Acute porphyric polyneuropathy in a pregnant patient with systemic lupus erythematosus

Dear Editor:

Guillain-Barré syndrome (GBS) is a heterogenous condition and may be mimicked by other acute polyneuropathies. Both acute porphyria and systemic lupus erythematosus (SLE) are included in this differential diagnosis. We report an instance of acute polyneuropathy in a pregnant patient with known SLE, whose neurological picture occurred during a flare of SLE but was found to be due to a previously undiagnosed hereditary coproporphyria (HCP).

We present the case of a 25-year-old Asian female with SLE with severe multisystemic involvement, diagnosed during a life-threatening flare in her first pregnancy. There was no other relevant personal or family history. Medica
tion included prednisolone 5 mg, azathioprine 100 mg, and hydroxychloroquine 400 mg. She was admitted for abdominal pain, vomiting, and constipation, followed by dark urine; she also described other self-limiting abdominal pain episodes over the previous 2 years. On examination, persistent tachycardia was noted. Laboratory studies were significant for hypocomplementemia, elevated erythro
cyte sedimentation rate and elevated ß-Human chorionic gonadotropin compatible with a 1–2-week pregnancy. There was no laboratory evidence of hematuria. Abdominal and obstetric ultrasound, and abdominal MRI were unremarkable. A provisional diagnosis of SLE-associated autonomic neuropathy was made and she was treated with IV methylprednisolone pulse plus an increase in prednisolone to 1 mg/kg/day. A rapidly progressive quadriaparesis developed over the first week after admission. On day 7 the patient was unable to independently walk, had a generalized areflexia, and patchy hypoesthesia. Electrodiagnostic studies showed increased F wave latency and absent H reflexes, suggesting GBS. CSF studies were normal. Despite treatment with intra
venous immunoglobulin, followed by plasma exchange, her neurological condition continued to deteriorate, with facial diplegia, worsening of quadriaparesis (grade 2 MRC in the proximal segments and grade 0 distally), marked hypopala
esthesia and proprioceptive errors up to the knees and elbows, and periods of severe dysautonomia. Repeat nerve conduction studies showed an acute sensory-motor axonal neuropathy (AMSAN). Meanwhile, the patient developed

| Table 1 Urinary porphobilinogen (PBG) and urinary porphyrins before treatment with hemin. ALA: delta-
| aminolevulinic acid. |
|---------------------|----------|
| PBG (<1.5 mg/L)     | 12.10    |
| PBG (24 h) (<2.0 mg/24h) | 18.15 |
| ALA (<0.6 mg/dL)    | 32.50    |
| ALA (24 h) (<8.0 mg/24h) | 42.25 |
| Coproporphyrin (<150 µg/L) | 3097 |
| Uroporphyrin (5–30 µg/L) | 4410 |

thrombocytopenia, prolonged clotting times, hypoproliferative anemia and elevated hepatic transaminases, and a provisional diagnosis of SLE flare with SLE-related acute polyneuropathy was made. The patient agreed to an interrup
tion of the pregnancy, followed by treatment with cyclophosphamide. Systemic manifestations resolved, with
tout any improvement of neurological symptoms. Additional investigations for GBS mimics were ordered, and urinary porphobilinogen and porphyrins were markedly elevated (Table 1). After withdrawal of potentially porphyrinogenic drugs and administration of IV hemin, the patient showed dramatic improvement, with resolution of sensory manifes
tations and plateauing of muscle strength. She was discharged to a rehabilitation center. At 20 months after onset, full recovery had occurred except for bilateral grade 4 MRC ankle dorsiflexion. Genetic testing revealed a previously unreported CPOX gene variant (NM_000097.5:c.245T>C [p.Leu82Pro]).

The present case illustrates a challenging differential diagnosis of acute polyneuropathy. Our patient had both an established diagnosis of SLE and laboratory evidence of increased disease activity. Still, she defied Occam’s razor and final diagnosis was of a second chronic disease, heredi
tary coproporphyria (HCP), as the cause of the neurological symptoms.

Clinical reasoning favors acute porphyric neuropathy against SLE-associated neuropathy: there had been self
limiting abdominal pain episodes accompanied by dark urine, abdominal pain and dysautonomia occurred before the acute neuropathy, and response to immunosuppression was absent while there was a response to hemin treat
mament and withdrawal of porphyrinogenic drugs. The lack of cutaneous manifestations is not unexpected, since they are far less frequent than neuropsychiatric manifestations in patients with HCP, occurring only in 5–30% of patients. The main limitations of the present report include limited bio
chemical testing (unavailable fecal and plasma porphyrin testing; urinary porphyrins and PBG unadjusted for creati
nine) and incomplete genetic testing, namely of unaffected
family members. However, clinical presentation was consistent with neurovisceral porphyria, no alternative causes were present for the expressive elevation of PBG and porphyrins, and a CPOX variant was found.

To the best of our knowledge, two other cases of SLE and hereditary coproporphyria have been reported. This association is most likely fortuitous, considering the low number of reports and weak evidence for shared pathological mechanisms. On the other hand, both entities present mainly in women of childbearing age, and can be precipitated by external factors. In the present case, pregnancy was likely the common factor precipitating flares of both SLE and HCP, although it is an infrequent precipitant for the latter. An SLE flare could precipitate a porphyric attack through caloric deprivation, but the presenting abdominal symptoms and dysautonomia were likely porphyrinic. In addition, drugs used to treat SLE could have aggravated the porphyria, since methylprednisolone, cyclophosphamide, and hydroxychloroquine are all possibly porphyrinogenic.

Though acute porphyrias are rare disorders, one study found a surprisingly high prevalence of 11% previously undiagnosed cases in patients with acute polynuropathy or encephalopathy in combination with abdominal pain or dysautonomic features.

Our case highlights the necessity of including porphyria in the differential diagnosis of an acute polynuropathy, even when alternative causes are present. The availability of specific therapy and preventive measures has important clinical implications, not only for the patient but also to family members, since without prompt treatment recovery is unpredictable and often incomplete.

Conflict of interest

The authors declare no conflicts of interest and no disclosures relevant to the manuscript. Informed consent was obtained from the patient for publication of this case report.

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References

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Recurrent intracranial hemorrhage in a patient with relapsing multiple sclerosis under interferon-β therapy

Hemorragia intracraneal recurrente en una paciente con Esclerosis Múltiple y tratamiento con Interferon-β

Dear Editor,

Interferon-β (IFN-β) is an immunomodulatory agent that has been used for the treatment of multiple sclerosis (MS) for more than twenty years now. Its efficacy and tolerability are well known as well as its side effects. We present a case of a woman diagnosed of relapsing-remitting multiple sclerosis (RRMS) who developed two spontaneous intracranial hemorrhage (ICH) while on subcutaneous IFN-β-1b and intramuscular IFN-β-1a.

A 56-year-old woman smoker of 10 cigarettes per day otherwise healthy, was diagnosed of RRMS in 2006 due to a left hemi-hypoesthesia relapse, three periventricular, two subcortical and an infratentorial lesion in a brain Magnetic Resonance Imaging (MRI) and positive IgG oligoclonal bands in cerebrospinal fluid. She had been treated with subcutaneous IFN-β-1b 250μg every two days for eight years. She suffered a new relapse (transverse myelitis) in

http://www.drugs-porphyria.org/