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A Case of Acute Opioid Withdrawal after Liposuction Surgery in a Patient on Extended-Release Buprenorphine

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Background: The US Food and Drug Administration approved the once-monthly injectable extended-release buprenorphine product to treat moderate-to-severe opioid use disorders. The patient in our case report had a liposuction procedure and immediately started having opioid withdrawal symptoms after the procedure.

Case Description: The patient is a 27-year-old African-American woman who injects drugs and has morbid obesity. She enrolled in a medications for addiction treatment program and opted to get treated with extended-release buprenorphine monthly injections. She tolerated them well for a span of 6 months. In one clinic visit, she reported opioid withdrawal symptoms and started purchasing and using sublingual buprenorphine from her acquaintances. On review of history, she underwent liposuction surgery and this triggered the opioid withdrawal symptoms. Examining her abdomen revealed surgical scars at the site of the buprenorphine injection and the residual buprenorphine depot was not palpable.

A subcutaneous injection of 300-mg extended release buprenorphine was administered in the right periumbilical area in this clinic visit. The following week, she was doing well and denied any withdrawal symptoms.

Discussion: This is a unique case of "iatrogenic opioid withdrawal" after a fairly common surgical procedure. The extended-release buprenorphine formulation solidifies when it comes into contact with bodily fluids forming a depot. The depot and surrounding adipose tissue may have been removed during the patient's liposuction procedure, causing an immediate drop in buprenorphine levels leading to acute opioid withdrawal.

This case report highlights the precautions that need to be taken before patients go for a surgical procedure like liposuction.

Key Words: opioid withdrawal, liposuction, extended-release buprenorphine

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In November 2017, the US Food and Drug Administration approved the first once-monthly injectable extended-release buprenorphine product for the treatment of moderate-to-severe opioid use disorders in adult patients.[1] This formulation is indicated for anyone who has been initiated on a transmucosal form of buprenorphine and has been on submucosal buprenorphine for at least 7 days.[2] The extended-release formulation of buprenorphine is given as a monthly subcutaneous injection, often in the abdominal region.[2]

Although this formulation of buprenorphine has been successfully used for managing moderate-to-severe opioid use disorder for approximately 5 years, there is a lack of awareness about this medication, particularly in nonaddiction medicine/addiction psychiatry and related fields. There is also limited literature and guidelines regarding using this form of buprenorphine.

In this case report, we present a unique case of opioid withdrawal in a patient who was on extended-release buprenorphine injection for almost 5 months and then began experiencing symptoms of opioid withdrawal after she underwent a liposuction procedure. Liposuction is a procedure that uses suction techniques to remove fat from certain areas of the body.[3]

In this article, we present the case, discuss the extended-release buprenorphine's mode of action, discuss the specifics of the liposuction procedure, and analyze possible causes for opioid withdrawal in our patient after the liposuction procedure. Informed consent was obtained from the patient for writing the manuscript for a publication.

CASE DISCUSSION

The patient is a 27-year-old African-American woman with a history of injection drug use in the Philadelphia region of the United States. She started using opioids and cocaine at age 14 years, using them intranasally and intravenously. She began misusing intravenous and intranasal cocaine at age 24 years. Along with opioid and stimulant use disorder, she had morbid obesity, bipolar disorder, major depression, generalized anxiety disorder, nicotine use disorder, and asthma. She had a family history of addiction, and her mother was also in recovery. Her brother also had a history of opioid misuse and died because of an overdose.

She was enrolled in an outpatient treatment program and received methadone but continued fentanyl use. After her brother's overdose, she discontinued attendance at the outpatient treatment program. She was incarcerated and subsequently enrolled in a residential treatment program where she started sublingual buprenorphine. After completion of 60-day residential treatment, she continued outpatient treatment with buprenorphine and weekly telehealth sessions.

In her next visit, she chose monthly extended-release buprenorphine injections to continue her treatment. She received the first injection in April 2022, when 300 mg of extended-release buprenorphine was injected subcutaneously in the

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right periumbilical area, and she tolerated it well without any adverse effects. She did not report any reactions or withdrawal symptoms during her subsequent monthly visits. A urine toxicology screen at each visit detected buprenorphine but no other opioids, fentanyl, or other substances. She again received a 300-mg subcutaneous dose in the month of June 2022. In the subsequent months of July and August 2022, she received 100-mg extended-release buprenorphine injections.

When she presented for the next injection in September 2022, she reported symptoms of opioid withdrawal, including anxiety, headaches, rhinorrhea, loose stools, and abdominal cramps. She also said that she started purchasing and using sublingual buprenorphine from her acquaintances in the community as the symptoms worsened.

During a review of her recent history, she reported having liposuction in late August, 2 days after she received the last injection. Within 24 hours after the surgical procedure, she started experiencing opioid withdrawal. On an abdominal examination, surgical scars at the buprenorphine injection site were noted, and the residual lump was not palpable. This office visit was 28 days after her last injection.

It was suspected that the residual buprenorphine might have been extracted by the liposuction procedure, which might have precipitated the opioid withdrawal. A subcutaneous 300-mg dose was injected in the right periumbilical area, and ondansetron, dicyclomine, and hydroxyzine were prescribed for opioid withdrawal symptoms if any. She was counseled not to use any illicit sublingual buprenorphine. One week later, she reported doing well in her next visit and denied withdrawal symptoms.

DISCUSSION

We present an unusual case of rapid opioid withdrawal after liposuction in a patient who had previously been stable on extended-release buprenorphine injections.

The US Food and Drug Administration approved the once-monthly injectable buprenorphine for the management of opioid use disorder in 2017. Buprenorphine, in all its forms (tablets, extended-release injections, and buccal films), is now the most widely used and easily accessible opioid treatment option in the United States.[4]

The extended-release formulation, just like all the other forms of buprenorphine, prevents opioid withdrawal by acting as a μ-opioid receptor partial agonist.[5] Buprenorphine has a high affinity at these receptor sites and is not easily replaced by other opioids. Current recommendations state that any patient using sublingual or oral buprenorphine can transition to an extended-release form after at least 7 days.[6]

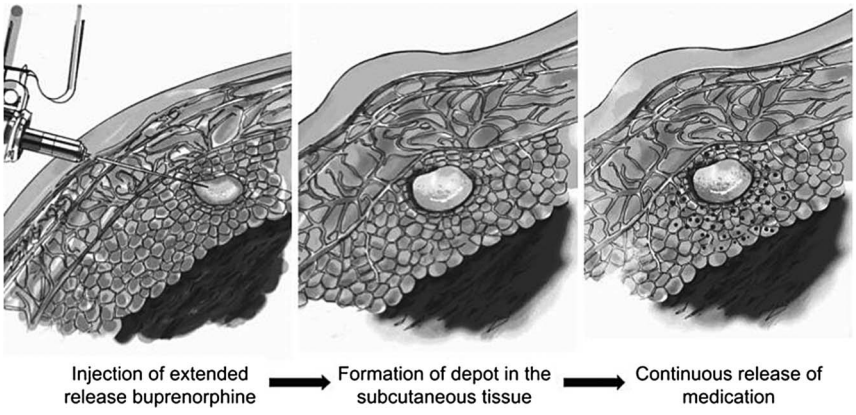
Injectable form of extended-release buprenorphine was developed to provide a sustained action on these receptors and improve long-term adherence compared with daily sublingual tablets or films to enhance overall effectiveness. After the subcutaneous injection, buprenorphine levels in the blood stay consistent throughout the month because of its sustained release.[7]

The extended-release injectable buprenorphine is subcutaneously injected as a liquid (Fig. 1). After the injection, it changes F1 into a solid form called a "depot." The depot can sometimes be felt as a small mass under the skin at the injection site for several weeks, and it gets smaller over time.[8]

The extended-release injectable buprenorphine is manufactured using the proprietary drug delivery system called Atrigel, a novel delivery system used for both parenteral and site-specific drug delivery.[9] It is known to have greater compatibility with a broad range of water soluble as well as lipid-soluble pharmaceutical compounds and can easily administer extended-release medications, vaccines, and natural products.[10] When buprenorphine is injected subcutaneously using the proprietary drug delivery system, it is delivered at sustained levels, and the levels stay consistent throughout the month.

The patient in this case report was stable for almost 5 months on extended-release buprenorphine. She experienced acute opioid withdrawal symptoms once had the liposuction procedure. Liposuction is a fairly common surgical procedure that is performed to contour and shape the areas like abdomen, hips, thighs, buttocks, arms, or neck. It uses a suction technique to remove fat from these areas of the body.[11] Small incisions are made on the surgical sites, and a cannula is inserted through these incisions to loosen the excess adipose tissue. The dislodged fatty tissue is then suctioned out of the body using a surgical vacuum suction catheter.[11]

When the patient had liposuction surgery done on her abdomen, we hypothesized that the depot might have been extracted along with surrounding adipose tissue, leading to a rapid decrease in the buprenorphine levels and thereby causing acute opioid withdrawal. This led to opioid withdrawal symptoms,



AQ4 FIGURE 1. Yyyy.

and the patient resorted to buying buprenorphine tablets off the street. Our patient had multiple scars on her abdomen, likely the result of the liposuction entry sites, including the site where she had the last injection. Liposuction procedure also leads to a significant amount of bruising, and this might have interfered with the absorption of the medication as well.

The suction cannulas used in the liposuction procedure can vary any way between 2 and 5 mm. In general, larger cannulas are used for liposuction of deep planes along with fat separation while smaller cannulas are more often used more for suctioning and contouring of the superficial parts. It is also possible that the depot probably was not suctioned all at once but might have been broken up.[12]

She did not report to the addiction medicine physician that she would get the procedure. In addition, she did not foresee the procedure's outcomes and failed to inform her surgeon where the depot injection was administered. In addition, the surgeon could have asked her about the location of buprenorphine, which could have potentially avoided the withdrawal symptoms either by leaving the injection site untouched or by switching to alternate forms before and after procedure.

The current recommendation is that if a patient takes the extended-release formulation but misses a dose, they should take the subsequent dose as soon as possible, no less than 26 days later.[10] When our patient returned for a follow-up visit, she received her next dose of extended-release medication, and her withdrawal symptoms resolved.

There are some rare cases reported in the literature where the depot had to be removed due to some unforeseen complications like skin necrosis after the injection. In those cases, the patients had to be treated to avoid acute withdrawal symptoms like the patient in this case.[13]

This case report presents a unique case of opioid withdrawal after a fairly common surgical procedure, fitting into the definition of "iatrogenic opioid withdrawal." In our case, neither the patient nor the surgeon anticipated this outcome when the patient had liposuction. This case adds to the literature about extended-release buprenorphine and the caution physicians and surgeons must take when patients undergo such surgical procedures. A detailed history should be obtained by the clinicians about the potential upcoming surgical procedures like liposuction when the patients are on extended release buprenorphine or any such similar products.

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