemia of Inflammatory disease. Elevated levels of procalcitonin, ESR, CRP were also found. Immunological workup yielded positive ANA, c-ANCA with titer 1:640, elevated P ANCA or MPO-ANCA, decreased C3, C4 and CH50 levels, elevated HSV 1 & 2 IgG Ab and high CMV IgG titer. Also we found elevated HCV RNA levels, Hepatitis C was 1 A genotype, negative cryoglobulins and elevated single and double stranded DNA antibodies. Urine drug test was positive for cocaine. HIV test was negative.

Her AST, ALT, Bilirubin, PT were normal with the exception of the albumin which was mildly decreased. Ultra-Sonogram of the liver and

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spleen was normal. CT of the chest and neck and Echocardiography of the heart were also normal.

Based on the presenting symptoms of inflammation, ulcerations and suspecting superimposed bacterial infection, IV broad spectrum antibiotics and antiviral drugs were begun without improvement of the skin, ear lesions and left ankle arthritis.

After the positive drug screen for cocaine on further questioning, the patient admitted using cocaine with levamisole by inhalation in the last 3-years.

She reported recurrent similar lesions in the last 3- years only after the usage of inhaled cocaine with levamisole, but never without its usage.

We suspected that some of the lesions ere related to Pyoderma gangrenosum and or vasculitis etc. and performed surgical biopsy of the right inguinal lesion and left lower extremity lesion. Pathology with light microscopy and direct immunofluorescence results were supportive of the diagnosis of pyoderma gangrenosum and leukoclastic vasculitis.

The biopsy sample grew also *Bacteroides fragilis*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Staphylococcus epidermidis* which we believed represented secondary bacterial infection of the PG/ vasculitis lesions and we continued the antibiotics but stopped the antiviral drugs.

The final Diagnosis of Pyoderma gangrenosum and Leukoclastic vasculitis secondary to Levamisole-cocaine was made based on the clinical presentation and association with their usage with the skin and ear findings. They were recurrent in the last 3- years and always happening only after the usage of the cocaine-levamisole. Also the ANCA positivity is strongly associated with cocaine- Levamisole usage. The inflammatory left ankle arthritis we believed was also due to cocaine-levamisole as described in the literature.

The patient was started on Steroids with significant improvement of the skin lesions in the right inguinal area, in the left lower extremity as well as improvement of the necrotic lesions on both upper extremities and tongue. The ear lesions and the monoarthritis of the left ankle completely resolved after the start of the steroids. The patient was discharged home on tapering doses of steroids and per oral antibiotics. She was extensively counseled against the usage of cocaine- levamisole.

Discussion

Initially described in 1978 in a patient treated for rheumatoid arthritis, levamisole-induced skin findings are becoming more evident in clinical practice these days. This is because, in the USA, it is now estimated that about 70% of the cocaine is adulterated with levamisole as it not only adds volume to the drug but is also believed to potentiate psychotropic properties of the cocaine

Pyoderma gangrenosum /PG/ is one of the neutrophilic dermatoses which is associated with SLE, Rheumatoid arthritis, Hepatitis C, Inflammatory bowel diseases, cryoglobulinemia etc. as well as medications like isotretinoin, sunitinib, propylthiouracil etc. Other neutrophilic dermatoses are Sweet syndrome, Behçet's disease and neutrophilic urticarial. Recently in the medical literature there have been few reports of association of PG with cocaine- levamisole.

In PG initially there is neutrophil infiltration (with or without lymphocytes), which often occurs diffusely in the dermis and involves

follicular structures. There are varying degrees of vascular damage, but usually without fibrinoid necrosis. Focal vasculitis is observed in fully developed lesions, which is apparently a secondary phenomenon. The infiltrate tends to be located in deeper levels of the dermis. A mixed inflammatory process and areas of necrosis are observed in fully developed lesions. There is a wide clinical variability, but the morphology of PG is the following: a) pustular b) ulcerated c) vesicobullous, d) verrucous vegetating. In general, there is predominance of one of the clinical forms, which can coexist in the same patient.

In our patient, the pustular and ulcerated form of PG coexisted. The bacterial infections were secondary. There was no response to the initial antibiotic and antiviral treatment of the lesions, but significant response to steroids.

Pathological diagnosis confirmed PG and leukoclastic vasculitis. The cause of it might have been SLE flare, or Hepatitis C but the previous as well as current flares of the PG leukoclastic vasculitis and ear changes were always associated with the use of inhaled cocaine with Levamisole which made us think that this was the most likely cause of the PG , ear changes and the leukoclastic vasculitis [4]

Additionally, the most pathognomonic lesions of cocaine-levamisole syndrome are those on the ears and association with ANCA positivity which our patient had. This is why we believed when we followed the association between the clinical, laboratory, histological and treatment picture with the cocaine-levamisole usage that the cause of the PG, leukoclastic vasculitis and ear changes was the cocaine-levamisole [5-8] rather than SLE flare or Hepatitis C.

The patient did not fulfill the criteria for Relapsing Polychondritis [9]. The cocaine-levamisole related syndrome comprises a set of immunological abnormalities, out of which, ANCA positivity is the most important one. Our patient was ANCA positive also.

Regarding pathological findings in cocaine adulterated with levamisole syndrome, this can range from the classic finding of leukocytoclastic vasculitis of small vessels to occlusive vascular disease without true vasculitis.

Although the mechanism of how tainted cocaine causes characteristically clinical and immunological findings is not well known, but there are there are suggested theories. The main theory nowadays relates the direct cytotoxic effect of levamisole to the cells, especially neutrophils, is of consideration. It is this direct effect due to which case reports of the association between pyoderma gangrenosum and the use of adulterated cocaine are emerging as pyoderma gangrenosum's pathophysiological basis is endothelial damage. Furthermore, ANCA translocation and increased recruitment of neutrophils all contribute to the damage of the vessel by oxidative reaction and degranulation. Also, cocaine- levamisole might act as immunomodulator and cause immune attack of the cartilaginous portion of the ears as in our patient. Also the inflammatory left ankle arthritis we believe was due to cocaine-levamisole. Few cases are described in the literature [10] as discussed.

Conclusion

In conclusion, we think that cocaine-levamisole syndrome is increasing and the clinicians should be aware of the clinical manifestation of the syndrome-skin findings suggestive of vasculitis, or non-vasculitis occlusive disease of the small vessels, neutrophil dermatoses like PG and inflammatory ear changes among others and not always attribute those changes to Rheumatological or Infectious

disorders like Systemic Lupus erythematosus/SLE/, Rheumatoid arthritis/RA/, Hepatitis C etc . Besides the thorough work up which we did the clinicians should follow the clinical presentations and temporary association of the symptoms with the disease flare or the drug use like in our patient when the skin and ear changes always happened with the use of cocaine-levamisole.

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