

# Paranoia and suicidality after starting treatment for lupus

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## How would you handle this case?

Answer the **challenge questions** throughout this article

Mr. L, age 28, presents with recent-onset suicidal ideation, paranoia, and hostile thoughts soon after starting treatment for subacute cutaneous lupus. What could be causing his unusual behavior?

### **CASE** Unusual behavior, thoughts

Mr. L, age 28, an immigrant from Burma, is brought to his primary care physician's clinic by his wife for follow-up on a rash. During the evaluation, his wife reports that Mr. L recently has had suicidal ideation, depression, and increased anger. She says Mr. L had made statements about wanting to kill himself with a gun. Mr. L had driven his car to a soccer field with a knife in hand and was contemplating suicide. She is concerned about her own safety and their children's safety because of Mr. L's anger. The physician refers Mr. L to the emergency department, and he is admitted to the medical floor for a rheumatological flare-up and suicidal ideation.

Mr. L starts displaying inappropriate behaviors, including masturbating in front of the patient safety attendant, telling the attendant "You are going to die today," and assaulting a female attendant by trying to grab her breasts. He is given IM haloperidol, 2 mg, which effectively alleviates these behaviors. Between episodes of unusual behavior and outbursts, Mr. L is docile, quiet, and cooperative, and denies any memory of these episodes.

One month earlier, Mr. L had been hospitalized for progressive weakness and inability to ambulate. He was diagnosed with necrotizing myositis and a rash consistent with subacute cutaneous lupus. He was started on

IV methylprednisolone, 1 g, and transitioned to oral prednisolone, 40 mg/d, which he continued taking after discharge. He also started taking azathioprine, which was increased from 50 to 100 mg/d. His condition improved shortly after beginning this regimen.

### Which diagnosis would you consider for Mr. L?

- a) brief psychotic disorder
- b) psychotic disorder secondary to neuropsychiatric lupus
- c) steroid-induced psychotic disorder
- d) amok

### The authors' observations

DSM-5 defines brief psychotic disorder as positive symptoms or disorganized or catatonic behavior appearing suddenly and lasting between 1 day to 1 month.<sup>1</sup> Mr. L had a sudden onset of his symptoms and marked stressors as a result of his worsening health. However, the possibility of his general medical conditions or medications causing his symptoms needed

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### Disclosures

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to be investigated and ruled out before this diagnosis could be assigned.

Another consideration is the culture-bound syndrome amok. Although DSM-5 does not use the term “culture-bound syndrome,” which was used in DSM-IV, it does recognize cultural conceptualizations of distress. Amok is described as a dissociative episode in which an individual has a period of brooding followed by outbursts that include violent, aggressive, and suicidal and/or homicidal ideation. The individual may exhibit persecutory and paranoid thinking, amnesia of the outbursts, and a return to typical behavior when the episode concludes.<sup>2</sup> However, it remained unclear whether Mr. L’s violent behavior was a manifestation of psychiatric or organic disease.

Identifying the possibility of amok is important not only for alleviating the patient’s distress but also for preventing violent outbursts that can result in injury or death.<sup>3</sup> Amok should be considered only in the context of possible psychiatric or organic brain disease, such as corticosteroid-induced psychosis (CIP) or systemic lupus erythematosus-induced psychosis (SLEIP).<sup>4</sup>

### EVALUATION Informants, labs

Mr. L immigrated to the United States when he was 5 years old. He does not speak English, and interviews are conducted with interpreting services at the hospital. Mr. L answers most questions with or 1 to 2 words. His medical and psychiatric histories are notable for hypothyroidism, hepatitis, non-ischemic cardiomyopathy, necrotizing myositis, subacute cutaneous lupus, and depression. Mr. L denies a personal or family history of mental illness; however, records show he has a history of unspecified depressive disorder.

Mr. L reports his current mood is “okay,” but he has felt different in the past few weeks. He denies auditory or visual hallucinations, or suicidal or homicidal ideation, but exhibits

paranoid thoughts. Mr. L believes everyone “lied” to him, and he repeats this frequently. Collateral information from friends reveals that he had threatened to burn down their houses. A family friend states that Mr. L has been depressed and angry over the past 5 days.

During his prior and current hospitalizations, many labs were completed. Thyroid, urine drug screen, C-reactive protein, urine analysis, ethanol, complete blood count, and comprehensive metabolic panel were negative. Erythrocyte sedimentation rate was 30. Lumbar puncture cell count was notable for mildly elevated lymphocytes at 84%. Antinuclear antibody (ANA) was positive. Lupus anticoagulant panel revealed a mildly prolonged partial thromboplastin time at 38.9 seconds. DNA double-stranded antibody (anti-dsDNA) was positive. Anti-Smith antibody was negative. Anti-Ro/SSA and anti-La/SSB antibodies were elevated. Albumin was low. A MRI of the brain showed dystrophic-appearing right parieto-occipital calcification and mild cerebral volume loss.

Based on Mr. L’s presentation and imaging, the rheumatology team suspects CNS lupus and that his prescribed steroids could be playing a role in his behavior.

### The authors’ observations

Differentiating CIP from SLEIP can be difficult. The clinical features and criteria for CIP and SLEIP are listed in *Table 1 (page 46)*.<sup>5-7</sup> Several studies have highlighted the difficulties in separating the 2 diagnoses:

- **Kampylafka et al**<sup>8</sup> found that CNS involvement, including stroke, myelopathy, seizures, optic neuritis, and meningitis, was present in 4.3% of their sample of patients with systematic lupus erythematosus (SLE), of whom 6.3% presented with SLEIP. Of patients with CNS involvement, 94% had positive ANA and 69% had positive anti-dsDNA antibodies. It remains difficult to definitively diagnose SLEIP rather than CIP, however, because 100% of

### Clinical Point

Consider amok when there is possible psychiatric or organic brain disease such as CIP or SLEIP

### Clinical Point

A distinguishing factor between CIP and SLEIP is the timing of the onset of symptoms; CIP occurs within 8 weeks of starting a corticosteroid

Table 1

## Criteria for diagnosing SLEIP vs CIP

SLEIP	CIP
<p><b>First stage</b> Evidence of exacerbation of SLE Other causes for neurological and/or psychiatric symptoms ruled out</p> <p><b>Second stage</b> Use clinical, laboratory, or imaging data to define lesion: Central and/or peripheral Diffuse and/or focal</p> <p><b>Third stage</b> Assess for signs/symptoms from 2 groups<sup>a</sup> <b>First group:</b> seizure, psychosis, cerebrovascular event, lesion of cranial nerves, quantitative alterations of consciousness <b>Second group:</b> cognitive dysfunction, lupus headache, peripheral neuropathy, MRI changes, EEG changes, ENMG changes, positive aRPA, positive aPL<sup>5</sup></p>	<ol style="list-style-type: none"> <li>1. Evidence of new-onset psychiatric disturbance (psychosis, mood disorder, anxiety)</li> <li>2. Corticosteroid dosage <math>\geq 40</math> mg/d<sup>6</sup></li> <li>3. Corticosteroid initiation within the past 8 weeks<sup>7</sup></li> <li>4. Response of psychosis to steroid reduction or withdrawal<sup>5</sup></li> </ol>
<p><sup>a</sup>Diagnosis of SLEIP requires <math>\geq 1</math> criterion from the first group and <math>\geq 2</math> criterion from the second group aPL: antiphospholipid-positive antibody; aRPA: replication protein A; CIP: corticosteroid-induced psychosis; ENMG: electroneuromyography; SLE: systemic lupus erythematosus; SLEIP: systemic lupus erythematosus-induced psychosis</p>	

patients in this study were taking corticosteroids, with 25% taking azathioprine, as was Mr. L.<sup>8</sup>

- **Appenzeller et al**<sup>9</sup> found that acute psychosis was associated with SLE in 11.3% of their sample. Psychosis in patients with SLE was accompanied by other manifestations of CNS involvement. On follow-up these patients had mild increases in white blood cell count in their CSF, and MRI demonstrated hyperdense lesions and cerebral atrophy. Hypoalbuminemia, although often seen in SLEIP, also is observed in patients with CIP and cannot be used to differentiate these 2 conditions.<sup>9</sup>

- **Monov and Monova**<sup>5</sup> recommended criteria for SLEIP that include 3 stages. The first stage is determining that there is evidence of an exacerbation of SLE, and ruling out other causes for neurologic and psychiatric symptoms. The second stage involves using clinical, laboratory, or imaging tests to define the lesion as central and/or peripheral and diffuse and/or focal. The third stage requires diagnosing SLEIP using criteria from 2 groups of signs and

symptoms: the first group includes seizure, psychosis, cerebrovascular event, lesion of cranial nerves, and quantitative alterations of consciousness; the second group includes cognitive dysfunction, lupus headache, peripheral neuropathy, MRI changes, EEG changes, electroneuromyography changes, and a positive replication protein A or antiphospholipid-positive antibody. Diagnosing SLEIP requires  $\geq 1$  criterion from group 1 and  $\geq 2$  criteria from group 2.<sup>5</sup>

- **Patten and Neutel**<sup>6</sup> found that patients taking prednisolone,  $< 40$  mg/d, had significantly higher rates of psychosis than those taking  $< 40$  mg/d.<sup>6</sup>

- **Bhangle et al**<sup>7</sup> found that one of the major distinguishing factors between CIP and SLEIP is the timing of the onset of symptoms, with CIP occurring within 8 weeks of initiation of a corticosteroid, and SLEIP being more likely to occur when additional CNS symptoms are present.<sup>7</sup>

### TREATMENT Decreased dosage

Mr. L starts quetiapine, 25 mg at bedtime, increased to 75 mg at bedtime. Prednisolone

Table 2

## Managing SLEIP vs CIP

## SLEIP

Acute exacerbations of SLE with psychosis, major depression, or severe confusion and cognitive dysfunction

1. Oral prednisolone, 1 to 2 mg/kg/d
2. Alternatively, IV cyclophosphamide
  - 0.75 to 1 g/m<sup>2</sup> body surface area 1 time/month for ≥2 months
  - 500 mg every 2 weeks for 3 treatments, followed by 500 mg every month for 6 months

Indications: severe, acute CNS disease; refractory to corticosteroids; or desire for control without corticosteroids

3. Failure of steroids or cyclophosphamide
  - Plasmapheresis
  - IV immunoglobulin
  - Intrathecal methotrexate
  - Azathioprine
  - Mycophenolate mofetil
4. Treatment for residual symptoms:
  - Antipsychotics: haloperidol, chlorpromazine, risperidone
  - Anticonvulsants: carbamazepine, valproate, lamotrigine
  - Antidepressants: fluoxetine<sup>10</sup>

## CIP

1. Decrease dosage of corticosteroid. Ideally, cessation of the offending agent  
Alternatively: taper to 40 mg/d, followed by tapering to 7.5 mg/d based on response to first taper and ability to safely continue reduction
2. For those who cannot cease corticosteroid therapy:
  - Antipsychotic therapy:  
First-line: second-generation antipsychotics  
Second-line: first-generation antipsychotics
  - Mood stabilizers: lithium, carbamazepine, valproic acid
  - Anti-anxiety, antidepressant therapy:  
SSRIs: fluoxetine, sertraline  
SNRIs: venlafaxine  
Avoid tricyclic antidepressants<sup>11</sup>

CIP: corticosteroid-induced psychosis; SLE: systemic lupus erythematosus; SLEIP: systemic lupus erythematosus-induced psychosis

## Clinical Point

For treating CIP, the corticosteroid dosage often is decreased.

For treating SLEIP, it often is increased

is decreased to 10 mg/d. Over the next few days Mr. L's mood, psychosis, and aggression improve. He becomes calm and cooperative, and denies suicidal or homicidal ideation. Mr. L's wife, who was initially scared to visit him, comes to see him and confirms that he has improved. After 3 consecutive days with no abnormal behaviors or psychiatric symptoms, Mr. L is discharged and continues taking quetiapine, 75 mg at bedtime, and prednisolone, 10 mg/d, with outpatient follow-up.

## The authors' observations

Table 2<sup>10,11</sup> describes approaches to treating CIP and SLEIP. Managing CIP typically consists of reducing the corticosteroid dosage. CIP treatment also includes adjunct therapy with psychotropics if the corticosteroid dose cannot be lowered enough to reduce

psychiatric symptoms while suppressing symptoms of the disease for which the corticosteroid was prescribed.<sup>6</sup>

When treating SLEIP, the corticosteroid dosage often is increased. Corticosteroids often are used to treat SLEIP while suppressing symptoms of SLE.<sup>10</sup> The main treatment of SLEIP is focused on the disease and using psychotropic medications to control symptoms that don't respond after exacerbation of the disease has been controlled.<sup>10</sup>

The presence of Mr. L's multiple SLE symptoms, as well as MRI findings, could indicate SLEIP. However, corticosteroids also were a possible cause of his psychotic symptoms. Mr. L's psychosis began within 8 weeks of starting a corticosteroid (prednisolone, 40 mg/d), and his symptoms improved when the corticosteroid dosage

**Clinical Point**

**Corticosteroids were a possible cause of Mr. L's psychotic symptoms, which improved once the dosage was decreased**

was reduced. The difference between CIP and SLEIP may best be distinguished by reducing the corticosteroid dosage and seeing if psychotic symptoms improve. Because it is important to control SLE symptoms in those with CIP, prescribing psychotropics may be warranted, as well as alternative treatments for immunosuppression.

**References**

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**Related Resources**

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- Lupus Foundation of America. Neuropsychiatric Lupus Research Program. <http://www.lupus.org/research/neuropsychiatric-lupus-research-program>.

**Drug Brand Names**

Azathioprine • Imuran	Methylprednisolone sodium succinate • Solu-Medrol
Carbamazepine • Tegretol	Mycophenolate mofetil • CellCept
Chlorpromazine • Thorazine	Prednisolone • Prednisone
Cyclophosphamide • Cytoxan	Quetiapine • Seroquel
Fluoxetine • Prozac	Risperidone • Risperdal
Haloperidol • Haldol	Sertraline • Zoloft
Lamotrigine • Lamictal	Valproate • Depakote
Lithium • Lithobid	Venlafaxine • Effexor
Methotrexate • Trexall	

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**Bottom Line**

Because steroids are frequently prescribed for lupus, it is important for clinicians to be aware of their psychiatric effects as well as how to manage those effects. When distinguishing CIP from SLEIP, consider decreasing the corticosteroid dosage and see if psychotic symptoms improve. Use adjunct therapy as needed.