## Case Report on Deep Vein Thrombosis Induced by Chronic Intravenous Drug Abuse

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#### ABSTRACT

Deep Vein Thrombosis (DVT), due to venous insufficiency commonly induced by chronic Intravenous (IV) drug abuse, is a major global health issue. This article discusses the interaction between these factors with the help of a case report of an adult male, Mr. X, who complained of persistent right lower limb ulcer. When physically examined, varicose veins, healed ulcers, and lipodermatosclerosis was noted, all suggestive of venous insufficiency. He was a chronic alcoholic and IV drug abuser. The diagnostic investigations established chronic DVT, which was associated to IV drug use and venous insufficiency. The required medical care was given, including anticoagulation therapy and wound care. Surgical, pharmacological and psychiatric support was provided. This case emphasis on the challenges presented by the IV drug use, in the context of venous pathology and also stresses on the necessity of comprehensive care in managing the systemic impact of substance abuse on overall health.

**Keywords:** Association, Deep Vein Thrombosis, Intravenous Drug Abuse, Management strategies, Management, Public health.

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## INTRODUCTION

Deep vein thrombosis is due to the blood clot forming in the major veins of the legs or pelvic region. DVT, which is a type of Venous Thromboembolism (VTE), is a significant avoidable factor contributing to morbidity and mortality on a global scale.1 The estimated occurrence of DVT is 1-2 cases per 1000 individuals annually.<sup>2</sup> The clinical presentation of acute lower extremity DVT varies with the anatomic location, extent, and degree of occlusion of the thrombus. Symptoms can vary from being absent to experiencing significant swelling and cyanosis with possible venous gangrene, pain, swelling, redness, tenderness, fever, noticeable superficial veins, Homan's sign, and cyanosis in the extremities. Factors such as Decreased blood flow, raised venous pressure, physical vein damage, increased blood thickness, and variations in venous structure can lead to DVT.<sup>3</sup> Venous insufficiencies can lead to the formation of varicose veins, which are enlarged and twisted veins that can be seen just below the skin's surface. A connection has been identified between venous insufficiency and DVT, a severe condition characterized by the formation of blood clots in the deep veins of the legs.<sup>4</sup> The



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disturbance in blood flow and pooling in veins due to backward flow in primary venous insufficiency may increase the risk of DVT in individuals with varicose veins. Even though varicose veins have been recognized as a potential factor that may increase the risk of developing DVT, it is crucial to understand that the connection between them is intricate and not completely clear. Additional elements, like age, gender, and preexisting health issues, can also play a role in the formation of DVT.<sup>5</sup> Moreover, specific factors may heighten the likelihood of contracting DVT, such as IV drug abuse. DVT poses a significant risk to Intravenous Drug Users (IVDU) with high morbidity rates. The issue of Intravenous Drug Use has become a significant concern for public health, with a noticeable rise in prevalence over the past ten years.<sup>6</sup> It is estimated that there are around 15.6 million people worldwide who are IVDU, although this number may not accurately represent the full extent of the issue due to the illegal and stigmatized nature of injecting drugs.7

IV drug use has the potential to cause DVT through multiple pathways. The primary concerns include vein damage from multiple punctures and lack of sterility, the nature of substances injected, introduction of insoluble drug particles and pills, irritation of veins from contaminants leading to hardening, infection, and inflammation.<sup>8</sup> Additional mechanisms could play a role, potentially akin to how cocaine causes a procoagulant effect in arteries, like vasoconstriction.<sup>9</sup> Furthermore, if IDUs can't inject in their arms anymore due to vein damage, they resort to using the femoral vein in the groin or other lower limb veins, despite the high risk of DVT. At times, IVDUs start injecting in their legs to hide needle marks.<sup>10</sup> The way DVT presents and progresses in individuals is typically distinct from the general population, frequently involving soft tissue infections, bacteremia, or septic embolism, and showing a higher occurrence of viral diseases that promote blood clotting, like hepatitis and HIV.<sup>9</sup>

Here we report a case of deep vein thrombosis secondary to chronic intravenous drug abuse associated with varicose vein and its complications. This case report highlights the intricate challenges of substance abuse, including IV drug use, which contributed to the development and progression of his medical issues, such as venous insufficiency and deep vein thrombosis. This highlights the systemic impact of substance abuse on overall health and the need for integrated treatment approaches.

### **CASE REPORT**

Mr. X, a 33-year-old male, presented with a complaint of a right lower limb ulcer persisting for 6 months. The infected ulcer, sudden in onset, had gradually worsened over time, causing significant pain. Upon examination, surgeons noted engorged veins over both lower limbs, along with a healed ulcer measuring 4x2 cm on the medial aspect of the right leg. Additionally, lipodermatosclerosis changes with hyperpigmentation and the inverted champagne bottle sign, indicative of venous insufficiency, were observed (Figure 1).

He had a history of smoking for 4-5 years (2-3 cigarettes/day) and chronic alcohol consumption (90 mL/day) for the past 9 months, with his last drink on the day of admission. He was diagnosed with bilateral varicose veins, a right venous ulcer, and lipodermatosclerosis. He was admitted to the general



Figure 1: The image shows a lower limb with hyperpigmentation, lipodermatosclerosis, and an 'inverted champagne bottle' appearance, indicative of venous insufficiency.

surgery male ward for further evaluation and management. Initial treatment included Tab. Amoxyclav 625 mg BD, Tab. Pan 40 mg OD, and Zerodol SP BD. Following ulcer evaluation, debridement and regular dressing changes, the patient received compression bandage application as part of the treatment regimen. Dermatological consultation was sought for verruca vulgaris, leading to the prescription of Dersol 12% ointment OD and Tab. Ascazin OD for 15 days.

Venous Doppler of the right lower limb revealed reduced caliber of the Common Femoral Vein (CFV) and proximal Superficial Femoral Vein (SFV) with an echogenic thrombus, suggestive of chronic DVT extending up to the common iliac vein. Additionally, a history of Intravenous (IV) drug abuse, superficial venous varicosities, and incompetent perforators were noted. Despite recommendations for a prothrombotic workup to investigate factors contributing to thrombosis, the patient opted to delay the procedure to a later date. Consequently, Mr. X was initiated on Inj. Clexane 60 g BD for 5 days to manage the thrombus.

Further questioning revealed Mr. X's history of IV drug use, including Loxoprofen (Rexogesic)/Buprenorphin (Lupigesics) (2 mL/day) and Phenergan (promethazine) 1 mL IV/Diazepam 1 mL IV occasionally over the past 5 years. However, he had abstained from substance abuse for the last 9 months. A psychiatric consultation diagnosed him with Alcohol Dependence Syndrome (ADS) with multiple substance abuse, currently in abatement. Treatment included Tab. Lopez 4 mg (with a tapering dose regime), Thiamine 100 mg 1-1-2, and Tab. Bacfen XL OD.

Inj. Clexane was bridged with Tab. Acitram 2 mg, with PT/ INR monitoring to manage thrombosis. The comprehensive management approach addressed both the physical and psychiatric aspects of Mr. X's condition. It aimed to promote ulcer healing, manage venous insufficiency, prevent thrombus extension, and support substance abuse rehabilitation. The multidisciplinary team collaborated closely to optimize treatment outcomes and ensure patient compliance and well-being.

At the time of discharge, the ulcer showed signs of being healthy and in the process of healing. The patient was discharged with Tab. ACITRAM 3 mg OD at 6 pm for five days, Tab. PAN 40 mg before food for 5 days, Tab. ZERODOL SP BD for 5 days, Tab. ASCAZIN OD for 5 days, DERSOL 12% ointment (L/A) OD for 5 days, Tab. THIAMINE 100 mg TID for 3 days, Tab. BACFEN XL OD for 3 days and Tab. LOPEZ 4 mg in tapering dose which was explained to the patient. The patient was asked for follow-up visit to the general surgery OPD with PT/INR reports after 5 days and a review with the dermatology and psychiatric department on ODP basis.

### DISCUSSION

For decades, the persistent issue of intravenous drug addiction has posed a major challenge in terms of public health. This form of substance abuse poses numerous public health concerns, including increased risk of infectious diseases, overdose fatalities, and societal consequences like crime and economic burden. Intravenous drug use also presents unique challenges in terms of treatment and rehabilitation, often requiring comprehensive approaches that address both the physical and psychological aspects of addiction. DVT is one of the most significant health complications among those related.<sup>8</sup> This discussion highlights the multifactorial nature of DVT development in the above case, exploring the underlying mechanisms, contributing factors, and clinical implications.

## Intravenous Drug Abuse and DVT: Understanding the association

Intravenous drug abuse involves the injection of the drug directly into the bloodstream, bypassing the body's natural barriers and exposing the vasculature to harmful agents. The act of intravenous injection itself poses a significant risk for vascular complications, including endothelial damage and thrombus formation. The repeated trauma inflicted on the vascular endothelium during the injection process can trigger an inflammatory response, leading to endothelial dysfunction and the activation of coagulation pathways.6 Vascular issues from injecting drugs typically occur following prolonged use. Because of superficial thrombophlebitis, individuals who use drugs for an extended period of time opt to inject the substance directly into deep veins.<sup>11</sup> The vascular complications resulting from the repeated administration of drugs via needles in this patient have led to venous insufficiency, contributing to various complications such as varicose veins, venous ulcers, and lipodermatosclerosis. Additionally, the patient was also infected with verruca vulgaris, adding to the complexity of their condition.

The repeated trauma inflicted by the administration of drugs through needles can cause endothelial damage and compromise the integrity of the venous valves, leading to venous reflux and increased venous pressure, this chronic venous insufficiency contributes to the development of varicose veins.

Furthermore, venous ulcers can develop as a consequence of prolonged venous insufficiency and increased venous pressure. These ulcers typically form on the lower legs, particularly in areas where the skin is subjected to pressure or trauma. The impaired circulation and tissue damage associated with venous insufficiency create an environment conducive to the development of ulcers, which can be painful, slow to heal, and prone to infection.

Lipodermatosclerosis is another complication of venous insufficiency characterized by inflammation and fibrosis of the skin and underlying tissue. It results from the chronic accumulation

of fluid and inflammatory mediators in the subcutaneous tissue, leading to changes in skin texture, pigmentation, and the appearance of the affected limb.

In addition to these vascular complications, the patient was also infected with verruca vulgaris, a common viral infection of the skin caused by the human papillomavirus. While verruca vulgaris may not be directly related to venous insufficiency, it adds to the patient's overall burden of skin-related issues and may complicate wound management and treatment.

Furthermore, the substances being injected play a crucial role in the pathogenesis of DVT in individuals with a history of IVDU. Drugs such as opioids, stimulants, and sedatives can exert direct effects on vascular tone, endothelial function, and blood coagulation, predisposing individuals to thrombotic events.<sup>12</sup> Buprenorphine, a partial agonist at the µ-opioid receptor commonly used in medication-assisted treatment for opioid dependence, has also been associated with an increased risk of thrombosis, particularly when abused intravenously. Despite being categorized as a Schedule III drug with a moderate-tolow potential for physical dependence, buprenorphine possesses inherent properties that contribute to vascular complications, including vasoconstriction and endothelial dysfunction.<sup>13</sup> The potential for abuse of these drugs is created by buprenorphine's interaction with opioid receptors and its ability to produce euphoria and opioid-like effects. The case series documented by Yeo et al. (2006) provides clinical evidence linking intravenous buprenorphine abuse to the development of infected thrombosis, highlighting the importance of recognizing and addressing the vascular risks associated with opioid abuse.14

Additionally, the lifestyle and behaviors associated with intravenous drug abuse further compound the risk of DVT. Individuals who engage in IVDU often experience prolonged periods of inactivity, particularly during and after drug use. Prolonged immobility and reduced muscle pump activity can impair venous return and promote stasis within deep veins, facilitating the formation of blood clots.<sup>15</sup> Moreover, the introduction of infections from contaminated needles and the development of superficial thrombophlebitis can further exacerbate the thrombotic risk in individuals with a history of IVDU.<sup>6</sup>

# The Role of Diazepam and Other Benzodiazepines in Thrombosis Risk

While opioids are often the primary focus in discussions of intravenous drug abuse and thrombosis risk, the role of other substances, such as benzodiazepines, cannot be overlooked. Diazepam, a benzodiazepine commonly used for anxiety and other conditions, is frequently abused in conjunction with opioids and other drugs. While diazepam itself is not directly associated with thrombotic events, its abuse or misuse may contribute to behaviors or circumstances that elevate thrombosis risk. One potential mechanism by which benzodiazepines like diazepam may increase thrombosis risk is through sedation-induced immobility. Sedative effects, commonly observed in individuals using diazepam, can lead to prolonged periods of inactivity and reduced muscle pump activity, predisposing individuals to venous stasis and thrombus formation. Furthermore, interactions between benzodiazepines and opioids may potentiate the sedative effects and exacerbate the risk of immobility-associated thrombosis.<sup>16</sup>

# Understanding the Mechanisms of Thrombosis in IVDU

The pathogenesis of DVT in this patient with a history of IV drug abuse is multifactorial, involving a complex interplay of vascular, pharmacological, and behavioral factors. The repeated trauma inflicted on the vascular endothelium during intravenous injection sets the stage for thrombus formation by inducing endothelial damage and triggering the release of procoagulant factors. The injected substances themselves, including opioids and other drugs, further contribute to thrombosis risk through their effects on vascular tone, endothelial function, and blood coagulation.

Endothelial dysfunction, a hallmark feature of intravenous drug abuse, disrupts the delicate balance between procoagulant and anticoagulant pathways, tilting the scales towards thrombus formation. The introduction of infections from contaminated needles exacerbates the inflammatory response, leading to endothelial injury and thrombotic cascades. Moreover, the sedative effects of certain drugs, such as benzodiazepines, compound the risk of thrombosis by promoting immobility and venous stasis.

### **Clinical Implications and Management Strategies**

Individuals with a past history of such abuses is a clinical challenge to diagnose the condition. The patient might be hesitant to inform about the drug use, presence of any comorbid conditions, and the atypical presentation of thrombotic events, delaying or complicating the diagnoses of DVT. In such cases the therapeutic management of DVT needs to addresses both the thrombotic event and the substance abuse disorder.

The therapy for DVT patients with a past abuse of IV drug includes of anticoagulation therapy, thrombolysis in severe cases, and supportive care management. In such cases, IV abuse of the drug and its associated risk factors must be addressed as it is one of the underlying cause of the thrombosis. Interventions from all departments including the general surgery and psychiatric department as well as dermatology department for the management of further complications is important to provide medical care.

Prophylaxis management must aim at decreasing the DVT recurrence in IVDU. Initiatives to create awareness regarding

the harm caused by needle exchange and rehabilitation facilities, can help reduce the risks associated to IVDU and further prevent thrombotic complications. Public health interventions for substance abuse prevention and treatment are also crucial in avoiding the societal implications of intravenous drug abuse and its associated health consequences.

### CONCLUSION

DVT in IVDU presents with a various clinical challenge with a significant implication for patient outcomes and public health. Association between the vascular injury, pharmacology of the drugs injected, and one's lifestyle attributes to thrombotic events in such case. Understanding the complexity underlying thrombosis in such cases is essential for a faster clinical management and for an effective prevention strategy. With this assessment of this complex associations of these factors that contributes to thrombosis risk, healthcare providers can optimize patient care and improve clinical outcomes in IVDU

## **CONSENT TO PARTICIPATE**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given his consent for his images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity.

## **CONFLICT OF INTEREST**

The authors declare that there is no conflict of interest.

### **ABBREVIATIONS**

IV: Intravenous; DVT: Deep Vein Thrombosis; VTE: Venous Thromboembolism; IVDU: Intravenous Drug Users; OD: Once a day; BD: Bis in die (twice a day); CFV: Common Femoral Vein; SFV: Superficial Femoral Vein.

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