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A loss of sensation

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CASE PRESENTATION

Chief complaint

The patient is a 21-year-old woman with acute loss of sensation, paresthesias, and difficulty walking.

History of present illness

The patient was in her usual state of good health until one week prior to presentation when she developed low back pain and numbness and tingling around her abdomen and lower back. Over the next several hours the numbness spread distally to involve her legs and feet, and it became difficult to walk. The following day she developed constipation and urinary retention. She became unable to sense an urge to urinate and would only void when she developed lower abdominal distention and pressure. These symptoms continued for four days, at which point she presented to the local county safety-net hospital. In the emergency room she had an elevated bladder post-void residual, and she excreted 600 milliliters of urine after Foley-catheter insertion. She was admitted to the neurology service for further evaluation and treatment.

Past medical history

The patient had a history of chronic urticaria. She experienced her first urticarial rash two years prior and reported “several” episodes since that time, two of which were treated by “traditional Chinese herbs.” She had no surgical history.

Social and family history

The patient was born and raised in China and moved to the United States with her family at age 19. She lived with her parents and attended the local community college. She never smoked cigarettes, had no history of illicit drug use, did not drink alcohol, and denied sexual

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activity. She had a maternal grandmother with rheumatoid arthritis. Her family history was negative for malignancy or neurologic disorders.

Review of systems

She reported nasal congestion and chills for two weeks prior to presentation. She endorsed Raynaud's phenomenon, which had been witnessed by her mother, as well as chronic pain in her right second proximal interphalangeal (PIP) joint without associated swelling. She also reported a pruritic migratory rash for the last two days, currently present on her hands and abdomen. She denied arthralgias elsewhere, joint swelling, morning stiffness, fevers, night sweats, and unintentional weight loss. She also denied cough, dyspnea, chest pain, palpitations, abdominal pain, nausea, emesis, photosensitivity, dry eyes, dry mouth, oral ulcers, or alopecia. A neurologic review of systems was negative for headache, seizures, decreased visual acuity, diplopia, facial numbness, dysphagia, slurred speech, vertigo, or extremity weakness.

Physical examination

In the emergency room the patient had a temperature of 36.8°C, heart rate of 67 beats per minute, blood pressure of 102/67 mm Hg, and respiratory rate of 16 breaths per minute with an oxygen saturation of 100% on room air. She was a young Asian woman in no apparent distress. Her mucous membranes were moist and her oropharynx was clear with no oral ulcers. Her neck was supple without cervical lymphadenopathy. Her cardiovascular exam was normal including absence of jugular venous distention, murmurs, rubs, or gallops. She had no subclavian or carotid bruits. Her radial and pedal artery pulses were normal. She demonstrated normal respiratory effort and had no wheezing, crackles or rhonchi. Her abdomen was soft and nontender without organomegaly. On musculoskeletal exam she had laxity of the proximal interphalangeal (PIP) joints without associated tenderness or swelling. The remainder of her musculoskeletal exam was normal.

On neurologic exam she was alert and oriented to person, place, and date. She had normal naming and comprehension in Cantonese. Her cranial nerve exam was normal, including her fundoscopic exam and visual acuity testing performed by ophthalmology. Her motor exam demonstrated normal bulk and tone, and 5/5 strength in all major muscle groups including the deltoids, biceps, triceps, wrist extensors, finger flexors, interossei of the hand, iliopsoas, hamstrings, quadriceps, anterior tibialis, gastrocnemius, and extensor hallucis longus. On sensory exam she had diminished sensation to light touch below the level of T8. Her brachialis reflexes were 2+ and symmetric whereas her patellar and Achilles reflexes were 4+ and symmetric. She had bilateral positive Babinski responses.

On examination of her skin there was a subtle patch of non-painful non-pruritic erythema on the right cheek. There were pruritic erythematous papules overlying the wrists and fingers, including the skin over the metacarpal joints and the dorsal surface of the fingers between joint spaces (Figure 1). Additionally, there was a patch of urticarial wheals over the right abdomen.

Laboratory evaluation

Her white blood cell count was 6,900/mm³, her hemoglobin concentration was 11.2 g/dl, and her platelet count was 303,000/mm³. Her creatinine was 0.45 mg/dl. Her electrolytes and liver function tests were within the normal range. Her INR was 1.0 and her PTT was 49 seconds (normal range 25–35). Her erythrocyte sedimentation rate and c-reactive protein were 46 and 22, respectively. Urinalysis demonstrated 1+ ketones, no protein, no blood, and no white blood cells. Her antinuclear antibody (ANA) was positive with a titer of greater than 1:640 in a speckled pattern.

A lumbar puncture was performed. The cerebrospinal fluid contained 39 white blood cells per mm³ (reference range 0–5) with 71% lymphocytes, 12% neutrophils, and 17% monocytes; a glucose concentration of 38 mg/dL (reference range > 0.6 serum glucose), a protein concentration of 55 mg/dL (reference range < 45 mg/dL). The CSF IgG concentration was 16.5 mg/dl (normal range < 5.8) and there were no oligoclonal bands.

Imaging

A chest x-ray showed clear lungs and normal cardiomedial silhouette. Magnetic resonance imaging (MRI) of her brain, with and without gadolinium contrast, was normal. She was further evaluated with a spinal MRI with and without gadolinium, which demonstrated extensive hyperintense T2 signal abnormality throughout the spinal cord from C1 to the conus, predominately involving the central cord with sparing of the dorsal column. T1-weighted post-contrast fat-saturated images demonstrated no abnormal cord enhancement, including no evidence of enhancement in the areas of edema on T2-weighted images (Figure 2). The other spinal structures including the epidural space and vertebral bodies were normal.

CASE SUMMARY

A 21-year-old previously healthy woman presented with acute onset back pain, urinary retention, constipation, and impaired sensation caudal to T8. She had a lymphocytic pleocytosis in her CSF, a high-titer positive anti-nuclear antibody, and MRI that demonstrated longitudinally extensive T2 signal abnormality of the spinal cord without associated contrast enhancement.

DIFFERENTIAL DIAGNOSIS

Our patient meets diagnostic criteria for “transverse myelitis” (TM), a heterogeneous group of inflammatory disorders characterized by bilateral sensorimotor and autonomic spinal cord dysfunction, spinal cord inflammation by CSF analysis or MRI, and exclusion of compressive, postradiation, and vascular causes [1–4]. The major etiologies for transverse myelitis include infectious, autoimmune, demyelinating, and paraneoplastic syndromes (Table 1). We consider each of these major diagnostic possibilities below.

Infectious Causes

Viral, bacterial, fungal, and parasitic infections can cause acute transverse myelitis either during an acute infection, or as a parainfectious phenomenon. Implicated bacterial infections include *treponema pallidum* (syphilis), *mycobacterium tuberculosis*, and *borrelia burgdorferi* (Lyme disease). There are numerous viruses known to cause TM, but the most commonly implicated are varicella zoster (VZV), enteroviruses, herpes simplex type-2 (HSV-2), and cytomegalovirus (CMV) [5]. Parasitic infections that warrant consideration in endemic areas include schistosomiasis, neurocysticercosis, gnathostoma, and angiostrongylosis.

Our patient reported nasal congestion and chills prior to the onset of numbness, suggesting the possibility of a viral prodrome. She had an urticarial rash on her hands and abdomen, which, given the association of acute urticaria and certain viruses [6], raised suspicion for an infectious process. However, urticaria is nonspecific and her skin examination was negative for vesicular lesions or genital ulcers as seen in the setting of VZV infection and HSV-2, respectively. Furthermore, she was afebrile and did not have signs of meningismus. Her normal vitals made an acute infection with spinal cord involvement unlikely [5], but a parainfectious process in response to a preceding viral infection such as EBV, CMV, HSV, or VZV, or to an atypical bacterial infection such as *mycoplasma*, was an important consideration in the differential diagnosis.

Systemic Lupus Erythematosus

Myelopathy is a rare manifestation of systemic lupus erythematosus (SLE) that affects an estimated 1–2% of patients with the disease [7, 8]. Among patients with newly diagnosed lupus in an international inception cohort study, 28% were identified to have a neuropsychiatric (NP) syndrome, and only 0.8% of NP syndromes were characterized as myelopathy [9]. In a meta-analysis of 105 cases of lupus myelitis, most patients developed TM either as the initial manifestation of SLE (46%) or within five years of the diagnosis [10]. The most common clinical presentation was a thoracic sensory level.

In the case of our patient, her epidemiology, the finding of a positive ANA, and history of Raynaud's phenomenon raised concern for an underlying connective tissue disease. The exam finding of an erythematous maculopapular rash involving the interphalangeal areas of her dorsal hands was characteristic of acute cutaneous lupus and further raised concern for SLE. However, she did not carry a diagnosis of lupus or other autoimmune disease known to cause TM, and did not have other findings on physical examination such as alopecia, synovitis, oral ulcers, or pleuritis to support a diagnosis of active lupus. Additionally, her initial spine MRI was notable for absence of contrast enhancement, suggesting a non-inflammatory etiology (such as viral, radiation, or vascular), as opposed to an inflammatory process. The MRI also showed longitudinally extensive T2 signal abnormality, a finding that is part of the diagnostic criteria for NMO and a known radiographic finding in patients with SLE-associated TM [11, 12].

Neuromyelitis Optica Spectrum Disorder

Neuromyelitis optica spectrum disorder (NMOSD), previously known as Devic disease, is a rare inflammatory disease of the spinal cord characterized by severe demyelination, axonal

damage, and a predilection for the optic nerves and spinal cord. The classic clinical manifestations of NMOSD are recurrent acute attacks of transverse myelitis and/or optic neuritis. The NMO-IgG antibody, also referred to as the aquaporin-4 (AQP4) autoantibody, is pathogenic and part of the diagnostic criteria [13–19].

While prior diagnostic criteria for NMO/NMOSD required optic neuritis and acute myelitis, the 2015 revised diagnostic criteria recognize 4 additional core clinical characteristics: area postrema syndrome (episodes of otherwise unexplained hiccups or nausea and vomiting), acute brainstem syndrome, symptomatic narcolepsy with associated MRI lesions, and symptomatic cerebral syndrome with MRI changes (Table 2) [14]. The hallmark laboratory finding is a positive serum AQP4 autoantibody, for which test characteristics depend on the specific assay used. The initial assay based on indirect immunofluorescence method had a reported sensitivity of 58–75% and specificity of 85–99%, whereas cell-based assays have both higher sensitivity (74–83%) and specificity (100%) [20–23]. Neuroimaging is also diagnostically useful: the classic finding is longitudinally extensive transverse myelitis (LETM), defined as T2 weighted high signal intensity extending across three or more vertebral segments on sagittal spinal MRI [24].

Our patient had LETM, which supported a diagnosis of NMOSD. She also had a positive ANA, which is a common laboratory finding in the setting of NMOSD [24]. However, she did not demonstrate overt vision loss to suggest optic neuritis and denied symptoms of area postrema syndrome such as intractable hiccups or vomiting. NMOSD was a strong possibility in the differential diagnosis, though she did not meet diagnostic criteria, and additional testing, including AQP4 serologies, was needed.

Multiple Sclerosis

Demyelinating disorders such as multiple sclerosis (MS) are a common cause of transverse myelitis. MS is a clinical diagnosis that relies upon demonstration of central nervous system lesions disseminated in both space and time [25]. Our patient represented an appropriate demographic for MS, and her symptoms of gait disturbance, sensory loss in the legs, and urinary retention are common associated symptoms. However, her neuroimaging was inconsistent; the cord lesions of MS tend to be located peripherally and typically involve short segments spanning less than one vertebral length [26], as opposed to the longitudinally extensive cord lesion observed in our patient. Additional data that points away from MS in this case are ANA positivity (serum autoantibodies are uncommon in MS) [24] and normal brain imaging.

PATIENT'S COURSE

Given concern for neuromyelitis optica, the patient was evaluated by ophthalmology to assess for the presence of optic neuritis. Her visual acuity, visual field testing, and dilated fundus exam were within normal limits. CSF and serum testing for aquaporin-4 receptor antibody was negative. The patient underwent an extensive infectious work-up. The following CSF PCR studies were negative: HSV-2, VZV, Human T-cell and Lymphotropic Virus (HTLV), West Nile Virus, and Enterovirus. Blood cultures and serum antibody testing for human immunodeficiency virus (HIV), hepatitis B virus, and hepatitis C virus was

negative. Screening for syphilis with the venereal disease research laboratory test (VDRL) on both serum and CSF specimens was also negative. The rheumatology service was consulted; given the patient's acute transverse myelitis in the context of her epidemiology and high-titer positive ANA, a connective tissue disease, specifically systemic lupus erythematosus (SLE), was deemed to be the most likely underlying etiology. She was treated with intravenous methylprednisolone 1000 mg daily for three days, followed by oral prednisone 1 mg/kg daily.

Additional autoantibody and immunologic tests were ordered. ANA subserologies were significant for positive anti-SSA (278) and positive anti-dsDNA (1:80). Tests for anti-Smith, anti-RNP, Jo-1, and anti-SSB were negative. Lupus anticoagulant was detected (dRVVT 78 seconds with correction to 62 seconds with mixing study, normal reference 33–44 seconds) but anticardiolipin antibodies (IgG and IgM) and anti-beta2glycoprotein I (IgG and IgM) antibodies were negative. Her C3 was 63 mg/dl (reference range 80–160) and C4 was 15 mg/dl (reference range 13–75).

The patient was started on hydroxychloroquine and steroid-sparing induction immunosuppression with intravenous cyclophosphamide. She received her first dose of IV cyclophosphamide (0.5 gm/m²) on hospital day 7, with the plan to continue monthly infusions as an outpatient for six months. She had a reported allergy to trimethoprim-sulfamethoxazole (TMP-SMX), so was started on dapsone for pneumocystis jirovecii pneumonia (PJP) prophylaxis. By the time she was discharged from the hospital, she had recovered normal bladder and bowel function. Her lower extremity sensation had improved to an estimated 80% of her pre-hospitalization baseline and she was able to walk without assistance. Repeat spinal MRI showed resolution of extensive spinal cord hyperintense T2 signal abnormality.

The patient continued to improve during the weeks following her hospitalization and two weeks after discharge her prednisone dose was reduced from 60 to 40 mg daily. However, three weeks following discharge, she re-presented to the hospital with two days of fever, facial edema, and diffuse rash. The rash had started on her face and spread to involve her trunk and arms. It was not painful or pruritic. She denied any recent medication exposures other than the medications she had started prior to discharge from the hospital three weeks prior. Her exam was notable for a temperature of 38.5, heart rate of 133 beats per minute, periorbital edema, and an erythematous morbilliform rash on her face, arms, trunk, and back (Figure 3). Laboratory studies revealed a white blood cell count of 13,000/mm³, absolute neutrophil count 8,200/mm³, absolute lymphocyte count 6,000/mm³, absolute eosinophil count 400/mm³ (reference range 30–350), hemoglobin concentration 9.8 g/dl, and platelet count 190,000/mm³. Her creatinine and electrolytes were within normal limits, but her AST and ALT had increased from normal during previous testing to 241 (normal range 10–40 units per liter) and 307 (normal range 7–56 units per liter), respectively. Her ESR was 23 and CRP 131.

Given her immunosuppressed status and SIRS physiology, her second hospitalization was highly concerning for a severe systemic infection. A robust attempt was made to identify an underlying infection, the results of which were negative. Specifically, her urinalysis was

within normal limits, her chest radiograph was clear, and stool testing for pathogenic organisms, including *Clostridium difficile*, was negative. Serologic testing for viral infections was negative for: EBV IgM, parvovirus IgM/IgG, CMV IgM/IgG, hepatitis A, hepatitis B, and hepatitis C. Serologic testing for HHV-6 was consistent with past exposure (IgG positive, IgM negative). She then underwent a skin biopsy (Figure 4), which demonstrated vacuolar interface dermatitis, a nonspecific finding that can be seen in a wide range of illnesses including drug or viral exanthem, connective tissue disease, and erythema multiforme.

Given the negative infectious work-up, recent initiation of dapsone, and the constellation of fever, rash, eosinophilia, and transaminitis, the patient was ultimately diagnosed with drug reaction with eosinophilia and systemic symptoms (DRESS) in the setting of recent dapsone initiation. Dapsone was stopped, her prednisone dose was increased from 40 mg daily to 60 mg daily, and she gradually recovered over the subsequent two weeks. Her rash resolved and her liver function tests normalized. Her second dose of intravenous cyclophosphamide was delayed by two weeks, but she was able to receive the subsequent doses as planned, every four weeks for a total of six doses. She was not re-started on PJP prophylaxis. Lupus anticoagulant was repeated over 12 weeks following the initial testing and was negative. Her prednisone dose was gradually tapered without recurrence of neurologic symptoms, and six months following her initial hospitalization, she resumed her undergraduate studies.

DISCUSSION

As seen in this case, acute transverse myelitis presents a challenging diagnostic and treatment dilemma. There is a wide spectrum of diseases known to cause the syndrome, appropriate treatment depends on the underlying etiology, and in many cases timing of treatment initiation impacts the risk of long-term disability [27, 28]. This challenge is compounded by the time consuming diagnostic evaluation—spine MRI with gadolinium, brain MRI, lumbar puncture, and autoantibody testing—required to narrow the differential diagnosis. When considering SLE-associated TM, myelitis is the initial manifestation of underlying disease in roughly 50% of patients [10], which means that for half of the cases there are no historical clues to support a new diagnosis of lupus. In other words, initial diagnostic uncertainty is common [3] and there is often insufficient time to establish a clear diagnosis within the recommended treatment window. Therefore, because inflammatory etiologies represent the majority of causes, once infectious etiologies have been excluded, high dose intravenous glucocorticoids should be initiated without delay, even if additional information such as serum and CSF biomarkers remain pending [3, 24].

Birnbaum et al have described two clinically distinct syndromes of SLE-associated myelitis, referred to as “gray matter” and “white matter” myelitis [28]. In their cohort of 22 patients, those with gray matter myelitis initially presented with urinary retention, fever, flaccidity, and hyporeflexia in the setting of active SLE, and demonstrated rapid clinical deterioration to irreversible paraplegia. In contrast, cases of white matter myelitis presented with spasticity, hyperreflexia, and less severe attacks characterized by slower progression of symptoms but greater likelihood of relapse. Additionally, the two syndromes demonstrated laboratory and radiographic differences: cases of gray matter myelitis were associated with

more inflammatory CSF (mean CSF WBC 385.5 cells/ml versus 10 cells/ml) and higher frequency of cord swelling on spine MRI, while white matter myelitis associated with higher probability of anti-Ro and lupus anticoagulant positivity. Our patient's presentation is consistent with the SLE-associated white matter myelitis subset: she presented with a relatively mild attack (eg preservation of antigravity strength), indolent progression of symptoms, and hyperreflexia, and was found to be anti-Ro and lupus anticoagulant positive. Additionally, she responded well to treatment despite a delay in diagnosis of several days.

Antiphospholipid antibodies (aPL) were present in our patient during her initial hospitalization and raised the question of their potential pathogenic role in the development of her spinal cord disease. A review of 105 patients with SLE-associated TM showed that 64% of affected patients were aPL positive [10]. Another study of patients who developed TM as the presenting manifestation of SLE found an aPL positivity prevalence of 73% [27]. The anterior medial longitudinal arterial trunk is smaller in the thoracic region as compared to the cervical and lumbar regions. The mid-thoracic spinal cord therefore represents a "watershed area" that is more vulnerable to arterial insufficiency in the setting of thrombotic disease. The observed association between aPL antibodies and TM in patients with SLE, as well as the predilection for thoracic cord involvement, has led to the hypothesis that aPL-induced vascular occlusion plays a role in the pathogenesis of this syndrome [29]. However, evidence to support this hypothesis is largely circumstantial and a review of 70 patients with SLE-associated TM did not find an association between aPL antibodies and involvement of the thoracic spine [30]. Furthermore, though anticoagulation has been tried in patients with SLE myelitis and aPL positivity, observational data does not show a therapeutic benefit for minimizing disability or preventing recurrence [30].

While the patient presented in this report responded well to immunosuppressive treatment, she developed a life-threatening reaction to antimicrobial therapy used for PJP prophylaxis. Both the underlying disease state [31] and the immunologic regimen [32–35] are important considerations in determining the risk-benefit ratio of PJP prophylaxis. A meta-analysis examining the efficacy of PJP prophylaxis among immunocompromised non-HIV infected patients found that the number needed to treat with trimethoprim-sulfamethoxazole (TMP-SMX) to prevent one PJP infection differed greatly by disease state: 11 for allogeneic bone marrow transplant and solid organ transplant, 32 for granulomatosis with polyangiitis, 73 for inflammatory myopathy, 110 for SLE, and 1099 for rheumatoid arthritis [32].

Trimethoprim-sulfamethoxazole is the recommended first-line prophylactic agent for PJP [36]. Alternative medications that can be used for PJP prophylaxis include dapsone, atovaquone, and aerosolized pentamidine, though the clinical efficacy of these medications is not as clear as that of TMP-SMX [31]. Dapsone, the medication used in our patient, has multiple known adverse effects, including hemolytic anemia, methemoglobinemia, agranulocytosis, and dapsone hypersensitivity syndrome [37]. Dapsone hypersensitivity syndrome is a severe idiosyncratic drug reaction with a reported mortality of 9.9% [38–40]. It usually develops 2 to 8 weeks after starting the medication and is characterized by fever, rash (often an erythematous morbilliform eruption), and systemic involvement [41]. The systemic involvement may include hepatic injury, renal dysfunction, hematologic

manifestations (such as eosinophilia and atypical lymphocytosis), and myocarditis [37, 42, 43].

Genetic testing may soon have the potential to identify patients who are at high risk for drug-induced hypersensitivity. In a genomewide association study of 872 leprosy patients who had been treated with dapsone, HLA-B*13:01 was significantly associated with the development of dapsone hypersensitivity syndrome (odds ratio: 21). Interestingly, the risk allele identified in the study is present in 2% to 20% of Chinese individuals, but is largely absent in Europeans and Africans [38]. Given our patient's ethnicity, she had a 2–20% risk of the allele being present for a disease with nearly 10% mortality. Meanwhile, based on available data, her risk of PJP infection was less than 1%. In retrospect, treatment for PJP prophylaxis with dapsone was not the correct choice for this patient. In the future, testing for HLA-B*13:01 in relevant populations, such as the Chinese patient described in this report, may enable identification of those at increased risk for dapsone hypersensitivity.

In summary, we present a case of a previously healthy young woman who presented with acute myelopathy and was ultimately found to have a new diagnosis of SLE. Her case highlights the importance of early aggressive immunosuppression in cases of suspected inflammatory myelitis as well as the need for a careful risk/benefit analysis prior to initiating antimicrobial therapy for PJP prophylaxis.

FINAL DIAGNOSIS

SLE white-matter myelitis and treatment complicated by dapsone hypersensitivity syndrome.

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References

1. Beh SC, et al. Transverse myelitis. *Neurol Clin.* 2013; 31(1):79–138. [PubMed: 23186897]
2. West TW, Hess C, Cree BA. Acute transverse myelitis: demyelinating, inflammatory, and infectious myelopathies. *Semin Neurol.* 2012; 32(2):97–113. [PubMed: 22961185]
3. West TW. Transverse myelitis—a review of the presentation, diagnosis, and initial management. *Discov Med.* 2013; 16(88):167–77. [PubMed: 24099672]
4. Proposed diagnostic criteria and nosology of acute transverse myelitis. *Neurology.* 2002; 59(4):499–505. [PubMed: 12236201]
5. Jacob A, Weinshenker BG. An approach to the diagnosis of acute transverse myelitis. *Semin Neurol.* 2008; 28(1):105–20. [PubMed: 18256991]
6. Imbalzano E, et al. Association between urticaria and virus infections: A systematic review. *Allergy Asthma Proc.* 2016; 37(1):18–22. [PubMed: 26637522]
7. The American College of Rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. *Arthritis Rheum.* 1999; 42(4):599–608. [PubMed: 10211873]
8. Theodoridou A, Settas L. Demyelination in rheumatic diseases. *Postgrad Med J.* 2008; 84(989):127–32. [PubMed: 18372483]
9. Hanly JG, et al. Neuropsychiatric events at the time of diagnosis of systemic lupus erythematosus: an international inception cohort study. *Arthritis Rheum.* 2007; 56(1):265–73. [PubMed: 17195230]

10. Kovacs B, et al. Transverse myelopathy in systemic lupus erythematosus: an analysis of 14 cases and review of the literature. *Ann Rheum Dis.* 2000; 59(2):120–4. [PubMed: 10666167]
11. Nardone R, et al. Longitudinally extensive transverse myelitis in systemic lupus erythematosus: case report and review of the literature. *Clin Neurol Neurosurg.* 2015; 129:57–61. [PubMed: 25544684]
12. Li XY, et al. Myelitis in systemic lupus erythematosus frequently manifests as longitudinal and sometimes occurs at low disease activity. *Lupus.* 2014; 23(11):1178–86. [PubMed: 24972897]
13. Bennett JL, et al. Intrathecal pathogenic anti-aquaporin-4 antibodies in early neuromyelitis optica. *Ann Neurol.* 2009; 66(5):617–29. [PubMed: 19938104]
14. Wingerchuk DM, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology.* 2015; 85(2):177–89. [PubMed: 26092914]
15. Sellner J, et al. EFNS guidelines on diagnosis and management of neuromyelitis optica. *Eur J Neurol.* 2010; 17(8):1019–32. [PubMed: 20528913]
16. Kim SH, et al. Clinical spectrum of CNS aquaporin-4 autoimmunity. *Neurology.* 2012; 78(15):1179–85. [PubMed: 22459676]
17. Wingerchuk DM, et al. The spectrum of neuromyelitis optica. *Lancet Neurol.* 2007; 6(9):805–15. [PubMed: 17706564]
18. Ghezzi A, et al. Clinical characteristics, course and prognosis of relapsing Devic's Neuromyelitis Optica. *J Neurol.* 2004; 251(1):47–52. [PubMed: 14999489]
19. Wingerchuk DM, et al. The clinical course of neuromyelitis optica (Devic's syndrome). *Neurology.* 1999; 53(5):1107–14. [PubMed: 10496275]
20. Lennon VA, et al. A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis. *Lancet.* 2004; 364(9451):2106–12. [PubMed: 15589308]
21. Flanagan EP, et al. Epidemiology of aquaporin-4 autoimmunity and neuromyelitis optica spectrum. *Ann Neurol.* 2016
22. Marignier R, et al. Aquaporin-4 antibody-negative neuromyelitis optica: distinct assay sensitivity-dependent entity. *Neurology.* 2013; 80(24):2194–200. [PubMed: 23658379]
23. Fryer JP, et al. AQP4 autoantibody assay performance in clinical laboratory service. *Neurol Neuroimmunol Neuroinflamm.* 2014; 1(1):e11. [PubMed: 25340055]
24. Kitley JL, et al. The differential diagnosis of longitudinally extensive transverse myelitis. *Mult Scler.* 2012; 18(3):271–85. [PubMed: 21669935]
25. Katz Sand I. Classification, diagnosis, and differential diagnosis of multiple sclerosis. *Curr Opin Neurol.* 2015; 28(3):193–205. [PubMed: 25887774]
26. McDonald WI, et al. Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the diagnosis of multiple sclerosis. *Ann Neurol.* 2001; 50(1):121–7. [PubMed: 11456302]
27. D'Cruz DP, et al. Transverse myelitis as the first manifestation of systemic lupus erythematosus or lupus-like disease: good functional outcome and relevance of antiphospholipid antibodies. *J Rheumatol.* 2004; 31(2):280–5. [PubMed: 14760797]
28. Birnbaum J, et al. Distinct subtypes of myelitis in systemic lupus erythematosus. *Arthritis Rheum.* 2009; 60(11):3378–87. [PubMed: 19877037]
29. Lavallo C, et al. Transverse myelitis: a manifestation of systemic lupus erythematosus strongly associated with antiphospholipid antibodies. *J Rheumatol.* 1990; 17(1):34–7. [PubMed: 2313670]
30. Katsiari CG, et al. Acute transverse myelitis and antiphospholipid antibodies in lupus. No evidence for anticoagulation. *Eur J Neurol.* 2011; 18(4):556–63. [PubMed: 20840379]
31. Stamp LK, Hurst M. Is there a role for consensus guidelines for P. jiroveci pneumonia prophylaxis in immunosuppressed patients with rheumatic diseases? *J Rheumatol.* 2010; 37(4):686–8. [PubMed: 20360202]
32. Green H, et al. Prophylaxis of Pneumocystis pneumonia in immunocompromised non-HIV-infected patients: systematic review and meta-analysis of randomized controlled trials. *Mayo Clin Proc.* 2007; 82(9):1052–9. [PubMed: 17803871]
33. Sepkowitz KA. Opportunistic infections in patients with and patients without Acquired Immunodeficiency Syndrome. *Clin Infect Dis.* 2002; 34(8):1098–107. [PubMed: 11914999]

34. Sepkowitz KA, Brown AE, Armstrong D. Pneumocystis carinii pneumonia without acquired immunodeficiency syndrome. More patients, same risk. Arch Intern Med. 1995; 155(11):1125–8. [PubMed: 7763117]
35. Suryaprasad A, Stone JH. When is it safe to stop Pneumocystis jiroveci pneumonia prophylaxis? Insights from three cases complicating autoimmune diseases. Arthritis Rheum. 2008; 59(7):1034–9. [PubMed: 18576286]
36. Stern A, et al. Prophylaxis for Pneumocystis pneumonia (PCP) in non-HIV immunocompromised patients. Cochrane Database Syst Rev. 2014; (10):CD005590. [PubMed: 25269391]
37. Hoogeveen RM, et al. A lethal case of the dapsone hypersensitivity syndrome involving the myocardium. Neth J Med. 2016; 74(2):89–92. [PubMed: 26951355]
38. Zhang FR, et al. HLA-B*13:01 and the dapsone hypersensitivity syndrome. N Engl J Med. 2013; 369(17):1620–8. [PubMed: 24152261]
39. Zhu YI, Stiller MJ. Dapsone and sulfones in dermatology: overview and update. J Am Acad Dermatol. 2001; 45(3):420–34. [PubMed: 11511841]
40. Lorenz M, Wozel G, Schmitt J. Hypersensitivity reactions to dapsone: a systematic review. Acta Derm Venereol. 2012; 92(2):194–9. [PubMed: 22307940]
41. Spriet S, Banks TA. Drug reaction with eosinophilia and systemic symptoms syndrome. Allergy Asthma Proc. 2015; 36(6):501–5. [PubMed: 26534757]
42. Hoetzenecker W, et al. Adverse cutaneous drug eruptions: current understanding. Semin Immunopathol. 2016; 38(1):75–86. [PubMed: 26553194]
43. Ang CC, et al. Retrospective analysis of drug-induced hypersensitivity syndrome: a study of 27 patients. J Am Acad Dermatol. 2010; 63(2):219–27. [PubMed: 20605253]
44. Cree BA. Acute inflammatory myelopathies. Handb Clin Neurol. 2014; 122:613–67. [PubMed: 24507538]

Figure 1.
Rash present on hands during initial hospital admission. There were pruritic erythematous papules on the dorsal aspect of the wrists, metacarpal joints, and fingers.

Figure 2.

A–C show images from T2-weighted fat-saturated magnetic resonance images (MRI), demonstrating diffuse spinal cord signal abnormality. On the sagittal cut (A), the upper arrow at the upper thoracic spine (T4 level) highlights edema confined to gray matter. The axial cut at T4 also demonstrates edema confined to gray matter (B). Axial imaging of the conus medullaris at the T12 level (panel C) shows edema extending beyond the confines of the gray matter, consistent with transverse myelitis. Panel D is from sagittal T1-weighted post-contrast fat-saturated imaging, and shows no abnormal cord enhancement in the areas of edema in Figure A.

Figure 3.
Erythematous morbilliform rash on abdomen on the first day of second hospital admission.

Figure 4. Skin biopsy pathology. Haematoxylin and Eosin (H&E) staining demonstrated lymphocytic infiltrate at the epidermis-dermis junction consistent with interface dermatitis.

Table 1

Differential diagnosis of transverse myelitis [2, 24, 44]

Demyelinating	
•	Multiple Sclerosis
•	Neuromyelitis Optica
•	Idiopathic transverse myelitis
•	Acute disseminated encephalomyelitis
Infectious	
•	Bacterial
	○ Syphilis, Mycobacterium tuberculosis, Lyme disease
•	Viral
	○ Herpes simplex virus type-2, Varicella-zoster virus, Cytomegalovirus, Epstein-barr virus, Coxsackie virus, Enterovirus, Hepatitis A and C
•	Parasitic
	○ Neurocysticercosis, Schistosoma, Gnathostoma angiostrongylosis
•	Fungal
	○ Actinomyces, Coccidioides immitus, Aspergillus, Blastomyces dermatitidis
Autoimmune/Inflammatory	
•	Systemic lupus erythematosus
•	Sjogren's syndrome
•	Antiphospholipid syndrome
•	Neurosarcoidosis
•	Behcet's disease
•	Mixed connective tissue disease

Table 2**2015 Diagnostic Criteria for Neuromyelitis Optica Spectrum Disorders^{*} [14]**

Core clinical characteristics	
<ul style="list-style-type: none"> • Optic neuritis • Acute myelitis • Area postrema syndrome (episodes of otherwise unexplained hiccups or nausea and vomiting) • Acute brainstem syndrome • Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions • Symptomatic cerebral syndrome with NMOSD-typical brain lesions 	
Diagnostic criteria for NMOSD with AQP4-IgG	
1	At least 1 core clinical characteristic
2	Positive test for AQP4-IgG using best available detection method
3	Exclusion of alternative diagnoses
Diagnostic criteria for NMOSD without AQP4-IgG or antibody status unknown	
1	At least 2 core clinical characteristics meeting all of the following characteristics: <ul style="list-style-type: none"> a. At least 1 core clinical characteristic must be optic neuritis, acute myelitis with LETM, or area postrema syndrome b. Dissemination in space (2 or more different core clinical characteristics) c. Fulfillment of additional MRI requirements <ul style="list-style-type: none"> i. Acute optic neuritis: brain MRI shows normal findings or nonspecific white matter lesions; OR optic nerve MRI demonstrates T2-hyperintense lesion or T1-weighted gadolinium enhancing lesion extending over at least half the optic nerve length or involving optic chiasm ii. Acute myelitis: spine MRI lesion extending over at least 3 contiguous segments (LETM) iii. Area postrema syndrome: associated dorsal medulla lesions iv. Acute brainstem syndrome: associated periependymal brainstem lesions
2	Negative test for AQP4-IgG, or testing unavailable
3	Exclusion of alternative diagnoses

^{*} Adapted from the 2015 International consensus diagnostic criteria for neuromyelitis optica spectrum disorders