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Silencing the Phantom - Pregabalin Misuse in Amputation Patients: A Case Report

Hayaleti Susturmak - Amputasyon Hastalarında Pregabalin Kötüye Kullanımı: Bir Olgu Sunumu

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Abstract

In the aftermath of amputation, individuals face not only physical pain but also psychological challenges as their body's integrity is suddenly disrupted. Phantom limb sensations, characterized by the feeling that the amputated limb still exists, are common after amputation. Phantom limb pain often accompanies these sensations. Beyond the physiological aspects, patients' psychological adaptation journey is pivotal. This case report delves into the intricate relationship between phantom limb sensations, psychological factors, and pregabalin use disorder in a right-arm amputee patient. A 25-year-old right-arm amputee male patient went to an addiction outpatient clinic for pregabalin addiction treatment. He had a history of cannabis use to cope with his sadness during his adolescence. While cannabis use initially provided emotional relief, it later turned to pregabalin misuse, escalating to alarming doses (3000mg/day). Many pharmacological agents, including pregabalin, are being tried to treat phantom limb pain. Beyond its positive effects in phantom limb pain treatment, many studies have been published about its addictive features recently. This case underscores the need for comprehensive care for amputees, including psychological support, early prosthetic intervention, social reintegration, and judicious medication management. This case report serves as a reminder that the post-amputation period is not just a physical struggle but also a complex psychological journey toward healing and reintegration into a fulfilling life..

Keywords: Amputation, phantom limb pain, phantom limb syndrome, pregabalin, substance use disorder

Öz

Ampütasyon sonrasında bireyler sadece fiziksel acı değil, aynı zamanda vücut bütünlükleri aniden bozulduğu için psikolojik zorlanmalarla da karşı karşıya kalırlar. Kesilen uzvun hala var olduğu hissi olarak tanımlanan hayalet (fantom) uzuv hissi, amputasyondan sonra yaygın olarak görülür. Hayalet uzuv ağrısı genellikle bu hislere eşlik eder. Fizyolojik uyumun ötesinde, hastaların psikolojik uyum yolculuğu da çok önemlidir. Bu olgu sunumunda, sağ kolu ampute bir hastada hayalet uzuv hissi, psikolojik faktörler ve pregabalin kullanım bozukluğu arasındaki karmaşık ilişki incelenmektedir. 25 yaşında sağ kolu ampute erkek hasta pregabalin bağımlılığı tedavisi almak için Alkol ve Madde Bağımlılığı Tedavi Merkezi (AMATEM) polikliniğine başvurdu. Ergenlik döneminde üzüntüsüyle başa çıkmak için esrar kullanım öyküsü mevcuttu. Esrar kullanımı başlangıçta duygusal rahatlama sağlarken, daha sonra pregabalin kötüye kullanımına dönüşmüştü ve olgu 3000 mg/gün pregabalin kullanmaktaydı. Hayalet uzuv ağrısını tedavi etmek için pregabalin de dahil olmak üzere birçok farmakolojik ajan denenmektedir. Hayalet uzuv ağrısı tedavisindeki olumlu etkilerinin ötesinde, pregabalinin bağımlılık yapıcı özellikleri hakkında son zamanlarda birçok çalışma yayınlanmıştır. Bu vaka, ampüte hastalar için psikolojik destek, erken protez müdahalesi, sosyal ilişkilerin yeniden sağlanması ve uygun farmakolojik tedavi yönetimi dahil olmak üzere kapsamlı bakım ihtiyacının altını çizmektedir. Bu olgu sunumu ampütasyon sonrası dönemin sadece fiziksel bir mücadele değil, aynı zamanda iyileşme ve tatmin edici bir hayata yeniden uyumlanmaya yönelik karmaşık bir psikolojik yolculuk olduğunu hatırlatmaktadır.

Anahtar kelimeler: Amputasyon, hayalet uzuv ağrısı, hayalet uzuv sendromu, madde kullanım bozukluğu, pregabalin

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Introduction

Aside from the physical pain it entails, amputation can lead to or exacerbate a range of difficulties that affect a patient's overall well-being as it may be seen as an assault on their body integrity. According to Desmond and MacLachlan (2002), amputation may significantly alter a patient's daily life, particularly affecting their emotional and social relationships (1). The physical disability resulting from amputation can lead to hopelessness, irritability, depression, anxiety, low self-esteem, social stigma, and isolation (2).

Phantom limb sensation (PLS), first described by Ambrose Parré in 1552 as the sensation that the amputated limb is still present, is a commonly observed phenomenon following amputation (3). These sensations may occur immediately after the effects of anesthesia wear off or may appear days or weeks later (4). Patients may articulate their PLSs in various ways. These sensations often include warmth or coldness, itching, tingling, squeezing, or even a sense of the limb as before. Phantom limb pain (PLP), which refers to pain experienced in the amputated limb, is recognized as a challenging pain syndrome for specialists to manage (5,6). Phantom limb syndrome (PLSynd) is listed under neuropathic pain disorders in the Eleventh Revision of the International Classification of Diseases (ICD-11), and its pharmacological management is based on treatments recommended for neuropathic pain syndromes (7,8).

In the mid-20th century, research into the influence of emotional and mental disorders on PLP began, leading to the development of two competing theories. Psychodynamic theories view the phantom limb phenomenon as a manifestation of an amputee's struggle to come to terms with the loss and its emotional impact, often involving a denial of this loss (9). However, psychological explanations for PLS have gradually moved away from this perspective, as it has become evident that even individuals who appear to have adapted well to their amputation can still experience PLS years after the amputation. The most widely accepted theory is the 'cortical reorganization' theory, which suggests that aberrant activation of the somatosensory cortex regions, once associated with the amputated limb, is responsible for PLSynd (10,11).

Commonly used drug classes in the treatment of PLP include traditional analgesics, opioids, tricyclic antidepressants, barbiturates, neuroleptics, beta-blockers, calcium channel blockers, calcitonin, ketamine, and myorelaxants (5,6). Among oral medications, anticonvulsants are the most prescribed for treating PLP. Few case reports suggest that gabapentin effectively alleviates PLP (12,13). Other anticonvulsants such as topiramate, pregabalin, and carbamazepine have been shown to be effective in a few case reports and a systematic review with a low quality of evidence (14). In addition to research suggesting the potential importance of early postoperative prosthesis use in the management of PLP, some non-pharmacological treatment methods have recently gained attention, including non-invasive mirror therapy (3,15).

Pregabalin is a new-generation antiepileptic that reduces multiple stimulus output by reducing depolarization-induced calcium flux (16). It is indicated for the treatment of epilepsy, peripheral neuropathic pain, fibromyalgia, postherpetic neuralgia, chronic pruritus, restless legs syndrome, generalized anxiety disorder and insomnia (17,18). Unfortunately, there is considerable evidence in the literature of pregabalin abuse (17,19,20), and studies have shown that pregabalin abuse can lead to addiction (20), poisoning (19), and drug withdrawal syndromes (17). Pregabalin addiction does not have a specific definition in the DSM-5 diagnostic criteria. Therefore, this issue is addressed in the criteria under the diagnosis of "other substance use disorders". This case report aims to discuss the relationship between phantom sensations, psychological factors, and pregabalin use disorder in a right-arm amputee patient.

Case

Twenty-five years old, single male, primary school graduate, living with his family, working as a taxi driver and courier, left-hand dominant, right upper extremity amputee patient applied to the AMATEM (Alcohol and Drug Addiction Treatment Centre) outpatient clinic to treat his pregabalin misuse. During the assessment, a comprehensive history was obtained to identify potential risk factors for misuse. The patient reported experiencing sensations in his right thumb and second finger (phantom limb) two to three days a week, with

episodes lasting from a few seconds to several hours. Remarkably, he had not previously sought professional assistance for these sensations. In August 2023, he was admitted to the Ankara Training and Research Hospital Alcohol and Drug Addiction Treatment Centre (AMATEM) inpatient clinic due to his PLSynd symptoms and in order to change his social environment.

He stated that when he was nine years old, he was admitted to the hospital in an unconscious state following a car accident, resulting in the amputation of his right humerus from approximately one-third of the proximal part of the shaft. He realized after the operation that his arm had been amputated.

A review of his medical records revealed that he was eligible for prosthesis surgery around 3.5 months after the accident. However, the prosthesis was not implanted, as the patient was unsuitable for a bionic prosthesis and did not request another one. Revision surgery was performed approximately nine months later. Subsequently, 15 months after the incident, he sought treatment for PLP at the orthopedic outpatient clinic. Approximately three years after the initial operation, the orthopedic department referred him to the child and adolescent psychiatry department with a preliminary diagnosis of PLSynd. We were informed by his father that the patient had not been attending his regular follow-up appointments with the child & adolescent psychiatrist. Additionally, it was mentioned that he had been prescribed a medication, the name of which they could not recall, and it had never been used.

Following the operation, he changed schools, experiencing difficulties adjusting to school life due to occasional peer teasing. At the age of 15, he began using cannabis upon the suggestion of a school friend, as he was unhappy with his situation. This cannabis use continued two to three days a week for two years, helping him manage his emotions. When he was 17, his father encouraged him to join an amputee football team. Influenced by his teammates, he voluntarily began using an arm prosthesis. His cannabis use subsequently decreased to once every 2-3 months during the two years as he was playing on the team and participating in tournaments. After leaving the football team and starting to work, he began experiencing unusual sensations in his right hand's thumb and index finger. He also felt an inability to open his right fist. These sensations were not present before, did not respond to painkillers, and lasted seconds to hours. To avoid questions about his prosthetic arm, he developed the habit of wrapping his right arm in bandages extending from the shoulder to the fingertips. Despite these discomforts, he never sought medical care for these complaints and on the recommendation of a friend who said it was good for pain, he started taking pregabalin. Although initially effective in reducing the frequency and severity of PLSynd symptoms, he gradually increased his pregabalin use. The patient's use of pregabalin, initially 2-3 tablets several days a week, has changed over the last year to 10 tablets daily (3000 mg/day), every day of the week. Additionally, he recently developed a habit of online gambling through virtual betting websites. He stated that he had not used to gamble. Interestingly, when asked, he reported that he perceived his body intact in his dreams and never saw himself as one-armed.

The patient has a class H driving license with the inscription "able to drive a specially adapted vehicle". His mother was a housewife and his father worked as a taxi driver. There was no known familial history of mental disorders or substance use disorder. He said his relationships with family and friends were generally good, but recently he had experienced recurrent interpersonal problems, particularly with his family.

The patient presented as conscious, coherent, and oriented during the mental status examination. No memory pathologies were found. He displayed regular and connected thought associations, primarily focused on his amputated arm. No perceptual problems were described. His mood was euthymic, his affect seemed anxious, and his psychomotor activity was normal. Psychometric tests (the MMPI and the Rorschach Test) were conducted. Although there was no significant increase in the MMPI subtests, it was reported that "individuals with this profile may be aware of the decline in their physical functioning and abilities. They may show attempts to deny or conceal these limitations, and may experience agitation due to the frustration caused by their physical limitations". There was no psychotic elevation on the Rorschach test, it was reported that “the primary defense mechanism observed was suppression, with poor physical investment noted. While the connection to reality was maintained albeit weakly, the test revealed a loss of boundaries overall, early-

stage issues, and no significant decline in the individual's identity perception. Taken together, these factors led to the consideration of a borderline personality structure in the person."

Only pregabalin metabolites were found in the patient's urine. Because the patient met at least two DSM-5 diagnostic criteria for "other substance use disorder," including duration of substance use, development of tolerance, impaired functioning and relationships, and intense craving, "pregabalin use disorder" was diagnosed, as well as comorbid depressive disorder (Beck Depression Scale score of 27).

To address any pain complaints after discontinuing pregabalin, duloxetine at 30 mg/day and lorazepam at 1.25 mg/day were prescribed. Mirtazapine (15 mg/day) was also prescribed for managing insomnia. He voluntarily requested discharge on the fourth day of his hospitalization, expressing that the frequency of his PLS was becoming increasingly disturbing and causing restlessness. The treatment plan included ongoing weekly supportive psychotherapy sessions, with a gradual plan to discontinue benzodiazepines during follow-up visits.

The patient reported feeling better starting the first week after discharge. Following discharge, the patient continued to receive outpatient follow-up care weekly. Throughout this period, no traces of drug or substance metabolites were found in the weekly urine tests. Despite occasional cravings for pregabalin, he reported that taking lorazepam helped him manage this situation more effectively. While the symptoms of PLSynd persisted, he ceased using pregabalin, ceased engaging in gambling behavior, altered his social environment, and developed an interest in gardening. The lorazepam treatment was discontinued during the follow-up period. Additionally, the patient was referred to an outpatient physiotherapy clinic to address his ongoing PLSynd symptoms.

Discussion

In this case report, we aimed to discuss a patient whose pregabalin abuse escalated upon realizing it could alleviate PLS. While the exact prevalence of PLS and PLP remains uncertain, it has been reported that approximately 80-90% of amputees experience PLS, often accompanied by PLP (21). According to the cortical reorganization theory, a significant link exists between neuroplastic changes in the somatosensory and motor cortex post-amputation and the development of PLSynd (11). Studies suggest young children are less likely to experience these sensations after amputation (22). The clinical manifestations of PLP vary among individuals (4). It may be intermittent for many patients (6,23), resolve within days or weeks post-amputation, or persist for years (15). In our case, the persistence of PLP for approximately 3 to 4 years after amputation, followed by its reappearance as PLS years after PLP subsided, aligns with existing literature.

Amputations are generally performed after sudden traumatic events or planned medical reasons, such as cancer. The most favorable scenario for patients is when they are fully convinced that amputation is the only path to survival and willingly consent to the procedure. Abrupt and unexpected limb loss without prior counseling can profoundly impact a patient's psychological adjustment (24,25). The fact that our patient underwent urgent surgery with parental consent without prior counseling about the procedure may have intensified emotions like shock, denial, anger, and sadness (26).

Bergo et al. (2018) observed that separation from social networks is a common experience among amputation survivors. Nevertheless, this isolation is typically temporary, especially after using a limb prosthesis, as patients gradually adapt and reconnect with their old social circles (26). Studies consistently show that a well-fitting prosthesis reduces pain and post-amputation depression (27). Conversely, delaying or failing to obtain a prosthesis can exacerbate the patient's adjustment issues (28). The fact that our patient did not use a prosthesis until approximately eight years after the amputation may have contributed to the onset of psychological complaints, triggering a substance use disorder and the development of PLSynd symptoms.

Amputees often experience common symptoms such as discomfort with how others perceive them, a perception of their body as defective, and a desire for isolation (2). In our case, the initiation of cannabis use

might be linked to his adaptation challenges during primary school. During this time, he may have been susceptible to peer acceptance and rejection, leading him to seek solace to detach from the effort of connecting with others (29). Interestingly, he displayed no difficulty using his prosthesis while participating in a team of amputees who shared similar life experiences and physical challenges. During this period, the frequency of his cannabis use significantly decreased, possibly due to the cathartic effect of group interaction (30). Research on the interplay between psychological factors and PLSynd symptoms suggests amputees often report increased phantom limb-related complaints following stressful events (31). As our patient began interacting with various people after he started work, his PLS intensified, particularly in response to inquiries about his prosthesis. This pattern aligns with findings in the existing literature.

The 'gateway hypothesis' proposes that substances like cannabis can make individuals more susceptible to addiction to other substances, like opioids (32). Even though cannabis was our patient's first exposure to drugs, the unanticipated lack of progression and the restriction to pregabalin use imply that the patient may have intended to self-medicate for PLSynd.

While various interventions exist for treating patients with PLP, none have demonstrated consistent long-term efficacy (33). Some case reports have indicated favorable outcomes with using pregabalin as a treatment for PLP. Pregabalin is structurally related to GABA; however, it is suggested that its effects do not primarily involve the GABA receptor complex. Instead, pregabalin is believed to suppress hyperexcitability by binding to the alpha-2-delta subunit of N-type voltage-dependent calcium channels at the axon tip (34). Doing so blocks calcium influx, limiting the neuron's ability to release glutamate and P into the synapse. Furthermore, studies have suggested that pregabalin may help reduce spontaneous nerve firing in damaged nerve fibers within the stump and adjacent fibers in patients with PLSynd (35).

However, alongside its positive effects, recent years have seen numerous studies on pregabalin abuse and addiction (36). Notably, our patient initially started using pregabalin to alleviate PLS but eventually escalated to doses as high as 3000 mg/day. This case underscores the importance of raising awareness about the risk of pregabalin addiction among amputee patients.

In conclusion, the post-amputation period poses physical and psychological challenges. Psychological support can help individuals to understand and cope with their emotional difficulties. Early prosthesis fitting may positively affect body image, contribute to functional independence, and help patients adapt to daily life faster. Following amputation, deviation from social norms, changes in body image, and fear of exclusion may lead to social isolation. Providing social support and reintegrating amputee individuals into social life is essential. It should not be forgotten that social isolation increases the risk of addiction.

In addition, phantom pain and sensations are common problems after amputation. Drugs such as pregabalin may effectively manage PLSynd symptoms but require professional oversight due to their addictive properities. Comprehensive care for amputees demands a multifaceted approach, integrating psychology, early prosthetics, social support, and cautious medication use to promote recovery and a better quality of life.

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