

Clinical Communications

Subcutaneous abdominal abscesses in a patient with common variable immunodeficiency receiving subcutaneous immunoglobulin therapy

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Clinical Implications

- Physicians should be made aware that subcutaneous hematoma and secondary infection might be a potential complication in patients receiving subcutaneous immunoglobulin therapy, in particular those with concomitant skin diseases.

TO THE EDITOR:

Antibody deficiencies are the most common primary immunodeficiency disorders for which immunoglobulin replacement therapy has been successfully used for preventing recurrent infections as well as long-term infection-related complications.¹ The introduction of subcutaneous immunoglobulin (SCIG) therapy has resulted in a decrease in some of the disadvantages associated with intravenous immunoglobulin (IVIG) therapy. However, some adverse effects exist with SCIG, in particular local tissue reactions. Fortunately, however, infections at the site of injection have rarely been reported.^{2,3} We describe a 59-year-old female patient with common variable immunodeficiency (CVID) who presented with subcutaneous abdominal abscesses due to SCIG administration.

Our patient was diagnosed with CVID on the basis of a history of recurrent sinopulmonary infections including multiple episodes of pneumonia requiring hospitalization at least once a year for about 13 years before her diagnosis. At diagnosis, she had hypogammaglobulinemia (IgG, 2.73 g/L [7.51-15.6]; IgA, 0.046 g/L [0.82-4.53]; and IgM, 2.07 g/L [0.46-3.04]) and impaired antibody responses to protein (tetanus, mumps) and polysaccharide (pneumococcal) vaccines. In addition to CVID, her medical history included type 2 diabetes, hypertension, renal insufficiency, cardiomyopathy, hypercholesterolemia, osteoarthritis, obstructive sleep apnea, asthma, hypothyroidism, psoriasis, and depression.

She initially received IVIG infusions beginning in 2003 but she was later switched to SCIG because of difficult intravenous access that required central venous catheter placement that was complicated by septicemia due to methicillin-resistant *Staphylococcus aureus*. She was dosed at approximately 500 mg/kg/mo, which resulted in a weekly total dose of 12.8 g (80 mL) of Vivaglobin. She administered 10 mL subcutaneously in both sides of her abdomen every Tuesday, Thursday, Saturday, and Sunday.

She tolerated this dosing without any adverse events. After 15 months, she developed multiple subcutaneous abdominal masses that became tender 1 week before the presentation, which led her to seek medical attention. On examination, she was afebrile and had mildly tender, indurated masses without fluctuation on the

lower left side of her abdomen with erythema of the overlying skin. Her IgG level about 2 months before her presentation was 10.7 g/L.

Abdominal ultrasonography revealed a complex collection in the left lower quadrant with several septations, and internal echoes, measuring 7.2 x 3.3 x 4 cm, surrounded by echogenic fat (Figure 1). Hemorrhagic purulent fluid was aspirated and grew methicillin-sensitive *Staphylococcus aureus*. IgG level was 9.01 g/L. She was treated with vancomycin, due to a history of penicillin allergy, and the abscesses were drained with a favorable response. Methicillin-sensitive *Staphylococcus aureus* was also isolated from the surveillance nasal swab. IVIG was restarted via a peripherally inserted central catheter line, which she tolerated without incident.

Immunoglobulin replacement is a fundamental therapy for antibody-deficient patients. Although immunoglobulin was first given subcutaneously in an agammaglobulinemic patient by Bruton in 1952, intramuscular immunoglobulin subsequently became the most widely used product in the early years. However, because of several disadvantages such as painful administration or inadequate serum immunoglobulin levels, IVIG had later emerged as the standard treatment for more than 3 decades.⁴

Systemic reactions can be found in approximately one-third of patients receiving IVIG within 72 hours after infusions.¹ They are usually mild such as headache, fever, chills, flushing, nausea, dizziness, fatigue, myalgia, urticaria, tachycardia, chest tightness, and musculoskeletal pain.^{1,5} Most reactions are related to the infusion rates and tend to diminish on subsequent infusions. Serious adverse events are uncommon and may include anaphylactic or anaphylactoid reactions, aseptic meningitis, acute renal failure, hemolytic anemia, thromboembolic events, and transfusion-related acute lung injury.^{1,4} Although IVIG is generally well tolerated, it still has some limitations particularly in those patients with difficult intravenous access, impaired quality of life, poor compliance, or intolerance due to systemic adverse reactions. SCIG was introduced in 1980 and has been recognized as an alternative delivery method to the population experiencing difficulties with IVIG since it was approved by the US Food and Drug Administration in 2006.⁵

Many studies have confirmed the safety and efficacy of SCIG as well as increased quality of life in patients treated with SCIG therapy.^{4,5} Systemic reactions are reported to occur in fewer than 5% of patients due to slower increasing and more constant serum immunoglobulin levels than with IVIG administration.^{1,5} However, local tissue reactions are common, albeit mild and transient, and can be found in up to 75% of patients.¹ The reactions may include swelling, redness, warmth, induration, soreness, bruising, and sensation of itching or burning at infusion sites. Most reactions decrease over time and generally do not require specific treatments or infusion withdrawal. Infusion site abscesses or skin infections are unusual.^{2,3} Although SCIG has been shown to obviate some disadvantages associated with IVIG, it might not be a suitable option for particular patients such as individuals with physical disability or requiring nursing

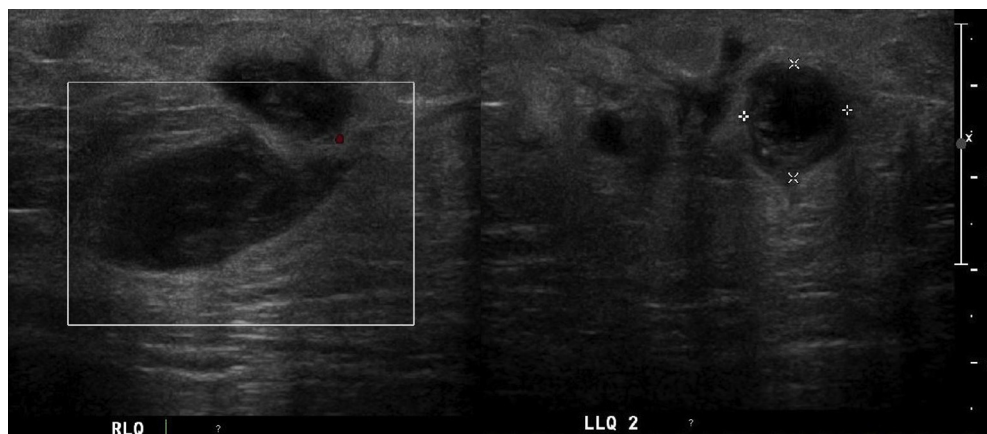


FIGURE 1. Subcutaneous abdominal collections were demonstrated on abdominal ultrasonography. LLQ, Left lower quadrant; RLQ, right lower quadrant.

assistance, widespread skin disease, limited subcutaneous fat, or a bleeding disorder.^{1,5}

Our patient had multiple comorbidities and concomitant skin disease that might have contributed to bacteria colonization and increased susceptibility to skin infections. It has been previously shown that *S aureus* was the most frequent organism isolated from the skin of patients with psoriasis.⁶ Underlying skin disease was also believed to be a predisposing factor to deep wound infections in another patient with CVID receiving SCIG therapy.³ In our patient, because the abdominal masses developed at the infusion site simultaneously with SCIG administration, her frequent infusion schedule might have played a contributing role in developing an infection due to repeated breaching of the skin barrier. We suggest that the subcutaneous abdominal abscess in this patient is likely to have developed from an infected hematoma secondary to blood vessel injury due to SCIG administration.

This patient illustrates a clinical dilemma for which making an appropriate selection of the delivery route of immunoglobulin therapy might be problematic, particularly in patients with coexisting dermatoses. Physicians should inform the patient that the risk of soft tissue infections, secondary to bacteria colonization, might increase with SCIG infusions. A strategy involving *S aureus* screening and decolonization before the initiation of SCIG should also be considered although its benefit remains controversial.⁷ Therefore, the route of immunoglobulin administration should be carefully selected and discussed with those patients.

In summary, although uncommon, abdominal hematomas should be recognized as a potential complication in patients receiving SCIG therapy. *S aureus* surveillance and eradication might also be considered before the initiation of SCIG therapy for prevention of secondary infections, particularly in patients who have a history of *S aureus* infections or

concomitant skin diseases that are susceptible to *S aureus* colonization.

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