Fatal diagnosis of hemophagocytic lymphohistiocytosis in a patient with a history of human immunodeficiency virus, Hodgkin’s lymphoma, and Epstein–Barr virus

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ABSTRACT

Introduction: Hemophagocytic lymphohistiocytosis (HLH) is a rare hyperinflammatory syndrome with high rates of mortality. Secondary HLH is acquired from an underlying illness and therefore difficult to diagnose because the underlying disease can mask the symptoms of HLH or have a similar presentation. Therefore, it is important for physicians and health care providers to be familiar with HLH to keep in mind as a differential diagnosis in critically ill patients. It is imperative to start treatment early to decrease mortality. Case Report: We describe a case of a 42-year-old African-American man with a past medical history of human immunodeficiency virus (HIV), Hodgkin’s lymphoma, and Epstein–Barr virus (EBV) who presented to the emergency department (ED) with diarrhea, nausea, and vomiting. He was ultimately diagnosed with acquired HLH. Early on during his admission he was treated with dexamethasone, but continued into multiple organ failure and succumbed on the 11th hospital day. Conclusion: Hemophagocytic lymphohistiocytosis is a rare disease and may not initially or come to mind at all as part of a differential diagnosis in critically ill patients. It is important for physicians to be aware of how the disease presents and the underlying diseases that can cause HLH as reported in this case report. Early diagnosis is crucial for early treatment before patient’s experience irreversible organ failure and death. This case report discusses the etiology, symptoms, diagnosis, and treatment of HLH to educate health care providers and decrease the mortality in this patient population.

Keywords: Epstein–Barr virus, Hemophagocytic lymphohistiocytosis, Hodgkin’s lymphoma, Human immunodeficiency virus

INTRODUCTION

Hemophagocytic lymphohistiocytosis (HLH) is a rare hyperinflammatory syndrome characterized by uncontrolled activation of T cells, macrophages, and histiocytes [1]. It is often fatal if not quickly diagnosed and treated. Mortality is high from terminal multiple organ failure that commonly occurs from overproduction of inflammatory cytokines. Hemophagocytic lymphohistiocytosis can be primary or secondary. Primary HLH is from familial inheritance or genetic causes. It usually presents in infants and young children and has a low likelihood of survival. Secondary HLH is acquired from an underlying illness [2]. Common triggers for
acquired HLH are malignancy, especially hematologic, and infections. Mycoplasma species, parasites, and fungal infections such as Cryptococcus, candida, and pneumocystis pneumonia are common sources of underlying infection. Epstein–Barr virus (EBV), HIV, cytomegalovirus (CMV), herpes simplex virus (HSV), and hepatitis are common viruses associated as well. Autoimmune diseases have also been linked to HLH [1]. Acquired HLH presents usually during adulthood in patients without a family history or genetic cause [3]. Here we report an adult patient with acquired HLH, with a past medical history of Hodgkin’s lymphoma, hepatitis B virus (HBV), EBV, Parvovirus B19, and HIV who presented with a week of diarrhea, nausea, and vomiting.

CASE REPORT

A 42-year-old African-American man with a past medical history of HIV, Hodgkin’s lymphoma, recurrent septic shock, HBV, steroid-induced hyperglycemia, Parvovirus B19, and EBV presented to the ED complaining of diarrhea and nausea. He was diagnosed with HIV 13 years prior and was treated with emtricitabine, dolutegravir, lamivudine, and tenofovir for the past 13 years prior and was treated with emtricitabine, dolutegravir, lamivudine, and tenofovir for the past 13 years. He also tested positive for EBV and hepatitis C virus (HCV) were negative. Procalcitonin was greater than 40,000 ng/mL, and CD4 count was 93 cells/uL. Cytomegalovirus, Histoplasma, blastomycosis, and malaria were ruled out. Computed tomography (CT) chest revealed lymphadenopathy throughout the mediastinum and retroperitoneum. Computed tomography abdomen and pelvis revealed an enlarged liver and spleen (Figure 1). He was diagnosed with acquired HLH.

Over the next 11 days, the patient quickly declined and went into multiple organ failure. He initially presented as alert and oriented, but prior to death was very lethargic, not oriented to self, place, or time, was unable to answer questions, and had difficulty following commands. Jaundice and scleral icterus worsened. His abdomen remained distended and diffusely tender with palpation. Peripheral edema was noted in his bilateral lower extremities. He also had ongoing singultus, which was refractory to baclofen and thorazine. He was continuously hypotensive requiring norepinephrine and vasopressin, but remained afebrile. Acyclovir, piperacillin-tazobactam, and linezolid were discontinued due to acute renal failure and atovaquone, meropenem, and micafungin were initiated along with continued home highly active antiretroviral therapy (HAART). He had a full workup to rule out an infectious or immunologic etiology for his presentation (Tables 2 and 3). His blood cultures and urine cultures were negative. Epstein–Barr virus reactivated and was 620,190 copies/mL, HIV quantitative polymerase chain reaction (PCR) was 1,290,000 copies/mL, HBV core was reactive, ferritin was greater than 40,000 ng/mL, and CD4 count was 93 cells/uL. Cytomegalovirus, Histoplasma, blastomycosis, and hepatitis C virus (HCV) were negative. Procalcitonin was 4.84 ng/mL.

He was pancytopenic requiring multiple packed red blood cell and platelet transfusions. Prior to death his white blood cells were 1.6 uL, hemoglobin 7.6 g/dL, and platelets 22 uL.
### Table 1: Patient’s lab results

| Lab                          | Initial presentation | Day 5 | Day 10 | Day 11 (Death) | 4 Months prior to admission |
|------------------------------|----------------------|-------|--------|----------------|-----------------------------|
| Sodium (mmol/L)              | 125                  | 142   | 140    | 142            | 128                         |
| Potassium (mmol/L)           | 3.6                  | 3.5   | 4.6    | 4.2            | 3.8                         |
| Anion gap (mmol/L)           | 10                   | 12    | 18     | 37             | 8                           |
| BUN (mg/dL)                  | 63                   | 79    | 83     | 44             | 65                          |
| Creatinine (mg/dL)           | 2.95                 | 2.58  | 3.95   | 2.31           | 3.10                        |
| AST (U/L)                    | 343                  | 137   | 220    | 493            | 268                         |
| ALT (U/L)                    | 98                   | 42    | 96     | 182            | 73                          |
| Total bilirubin (mg/dL)      | 7.3                  | 19.5  | 32.4   | 37.6           | 7.6                         |
| Direct bilirubin (mg/dL)     | 5.8                  | 14    | 24.2   | 26.8           | 6                           |
| Ammonia (ug/dL)              | 73                   | 86    | 125    | 45             |                             |
| Lipase (U/L)                 | 62                   | 727   |        |                | 129                         |
| WBC (uL)                     | 2.4                  | 3.1   | 2.1    | 1.6            | 1.9                         |
| Hemoglobin (g/dL)            | 9.6                  | 8.6   | 7.8    | 7.6            | 6.6                         |
| Platelets (uL)               | 132                  | 68    | 11     | 22             | 190                         |
| INR                          | 1.6                  | 1.4   | 2.4    | 2.7            | 1.8                         |
| Pro time (seconds)           | 18.3                 | 15.7  | 28.2   | 31             | 20.6                        |
| Lactate (mmol/L)             | 5.73                 |       | 19.56  |                | 2.34                        |
| Ferritin (ng/mL)             | >40,000              | >2000 | >40,000 |                | >40,000                      |
| Other labs                   |                      |       |        |                |                             |
| LDH (U/L)                    | 528 (Day 1)          | 426   | (Day 3) |                | 794                         |
| Triglycerides (mg/dL)        | 279 (Day 2)          | 325   | (Day 5) |                |                             |
| ACTH stimulation cortisol (ug/dL) | 21 (0 min)           | 23.2  | (30 min) | 24.1 (60 min) |                             |
| Procalcitonin (ng/mL)        | 4.85                 |       |        |                | 12.12                       |

WBC: white blood cell; INR: international normalized ratio.

### Table 2: Immunology and microbiology labs

#### Immunology labs

| Lab                          | Initial presentation | 4 Months prior to admission |
|------------------------------|----------------------|-----------------------------|
| ANA                          | Negative             | Negative                    |
| ANCA screen                  | Negative             | Negative                    |
| C3 Complement (mg/dL)        | 75                   | 79                          |
| C4 Complement (mg/dL)        | 37                   | 20                          |
| Hep A IgM                    | Nonreactive          | Nonreactive                 |
| Hep B core total Ab          | Reactive             |                             |
| Hepatic C RNA QUANT PCR      | Nonreactive          | Nonreactive                 |
| HIV-1 genotype               | Detected             |                             |
| HIV 1 RNA QN PCR (log copies/mL) | 6.11               | Not detected four months prior |
| HIV 1 RNA QN PCR (copies/mL) | 1,290,000            | Not detected four months prior |
| IL-2 (pg/mL)                 | <38                  | <38                         |

#### Microbiology labs

| Lab                          | Initial presentation | 4 Months prior to admission |
|------------------------------|----------------------|-----------------------------|
| EBV DNA PCR (copies/mL)      | 620,190              | 13,896                      |
| CMV, HSV1 HSV2, Influenza A, Influenza B, Varicella-zoster | Not detected | Not detected |
| Histoplasma, blastomyces, cryptococcus | Not detected | Not detected |
| GI panel                     | Not detected         |                             |

ANA: antinuclear antibody; ANCA: antineutrophil cytoplasmic antibodies.
The patient continued to have diarrhea with minimal improvement. A gastrointestinal (GI) panel including Clostridium difficile was negative. The patient had progressively worsening transaminitis and hyperbilirubinemia that prompted multiple abdominal images. His AST and ALT peaked at 493 and 193 U/L. Total bilirubin and direct bilirubin peaked at 37.6 and 26.8 mg/dL. A right upper quadrant ultrasound revealed gallbladder thickening and sludge and a hepatobiliary iminodiacetic acid (HIDA) scan noted no biliary excretion after five hours. Magnetic resonance cholangiopancreatography was difficult to visualize secondary to singultus but there was no evidence of biliary duct dilation. Gallbladder edema, trace ascites, and mild anasarca were noted along with abdominal and retroperitoneal lymphadenopathy. The abdominal pain and distension of the patient continued to worsen over his hospital course, so an additional abdominal ultrasound was ordered and only revealed small ascites and splenomegaly. Ammonia levels peaked at 125 ug/dL and the patient received multiple doses of rifaximin and lactulose. A liver biopsy was performed which revealed classic Hodgkin’s lymphoma. Lipase was elevated at 727 U/L, but trended down with multiple fluid boluses and an increase of continuous intravenous (IV) fluids. Initial CT of abdomen and pelvis was negative for pancreatitis. His acute kidney injury initially improved with fluid replacement, but the patient eventually went into acute renal failure with worsening metabolic acidosis. He required continuous renal replacement therapy (CRRT) and multiple amps of sodium bicarbonate. He was given albumin and started on a sodium bicarbonate drip. His lactate dehydrogenase (LDH) was 426 U/L and lactate continued to increase peaking at 19.56 mmol/L.

A ferritin level was initially checked upon admission in further supporting HLH versus sepsis in this patient. Ferritin was negative. The patient’s worsening mental status, hypotension requiring norepinephrine and vasopressin, and multiple organ failure, oncology felt he was too clinically ill to tolerate chemotherapy treatment for the underlying Hodgkin’s lymphoma. He succumbed on the 11th hospital day.

### DISCUSSION

Hemophagocytic lymphohistiocytosis is a rare hyperinflammatory hyperferritinemic syndrome driven by over activation of T cells and a cytokine storm which is often fatal [4]. It was not listed in the Surveillance, Epidemiology, and End Results (SEER) program until 2010, so the incidence and prevalence is unknown and cases are most likely undiagnosed and underreported. In the United States, the prevalence is estimated to be 1/100,000 live births [1]. Primary HLH is familial or genetic in origin, usually presents in infants or children, and is usually fatal within two months without treatment [2]. Secondary HLH, which was seen in our patient, is secondary to an underlying illness such as malignancy, infection, or autoimmune diseases. The mean age of onset is 49 years old and is more commonly seen in males [4]. Out of the infectious etiologies, EBV is the most common affecting approximately 70% of patients diagnosed with HLH [5]. Lymphomas are the most common underlying malignancy associated with HLH [3]. With our patient having a past medical history of EBV, Hodgkin’s lymphoma, HIV, HBV, and Parvovirus B19, it was difficult to determine the underlying illness driving the HLH and differentiating it from sepsis due to his history of multiple admissions for sepsis and being immunosuppressed.

Most patients present with fever, pancytopenia, liver dysfunction, hepatosplenomegaly, hyperglycemia, hyperfibrinogenemia, neurological symptoms, and sepsis like syndrome that can rapidly progress into multiple organ failure [4, 6]. Our patient did present initially with a sepsis like picture with hypotension, pancytopenia, hepatosplenomegaly, transaminitis, and hyperbilirubinemia. Although, he remained afebrile for most of his hospital course, but this could have been masked with multiple days of CRRT. Also, a bone marrow biopsy was not performed, which would have been helpful in further supporting HLH versus sepsis in this patient.

### Table 3: Flow cytometry

| Lab                             | Initial presentation | Four months prior to admission |
|---------------------------------|----------------------|-------------------------------|
| CD16 B cell (cells/uL)          | <20                  | 24                            |
| CD3 total T cells (cells/uL)    | 410                  | 119                           |
| CD4 helper T cell (cells/uL)    | 93                   | 60                            |
| CD8 suppressor T cell (cells/uL)| 307                  | 59                            |
| CD4/CD8 ratio                   | 0.30                 | 1.01                          |
| CD16/56 NK cell (cells/uL)      | 49                   | 57                            |

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In patients with underlying illness, especially in the ICU, it is difficult to differentiate HLH from other diagnoses such as septic shock, Langerhans cell histiocytosis, infections, and metabolic disease [1]. The HLH-2004 diagnostic criteria is a useful tool to help make a diagnosis in these patients if 5/8 of the criteria is met (Table 4). Our patient met 5/8 criteria of the diagnostic criteria. He had splenomegaly, cytopenia involving three cellular lineages (anemic, thrombocytopenic, and leukopenic), hypertriglyceridemia at 325, CD16/56 NK cells decreased at 49, and ferritin >40,000 [4, 6, 7]. Hyperbilirubinemia, hepatomegaly, transaminitis, and elevated lactate dehydrogenase are not included in the diagnostic criteria but also support the diagnosis of HLH, especially an increased ferritin over 7000–10,000, which was also seen in our patient [4]. The patient did have a liver biopsy done, which Reed–Sternberg cells were seen and consistent with classical Hodgkin’s lymphoma. Also, atypical cells PAX-5, CD30, and focally CD15 were positive and EBV in situ hybridization was positive as well. Hemophagocytosis was not noted in the pathology report from the liver biopsy and a bone marrow biopsy was not done. A study done in 2018 by Qiaolei et al. reported 174 patients diagnosed with HLH who nearly all had hyperferritinemia, high LDL, fever, low albumin, and hemophagocytosis seen in a bone marrow biopsy [6]. Another study done in 2018 by Lai et al. revealed that out of 133 patients diagnosed with EBV associated HLH, 92% had an elevation of serum ferritin, 93.2% had a reduction of 2–3 different cell type lineages, 91.2% were febrile, 89.5% had splenomegaly, and 80% had liver function damage [5]. Our patient’s presentation is similar to how the patients were reported in these prior studies, which further supports his diagnosis of HLH.

The HLH probability calculation (H-score) was developed retrospectively in adult patients based on a point system (Table 5). This scoring system is an additional tool that is useful when diagnosing HLH and is less restrictive than HLH-2004 diagnostic criteria. It has been reported to be the most useful in adults based of their initial labs at presentation instead of going off extreme values later during their hospital course [4, 8]. After using the patient’s initial labs before his condition worsened and the scoring criteria from the manuscript by

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### Table 4: HLH-2004 diagnostic criteria

| Molecular diagnosis consistent with HLH | Mutations of PRF1, UNC13D, Munc18-2, Rab27a, STX11, SH2D1A, or BIRC4 |
|----------------------------------------|---------------------------------------------------------------------|
| OR                                     | Temperature >38.5 for great than 7 days                             |
| Fulfillment of 5/8 of the below criteria:| Affecting 2 of 3 lineages in peripheral blood                       |
| Fever                                  | • Hemoglobin 9 g/dL                                                  |
| Splenomegaly                           | • Platelets <100 × 10⁶/mL                                            |
| Cytopenias                             | • Neutrophils <1 × 10⁹/mL                                            |
|                                        | Fasting >265 mg/dL and/or <150 mg/dL                                |
| Hypertriglyceridemia and/or hypofibrinogenemia | Alpha-chain of sIL-2 receptors                                    |
| Hemophagocytosis in bone marrow, spleen, lymph nodes, or liver | >500 ng/mL                                                          |
| Low or absent NK-cell activity          |                                                                     |
| Ferritin                               |                                                                     |
| Elevated sCD25                         |                                                                     |

Adapted from Jordan et al. and Tothova et al.
Fardet et al., our patient scored a 193. This score did not consider fibrinogen and hemophagocytosis from a bone marrow biopsy. A score of 193 has an 82% probability of having HLH. The best cutoff value for the H-score is 169, which has an accurate classification of 90% of patients based on a sensitivity of 93% and specificity of 86% [9].

The importance of rapid recognition of HLH is pivotal, so patients can receive appropriate treatment quickly to increase survival. If the diagnosis is made too late, the patient may not be able to receive treatment [1]. The HLH-94 protocol consists of corticosteroid initiation, typically dexamethasone, cyclosporine A, and etoposide to delete activated T cells and suppress inflammatory cytokine production [4]. Dexamethasone is typically given at 10 mg daily for two weeks and then tapered to 5 mg for two weeks, 2.5 mg for two weeks, and 1.25 mg for one week. This was how the patient was treated during his prior admission and was discharged with the remaining dexamethasone taper. During the most recent admission, the patient was started on 10 mg twice daily, but due to his worsening clinical condition, the dose was increased to 10 mg three times a day, which no improvement was seen.

He was not given cyclosporine A or etoposide. It was difficult to determine what was driving the HLH due to his extensive past medical history including EBV, HIV, and Hodgkin’s lymphoma. The patient failed to follow up with treatment for his Hodgkin’s lymphoma, so this was the most likely underlying cause of the recurrent HLH. Although, due to the patient’s noncompliance, it is difficult to determine if he was compliant with taking his antiviral medications as an outpatient. He continued his home regimen of emtricitabine, dolutegravir, tenofovir, and lamivudine inpatient. Studies have been reported in patients with acute HIV-associated HLH that clinical improvement is seen after HAART therapy for 5–7 days, but continuing antiviral therapy in our patient did not improve his clinical outcome [10]. It has been reported in patients with lymphoma-associated HLH should be rapidly treated with specific anti-lymphoma therapy, although it was felt by oncology that our patient was too clinically ill with associated altered mental status, hypotension requiring norepinephrine and vasopressin, and multiple organ failure to tolerate the chemotherapy without worsening his condition [6].

### Table 5: HLH probability calculator (H-score)

| Parameter                              | H-score                                      |
|----------------------------------------|----------------------------------------------|
| Fever (°C)                             | • 0 (<38.4)                                 |
|                                        | • 33 (38.4–39.4)                             |
|                                        | • 49 (>39.4)                                |
| Organomegaly                           | • 0: no                                      |
|                                        | • 23: hepatomegaly or splenomegaly          |
|                                        | • 38: hepatomegaly and splenomegaly        |
| Cytopenia                              | • 0: one lineage                             |
|                                        | • 24: two lineages                          |
|                                        | • 34: three lineages                        |
| Ferritin (ng/mL)                       | • 0: <2000                                   |
|                                        | • 35: 2000–6000                             |
|                                        | • 50: >6000                                  |
| Triglycerides (nmol/L)                 | • 0: <1.5                                    |
|                                        | • 44: 1.5–4                                 |
|                                        | • 64: >4                                    |
| Fibrinogen (g/L) (not added if there is a point for elevated triglycerides) | • 0: >2.5                                    |
|                                        | • 30 or equal to 2.5                         |
| Hemophagocytosis in bone marrow       | • 0: no                                      |
|                                        | • 35: yes                                    |
| Aspartate aminotransferase (AST) IU/L  | • 0: <30                                     |
|                                        | • 19: ≥30                                    |
| Known underlying immunosuppression     | • 0: no                                      |
|                                        | • 18: yes                                    |

Adapted from Fardet et al.
The overall prognosis in patients diagnosed with HLH is poor. The mortality in secondary HLH, even though lacking specificity, ranges from 20% to 88% depending on the underlying illness. The worst prognostic factors are patients aged greater than 60, male sex, lymphocytopenia, hypofibrinogenaemia, bilirubin >2 mg/dL, and BUN >20 mg/dL. Also, patients with HLH associated with lymphomas have a higher mortality than if the underlying etiology is an infection or autoimmune condition [6]. Elevated LDH, AST, c-reactive protein, ferritin, and procalcitonin were also reported by Gavand et al. to be related to poor prognosis [6, 11]. Our patient is a male who presented with lymphocytopenia, increased bilirubin, BUN, AST, ferritin, and procalcitonin, which are all characteristics of a poor prognosis.

CONCLUSION

In conclusion, HLH is a rare hyperinflammatory syndrome with high rates of mortality. It is difficult to diagnose these patients, especially with secondary HLH, because of underlying illnesses and similar presentations to other conditions. Due to the difficulty of diagnoses, HLH can often be missed and treatment is delayed. It is crucial for patients to be diagnosed and treated quickly before their condition becomes too clinically severe for treatment to be initiated. With our patient, he was noncompliant and initially presented with a sepsis-like picture with multiple underlying comorbidities. Although, with the known possible diagnosis of HLH in the past, he was treated with dexamethasone, but became too clinically ill to receive further chemotherapy treatment for the underlying Hodgkin’s lymphoma. The Hodgkin’s lymphoma seemed to be the most likely associated etiology for the HLH because he was noncompliant with following up with treatment after diagnosis. Also, CT chest, abdomen, and pelvis revealed diffuse lymphadenopathy and the liver biopsy revealed classic Hodgkin’s lymphoma suggesting extensive disease. It is important for physicians, especially in the ICU, to include HLH in their differential and to be familiar with the diagnostic criteria for early recognition and treatment to increase potential survival in these patients.

REFERENCES

1. Tothova Z, Berliner N. Hemophagocytic syndrome and critical illness: New insights into diagnosis and management. J Intensive Care Med 2015;30(7):401–12.
2. Narendra AM, Varun Kumar G, Krishna Prasad A, Shetty M, Uppin MS, Srinivasan VR. Hemophagocytic lymphohistiocytosis. Indian J Hematol Blood Transfus 2014;30(3):204–7.
3. Fatima Z, Khan A, Tariq U, Sohail MS. Hemophagocytic lymphohistiocytosis: A case series. Cureus 2018;10(4):e2545.
4. La Rosée P, Horne A, Hines M, et al. Recommendations for the management of hemophagocytic lymphohistiocytosis in adults. Blood 2019;133(23):2465–77.
5. Lai W, Wang Y, Wang J, Wu L, Jin Z, Wang Z. Epstein-Barr virus-associated hemophagocytic lymphohistiocytosis in adults and adolescents-a life-threatening disease: Analysis of 133 cases from a single center. Hematology 2018;23(10):810–6.
6. Zhang Q, Li L, Zhu L, et al. Adult onset haemophagocytic lymphohistiocytosis prognosis is affected by underlying disease: Analysis of a single-institution series of 174 patients. Swiss Med Wkly 2018;148:w14641.
7. Fitzgerald BP, Wojciechowski AL, Bajwa RPS. Efficacy of prompt initiation of antiretroviral therapy in the treatment of hemophagocytic lymphohistiocytosis triggered by uncontrolled human immunodeficiency virus. Case Rep Crit Care 2017;2017:8630609.
8. Debaugnies F, Mahadeb B, Ferster A, et al. Performances of the H-score for diagnosis of hemophagocytic lymphohistiocytosis in adult and pediatric patients. Am J Clin Pathol 2016;145(6):862–70.
9. Fardet L, Galicier L, Lambotte O, et al. Development and validation of the HScore, a score for the diagnosis of reactive hemophagocytic syndrome. Arthritis Rheumatol 2014;66(9):2613–20.
10. Jordan MB, Allen CE, Weitzman S, Filipovich AH, McClain KL. How I treat hemophagocytic lymphohistiocytosis. Blood 2011;118(15):4041–52.
11. Gavand PE, Sério I, Larroche C, et al. Association syndrome lymphohistiocytaire (HLH) et lupus systémique: Étude multicentrique française de 103 épisodes chez 89 patients adultes. La Revue de Médecine Interne 2016;37(Suppl 2):A122–3.

Author Contributions
Chelsea Taylor Schwartz – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Christopher B Schmitt – Conception of the work, Design of the work, Analysis of data, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.

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