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Case Report

Urologic Presentation of Stevens-Johnson Syndrome: A Case Report

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Introduction and Case Description

This case report describes a case of a rare skin condition, Stevens-Johnson Syndrome, which was localized almost solely to the genitourinary region.

The patient is a 53 year-old gentleman with a C4-5 spinal cord injury resulting from a motor vehicle accident with a neurogenic bladder which has been managed by urology with suprapubic catheter. Prior to presentation, he had a prolonged admission for aspiration pneumonia treated with intravenous cefepime. Within a few days from discharge, he was transferred back to the emergency room due to altered mental status and hypothermia. His chest X-ray showed persistent pneumonia and he was reinitiated on antibiotic treatment with metronidazole and cefepime. At this time, nursing in the emergency room noted significant skin changes of the penis and scrotum and urology was called to rule out a Fournier's gangrene. The skin was noted to be desquamating and sloughing, which was not consistent with necrotizing fasciitis (Figure 1).

Figure 1: Genitourinary Physical Presentation

Intensive care unit admission and dermatology consult were recommended given concern for Stevens-Johnson Syndrome in the setting of hypothermia and tachycardia. Infectious disease was then consulted to address his antibiotics as the possible offending agent. Skin exam was notable for mild right–sided scleral injection, upper and lower lip mucosa with shallow denudation, left axillary fold with ~3 cm denudation and most significantly, 75% denudation of scrotum and almost complete denudation of penis with dusky borders, positive Nikolsky sign (Figure 2).

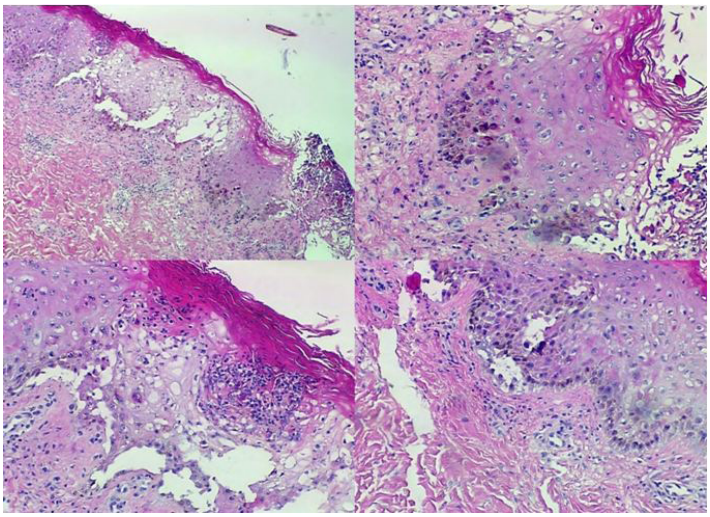

Figure 2: Histopathology from patient's skin biopsy from right medial thigh.

Skin surrounding the suprapubic catheter was unaffected. Body surface area calculated was approximately 10%. A biopsy was obtained and pathology revealed the following:

Skin biopsy obtained from the right medial thigh demonstrates epidermal separation with focal full thickness epidermal necrosis and subepidermal bullae. Apoptotic keratinocytes align the basal layer of the epidermis with perivascular lymphocytic in-

filtrate and occasional eosinophils in the superficial dermis. This is consistent with Stevens-Johnson Syndrome.

Within the spectrum of severe cutaneous adverse reactions (SCAR) affecting skin and mucous membranes, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis are two entities that belong.Both involve cutaneous erythema with blister formation and hemorrhagic erosions of mucous membranes and therefore, findings can be characterized with stomatitis, balanitis, colpitis, conjunctivitis and blepharitis [1].

The disease is fairly rare, incidence of 1-2 cases per 1,000,000 annually but mortality rates can be high based on degree of skin involvement.The spectrum of these skin conditions is defined specifically based on the type, extent and body surface area of coverage of the lesions [2]. The surface area involved in SJS is typically less than 10%, and toxic epidermal necrolysis (TEN) is typically greater than 30%, with SJS/TEN falling between 10% and 30%. True TEN, encompasses > 30% body surface area and can involve large epidermal sheet losses.A related entity is Mycoplasma-pneumonia associated mucositis, an atypical form of SJS, predominately mucus membrane involvement without significant cutaneous involvement.

Revuz et al. reviewed 87 with clinical features observed in SJS/TEN and followed their clinical and dermatologic manifestations[3]. Generally, the patients present with fever, malaise and a respiratory infection that progresses to the eruption of a rash with the presence of atypical target lesions or purpuric macules that begin on the torso and limbs and spread to involve the rest of the trunk and limbs, eventually coalescing into large areas that blister. The lesions are characterized by the Nikolsky sign in which the epidermis or blister can be pushed away, causing desquamation. This results in significant insensible losses and energy expenditure, as similar to the case of burns. Ocular symptoms tend to start before the skin signs. Patients can also develop gastrointestinal symptoms, involvement of upper airway, and oromucosal ulcers.

Differential and Characterization

The differential diagnosis includes other desquamating lesions including erythema multiforme, staph-scalded skin syndrome, drug-induced linear immunoglobulin A dermatosis, acute graft versus short disease, acute generalized exanthematouspustulosis, and generalized morbiliform eruption. In adults, they are usually due to drug use, high risk being anti seizure medications, sulfonamides, NSAIDS and phenobarbital followed by other antibiotics including cephalosporins, macrolides, quinolones, tetracyclines [2].

It is notable to mention the compilation called Severity of Illness score for Toxic Epidermal Necrolysis (SCORTEN) used to predict mortality in cases of acute TEN. It was developed from a study of two databases including 78 females and 87 males with SJS/TEN spectrum, essentially allocates points for certain variables that contribute to an overall score that predicts morality rates [3]. The variables include age, heart rate, presence of cancer, BSA, serum levels of urea, bicarbonate and glucose. With equal weight to each variable, a value ≥ 5 (10 patients) was associated with 90% mortality for the 165 patients reviewed in their study.It is a level C recommendation by the UK guidelines to calculate a SCORTEN grade within 24 hours of admission [5].

The histology can be varied, from cell apoptosis to necrosis of the epidermal layers and changes with basal cell vacuolar degeneration and subepidermal vesicle or bullous changes. The dermis is less often involved, only found typically to have cellular infiltration with lymphocytesand histiocytes [6].

Genitourinary involvement

Many of the studies of SJS and GU involvement stem from the pediatric population, for whom desquamating conditions, although still rare, are more often seen due to infections.Genitourinary complications include penile adhesions and meatal stenosis, urethral strictures and phimosis for males. For females, this can include vaginal synechia, stenosis and obstruction. Batavia et al performed a comprehensive retrospective review of 31 patients with SJS/TEN in patients aged 2-18 years from mycoplasmia (48%) or medications (45%) and found 74% of them to have genial involvement [7]. Of note 20 patients (61%) complained of dysuria and 8 patients required placement of a urethral catheter.In the short term, 2 males underwent lysis of penile adhesions and in long term, a single male and female had lysis or penile and vaginal adhesions. No patients developed any long-term sequelae of clinical significance from the genitourinary involvement or catheterization in this study. Skin and ocular sequelae have the most long-term complications but there are other studies that found two of 55 children with SJS/TEN to have phimosis on long-term follow-up [8]. There are, however, more case reports with long-term vulvovaginal sequelae in female patients, resulting in difficulties with menstruation, intercourse and pregnancy at a later date [9]. One of many case reports describes vaginal stenosis in a pregnant female requiring dilation and topical therapy who required multiple surgical interventions and continues to self-dilate to prevent recurrence [10]. Involvement in adults can be detrimental. Meneux et al studied 40 women retrospectively and found 28 (70%) to report acute genitourinary symptoms, of which 5 developed vulvovaginal sequelae of which three were unable to have vaginal sexual intercourse, 2 of which required surgical intervention and one with persistent dyspareunia [11].

Management

In 2016 a team of dermatologists and plastic surgeons published a set of guidelines from the United Kingdom regarding management for this population [5]. The guidelines recommends evaluation of critical disease components with appropriate level of

care (burn center for >10% body surface area involvement), cessation of the offending agent (usually assumed via drug history for patient and referring to list of commonly offending agents) with detailed history outlining any bowel or urinary, other mucous site involvement, and symptoms indicating involvement with respiratory tract. Sassolas et al developed an algorithm called ALDEN (Algorithm of Drug causality in Epidermal Necrolysis) as a tool for retrospective assessment of offending agent but parameters within the algorithm are often used in practice in the acute setting to determine the drug culpability [12].

Patients should be managed by multidisciplinary teams that involve skin experts such as dermatology and plastic surgery, and may include other medical specialists depending on cause and presentation including allergy, pulmonary, gastroenterology, infectious disease, oral surgery or otolaryngology, ophthalmology and urology or gynecology. Other specialists including dieticians, pharmacists, and wound care specialists are often involved. Patients should be in an environment in which the room temperature may be raised to prevent acceleration of the patient's basal metabolic rate. Fluid resuscitation should be performed early in management to account for the insensible losses. Nutrition should be provided in the appropriate manner, which may be parenteral or enteral pending orogastric involvement.

Careful handing is paramount, particularly with repositioning, to prevent excessive shear force that can result in separation of the dermis from the epidermis. Though there is little data to support this, any epidermis that has sloughed should not be removed and should be kept intact, covering he exposed dermis. Extensive bullae may be trained but overlying skin should remain intact to function as a biologic dressing. Bland emollients should be used over the sites to keep the moisture in place. Should this approach fail or skin becomes infected, more aggressive approaches can be taken with removal of the denuded skin and replacement with allograft or xenograft. Simple inpatient preventative tasks including avoiding telemetry leads, skin adhesives, pressure items such as venodyne boots and sphygmomanometer cuffs can reduce risk of further denudation.

Management of topical wounds centers around moisture conservation and non-irritants. Wounds should be irrigated with warm sterile saline or chlorhexidine followed by a greasy emollient such as paraffin.Once can consider an antimicrobial topical agent in areas that are starting to denude can. Silver-containing products can be used sparingly, as absorption can occur and non-adherent dressings are recommended. Specific recommendations for genitourinary involvement have also been made (grade D). Daily exams are important to document involvement if present, and if identified, to prevent serious long-term morbidity from urethral strictures or stenosis, phimosis in males and vaginal synechiae in females. Topical management is similar to management of skin lesions as listed. Non-adherent dressings should be used to prevent irrigation from blankets or clothing. Though there is no evidence to suggest catheterization prevents complications from stricture formation, The UK recommends catheterization of all patients to prevent strictures and for females, dilator or tampon should be wrapped in Mepitel and inserted into the vagina to prevent synechiae (grade D, level 4 evidence). Often patients require systemic treatment with intravenous immunoglobulin, cyclosporine or systemic corticosteroids but data is limited to support these treatments. The use of these agents is to the discretion of the clinician based on the patient's clinical course.

Case Conclusion

In the case of our patient, SCORTEN grade was 2. He was managed in the intensive care unit for several weeks with fluid resuscitation, antibiotic treatment for pneumonia and candida urinary tract infection with micafungin, linezolid and meropenem and was given intravenous immunoglobulin.Consulting teams included pulmonary, otolaryngology, urology, infectious disease, dermatology, wound nurse, renal, ophthalmology, neurology, nutrition and allergy. The patient's wounds were managed with Hydrogel (emollient), xeroform gauze and Exu-Dry dressing. He was eventually discharged after 2.5 months and when seen again in follow-up almost 10 months later, was noted to have re-epithelialization of his skin.

Discussion

The SJS/TEN spectrum can be a life-threatening skin condition that can manifest with many mucosal and cutaneous lesions that can rapidly denude the skin, resulting in significant fluid loss and increased risk of infection, leading to higher morbidity rates. Early recognition and prompt treatment with both preventative precautionary skin care measures, supportive care with nutrition and fluids, topical and systemic treatments can ameliorate some of this rapid decline. There should be a multidisciplinary approach to these patients to address every aspect of their care, and efforts should be made to quickly identify and cease administration of the offending agent. Genitourinary presentations are common, but in this unusual case, the patient's primary presentation was of the penile skin and scrotum. Understanding the principles of this disease and populations at risk can expedite diagnosis and care.

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