Title

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CLINICAL VIGNETTE

Rare Presentation of Cutaneous Stevens-Johnson/ Toxic Epidermal Necrolysis-Like Lupus Erythematosus

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Case

A 50-year-old female with hyperlipidemia presented to the Emergency Room with three days of sore throat, eye discharge and rash. The patient initially noted subjective fevers and chills, followed by bilateral eye swelling with yellow crusting discharge. One day prior to presentation, she developed lip swelling, odynophagia, and dysphagia to solids and liquids. An erythematous rash started, spreading from her trunk outwards throughout her upper body and arms. Other symptoms included a productive cough, rhinorrhea, diarrhea, and dysuria. She denied prior similar rashes or sick contacts. Her only medication was a multivitamin and denied any recent antibiotics or herbal supplements. One month prior, she had travelled to Mexico for two days. She receiving her childhood vaccinations in the Philippines.

In the ER, she was febrile to 39.3. Her exam was significant for bilateral conjunctival injection with yellow crusted exudates. Her oral mucosa was dry with white spots on the buccal mucosa. There was edema of the lips with some desquamation and a diffuse maculopapular rash of the face, chest, back, arms, and palms. Initial labs included: unremarkable BMP, normal WBC of 3.9 /mm3 with 90.8% neutrophilia, platelets of 155 K/cumm, a mild transaminitis of AST 97 U/L, ALT 146 U/L, ALP 141 U/L. Urinalysis showed large leukocytes and 68 WBC's. Chest xray showed mild bilateral posterior infrahilar consolidations and CT chest showed ground glass opacities and trace pleural effusions.

The patient's fever, cough, coryza, and rash on exam raised initial concern for measles, and she was placed in airborne isolation, pending measles serologies and Infectious Disease was consulted. Additional testing for broad–infectious and rheumatologic workup was sent. Dermatology performed skin biopsy and Ophthalmology considered a diagnosis of hemorrhagic blepharoconjunctivitis. The patient was started on empiric ceftriaxone, azithromycin, acyclovir, ciprofloxacin eye drops, and pred forte eye drops. Her fever and rash persisted despite antibiotics and the oral lesions progressed to ulcerations.

On hospital day #5, the anti-nuclear antibody (ANA) resulted positive with a titer of 1:1280 with a centromere pattern. Rheumatology felt her positive ANA, lymphocytopenia, thrombocytopenia, malar rash, photosensitivity, and symptoms were highly suggestive of systemic lupus erythematosus (SLE) with severe cutaneous/mucocutaneous manifestations. She was started on IV methylprednisolone 60mg BID. Initial extensive infectious testing including: HIV, HCV Ab, RPR, coccidioidomycosis, mycoplasma, HSV swab, VZV swab, measles serology, mycoplasma, rickettsia serology returned negative and antibiotics were discontinued. The final skin biopsy resulted on hospital day #10, showing deep perivascular and periadnexal lymphocytic infiltrate and full thickness epidermal necrosis with features raising the possibility of erythema multiforme/toxic epidermal necrolysis/Stevens-Johnson syndrome. Given the clinical presentation, lab findings, and skin biopsy results, the patient was diagnosed as likely SLE presenting as Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN). Her symptoms improved and she was discharged on hospital day #19 with a prednisone taper, hydroxychloroquine, and mycophenolate mofetil. On outpatient follow up two months later, the patient's conjunctivitis resolved, discharge had not returned, her oral mucosal ulcerations healed, and her skin rash had nearly resolved with residual scattered cutaneous hyper- and hypo-pigmentation.

Discussion

This illustrates a rare presentation of SLE presenting as a SJS/TEN like picture. There have been case reports of SJS/TEN-like lupus erythematosus (LE) presentations in both pediatric and adult patients.[1-3] Presentations ranged from isolated skin manifestations to concomitant degrees of oral, mucosal, and conjunctival involvement. SJS/TEN-like LE is considered a separate entity from SJS/TEN, but is often difficult to distinguish between the two conditions.

SJS and TEN are life threatening mucocutaneous reactions with a mortality rate as high as 50% in TEN. Both represent a disease continuum distinguished by the degree of body surface involvement. SJS involves less than 10%, SJS/TEN involves 10-30%, and TEN involves >30% of the total body surface area. The incidence of the SJS/TEN continuum is reported as two to seven cases per million people per year, with SJS outnumbering TEN in the United States three to one.[4] Certain patient populations have a higher incidence of SJS/TEN, including HIV patients and active cancer patients.[5,6] One retrospective study noted that out of 1366 patients with SJS/TEN, 17 had SLE (1.2%).[7]

The leading cause of SJS/TEN is medication induced, with the most common being allopurinol, aromatic antiepileptics, sulfonamides, nevaripine, and NSAIDs.[4] The clinical presentation of SJS/TEN often starts with fevers and flu like symptoms that precede the skin manifestations by one to three days. Skin lesions begin as erythematous macules with purpuric centers and usually first appear on the face and trunk and spread outwards. The Nikolsky sign may also be positive. This is positive when there is superficial skin sloughing with application of lateral pressure at an adjacent, unaffected site. Characteristic mucosal manifestations include stomatitis, mucositis, conjunctivitis with discharge, and genital erosions. Pharyngeal involvement can present as odynophagia.[4] Associated lab abnormalities include lymphopenia, anemia, and a mild transaminitis.[4] Histologic findings include superficial perivascular and interstitial lymphocytic infiltrates and necrotic keratinocytes throughout the lower epidermis.[7]

The diagnosis of SJS/TEN is made clinically in conjunction with histological findings. The recognition and diagnosis of SJS/TEN is crucial given the high associated mortality. The SCORETEN is a severity score ranging from zero to seven used to estimate prognosis in SJS/TEN. The index includes age, presence of malignancy, percentage of body surface involvement, heart rate, blood urea nitrogen, serum glucose, and serum bicarbonate. Higher score are associated with higher mortality.[8-10] Treatment includes prompt withdrawal of the offending agent and supportive care similar to that of burns or large surface wound management. There is no established therapy outside of supportive care, although clinical use of systemic corticosteroids, intravenous immune globulin, cyclosporine, plasmapheresis, and anti-tumor necrosis factor monoclonal antibodies have been reported but not studied adequately in randomized trials.[8]

Cutaneous LE encompasses three subsets: acute cutaneous lupus erythematosus (ACLE), subacute cutaneous lupus erythematosus (SCLE), and chronic cutaneous lupus erythematosus (CCLE). These can occur as a manifestation of SLE or independently. Each subset has different variants, with SJS/TEN-like LE being the most severe presentation of ACLE. SJS/TEN-like LE presents as an erythematous maculopapular eruption, mainly in sun exposed areas of the skin, but can become generalized to include mucosal areas.[1] Conjunctival involvement may also be seen.[3] As with SJS/TEN, the diagnosis of SJS/TEN-like LE is made clinically, with support from histopathologic data if needed. Because these two entities share an almost identical clinical presentation, differentiating between the two may be extremely difficult. Features that help support a SJS/TEN-like LE diagnosis over SJS/TEN include a recent SLE diagnosis or exacerbation, minimal mucosal involvement, photo distribution of the lesions, and insidious onset (days to weeks).[1] SJS/TEN will usually be associated with an antecedent medication use. On histology, SJS/TEN-like LE can show a basement membrane complement and IG deposition, perivascular and periadnexal lymphocytic infiltrate, vacuolar degeneration, and dermal mucin deposition, whereas SJS/TEN shows epidermal necrosis and minimal lymphocytic infiltrate.[1]

Given the rarity of SJS/TEN-like LE, there are no current standard treatments. Acute management has been largely based on case reports and limited reviews. One report reviewed 25 other cases of SJS/TEN-like LE, with nearly all treated with high dose IV corticosteroids. Of the 23 cases that used IV corticosteroids, 13 resolved with steroids alone. Eight cases employed intravenous immunoglobulin (IVIG) with six cases reporting resolution either with IVIG alone or in combination with IV steroids. It was postulated that since IVIG blocks Fas from binding to the Fas ligand to induce epidermal cell death, it may have potential utility in SJS/TEN-like LE where it is believed that the underlying pathology is due to the upregulation of keratinocyte apoptosis.[1] The literature also reports use of antimalarials, plasmapheresis, and tumor necrosis factor inhibitors.[1,11] Plasmapharesis removes antibodies and immune complexes from the blood. While the use and efficacy of plasmapheresis in SLE has only been supported by non-controlled or retrospective studies, it has been recommended in life threatening or therapy resistant SLE.[12] A case report noted success with plasmapheresis for severe SJS/TEN-like LE when there had been no response with IV steroids and IVIG.[1]

Conclusion

SJS/TEN-like LE is a rare presentation of cutaneous LE, but is specifically described in acute cutaneous lupus erythematosus. Given the high mortality rate of SJS/TEN, prompt diagnosis of either disease may help proper care and treatment. Due to the rarity of disease, there is no standard of care for SJS/TEN-like LE, however systemic corticosteroids, IVIG, and plasmapheresis have reported efficacy. In addition to illustrating a rare presentation of what can be a common rheumatologic diagnosis, this case highlights the importance of a multidisciplinary approach to cases with overlapping multi-specialty clinical presentations.

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