1. Introduction

While the usage of illicit drugs in itself carries significant health risks and associated toxicities, drugs that are adulterated to give them volume, alter their psychogenic properties, and make them cheaper to produce are to be considered even more dangerous. Cocaine is one of them, and it is now most commonly being adulterated with levamisole. We report a case of a 37-year-old female with the chief complaint of painful skin lesions and wounds on both of her upper and lower extremities for three weeks duration. She was tested positive for cocaine and had classical purpuric, ecchymotic, and necrotic patches on both ears, which are pathognomonic. She also had multiple wounds in extremities. 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. 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. Our case’s biopsy showed no vasculitis, and this is why it is important to highlight that cocaine can also cause a pseudo-vasculitic picture. The other possibility that we entertained was that of pyoderma gangrenosum as the skin finding in levamisole-contaminated cocaine, and the lesion was consistent in appearance. Recently, there have been a few case reports of pyoderma gangrenosum from adulterated cocaine with levamisole, where skin findings were consistent with pyoderma gangrenosum; however, serological findings rather favored levamisole vasculopathy or vasculitis. Therefore, we should familiarize ourselves with the multitude of pathological and skin findings that adulterated cocaine can cause and, finally, make ourselves aware that the classical pathological finding of vasculitis in such cases is not always seen.

2. Case report

A 37-year-old female presented with the chief complaint of painful skin lesions and wounds on both of her upper and lower extremities for three weeks’ duration.

Per patient, this started with abrasions on both of her forearms and elbow areas, which she claimed to have gotten by scrapping against car doors. These ‘abrasions’ were small, to begin with, but gradually turned into open and painful flesh wounds. The wounds were bleeding and foul smelling on presentation.

Initially, the patient denied illicit drug usage, but upon further prompting, she did admit to snorting cocaine and using acetaminophen/oxycodone for the pain. The patient otherwise denied fever or chills. She denied any travel, hiking, or camping. She also denied any specific trauma.

On examination, purpuric, ecchymotic, and necrotic patches on both ears were present (Figure 1). Extremities revealed bilateral forearm and lower extremity wounds, which were purpuric and necrotic.

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Full thickness dermal necrosis with sloughing in the wounds was also noted (Figure 2).

Labs were significant for leukopenia, neutropenia, and microcytic anemia. The patient was positive for cocaine along with cannabinoids and opiates. HIV and acute hepatitis panel screening were negative. Quantitative Gas Chromatography–Mass Spectrometry revealed cocaine in urine to be >5000 ng/mL. Other significant lab work revealed ANCA IFA positivity.

Figure 1. Images showing purpuric, ecchymotic, and necrotic patches on both ears in our patient. These lesions are pathognomonic as ears are very rarely affected by other types of vasculitides.

Figure 2. Images showing multiple wounds, both purpuric and necrotic. Full thickness dermal necrosis with sloughing in the wounds also noted. Some of the lesions almost appear like pyoderma gangrenosum.
Biopsy of the skin lesion was obtained from the patient's skin lesion from the distal right arm, which showed organizing cutaneous abscess with pseudoeiphielomatous hyperplasia, but negative for granuloma or vasculitis. The patient was empirically treated with Vancomycin and Zosyn. The patient's skin findings began to improve gradually along with her leukopenia throughout her admission and clinical course.

3. 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 [2].

Levamisole-induced skin lesions are a characteristically stellate purpuric rash with bright red border, non-blanching, and when severe, can cause bullae or central necrosis. Levamisole-induced lesions have a predilection for the ears and extremities. Also, the most pathognomonic lesions are those on the ears [2].

It is unique from other systemic vasculitides due to its isolation to the skin most of the time. However, severe cases can involve deeper skin structures requiring skin grafts [2]. Neutropenia and agranulocytosis can either occur in isolation or precede cutaneous vasculopathy.

The cocaine–levamisole related syndrome comprises a set of immunological abnormalities, out of which, ANCA positivity is the most important one [3]. Our patient was ANCA positive.

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 [3]. Moreover, in one review, vasculitis was not observed in 48% of the biopsies [4].

Although the mechanism of how tainted cocaine causes characteristically clinical and immunological findings is not well known, there are suggested theories. First of all, the direct cytotoxic effect of levamisole to the cells, especially neutrophils, is a consideration [5]. 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 [6]. Furthermore, ANCA translocation and increased recruitment of neutrophils all contribute to the damage of the vessel by oxidative reaction and degranulation [5].

As discussed, the direct toxic effect of the adulterant and cocaine is apparent, but there is also an indication towards synergy with the immune system that perhaps results in typical clinical findings. We do know that levamisole is an immunomodulator that causes chemotaxis of neutrophils, and metabolites of it can, therefore, contribute to the pathogenesis. For instance, the MPO enzyme, present in peripheral leukocytes, is involved in metabolizing the drug to its active metabolites which are capable of haptenization and therefore, autoantibodies to this molecule may play a pivotal role in the levamisole-induced vasculopathy and agranulocytosis [5,7]. The antibody titer correlating with disease activity is further supportive of the direct effect. In one case report, a bone marrow biopsy was done, which was consistent with recently injured bone marrow showing early recovery [8], suggesting that levamisole can also have an impact on bone marrow.

Moreover, levamisole itself can act as the hapten and thus can potentiate the formation of antibodies to antigens resulting in an immune response that can cause leukocyte destruction [9]. Recent findings are also pointing towards the release of inflammatory NETS (neutrophil extracellular traps) in the pathogenesis of cellular and tissue injury [10]. Finally, it is proposed that certain individuals may just be more prone to developing autoimmunity and autoantigens, resulting in immunological insult, as the typical clinical picture is not seen in every patient [5].

Treatment involves discontinuing cocaine use to which almost all patients respond. There is no definitive role of using corticosteroids, and use of plasmapheresis is very limited too. In some cases, due to necrosis and extensive wound formation, patients can also develop superimposed infection; in such cases, surgical debridement and skin grafting prove beneficial. It is important to note that infections can be more dreadful as patients are already in an immunocompromised state due to neutropenia that follows the use of levamisole [2].

Coming back to our case, as the biopsy showed no vasculitis, a diagnostic inquiry stirred up, and other causes were sought out. However, it is important to highlight that cocaine can also cause a pseudo-vasculitic picture, meaning a disease that presents with lab findings that would be consistent with true vasculitis but the biopsy would fail to show the classical picture of a vasculitis [11].

The other possibility that we entertained was that of pyoderma gangrenosum as the skin finding in levamisole-contaminated cocaine and the lesion was consistent in appearance. Recently, there have been a few case reports of pyoderma gangrenosum from adulterated cocaine with levamisole, where skin findings were consistent with pyoderma gangrenosum; however, serological findings rather favored levamisole vasculopathy or vasculitis [12]. The study was limited to eight serological and pathological findings from only eight patients, but this tends to highlight the uncommonness of such a presentation and the diagnostic challenge that it therefore poses.
4. Conclusion

In conclusion, we should take adulterated cocaine seriously, especially cocaine with levamisole, as the rise of its use is more prevalent for reasons already mentioned. In addition, we should be aware of the mimickers of vasculitis and not solely rely on serologic tests alone but rather make an accurate diagnosis based on clinical findings, presentation, and complete work up. We should familiarize ourselves with the multitude of pathological and skin findings that adulterated cocaine (especially with levamisole) can cause, and finally, make ourselves aware that the classical pathological finding of vasculitis in such cases is not always seen.

Disclosure statement

No potential conflict of interest was reported by the authors.

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