STAPHYLOCOCCAL SCALDED SKIN SYNDROME: CRITERIA FOR DIFFERENTIAL DIAGNOSIS FROM LYELL'S SYNDROME. TWO CASES IN ADULT PATIENTS

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SUMMARY. A review of the relative international literature of the last few years is followed by a description of two cases of staphylococcal scalded skin syndrome in adults. As in both cases the initial diagnosis was that of Lyell's syndrome, the main criteria for the differential diagnosis of the two pathologies are considered in order to permit specific and effective treatment.

Introduction

Staphylococcal scalded skin syndrome (SSSS) is a bullous disease of the skin caused by toxins (exfoliatins) secreted by certain types of *Staphylococcus aureus*.

These toxins (ET A, ET B, and recently also ET D) may act as superantigens, stimulating the proliferation of T lymphocytes, with a massive release of cytokines and consequent epidermal damage.[1]

On the other hand, exfoliatins may also affect Desmoglein 1 (a protein of the desmosomes of the stratum granulosum of the epidermis), provoking the loss of cellular adhesion. Histological findings show conditions compatible with this lithic activity.[2-5]

Epidemiology. SSSS is a paediatric disease. In 1979, Lyell identified only 12 cases of SSSS in adult patients, to which he added one that in 1956 he had described as toxic epidermal necrolysis.[6]

A later survey of the literature (1994) produced only 32 cases of SSSS in adults and the description of one further case.[7] Since then the disease has been reported a few times to have affected adults or elderly persons with chronic debilitating diseases, immune suppression/depression (antitoxin antibodies deficit), or kidney failure (toxin elimination deficit), always occurring in the presence of an imbalance between production, detoxification, and elimination of toxins.[1,8]

Table I presents some cases of non-paediatric SSSS reported after 1994.

Table I - Survey of the literature after 1994

Author and bibliographical reference	Patient's sex/age (yr)	Focus of infection	Disease or drugs
Hardwich, 1995, UK[9]	F, 77	Surgical wound	Kidney failure, NSAIDS
Farrell, 1996, UK[10]	F, 38	Pneumonia	HIV-1+
Oono, 1997, Japan[11]	F, 68	Abscess	NSAIDS
Shelley, 1998, USA[12]	M, 50	Conjunctivitis Otitis	Epilepsy, Ataxia
Shirin, 1998, USA[13]	M, 51	?	Steroids
Ansai, 2000, Japan[14]	F, 67	Endocarditis	Cardiopathy
Oyake, 2001, Japan[15]	M, 65	Conjunctivitis, Rhinopharyngitis	–
Fumal, 2001, Belgium[16]	M, 50	Pharyngitis	–
Sharkey, 2002, Australia[17]	M, 60	Pustolar psoriasis	Cyclosporin, Kidney failure
Ito, 2002, Japan[18]	F, 71	Empyema, Gallbladder	Diabetes, Kidney stones
Suzuki, 2003, Japan[19]	F, 62	Peritonitis	Peritoneal dialysis
Paquet, Pierard, 2003, Belgium[1]	F, 46	Skin ulcer	Alcoholism, Epilepsy
	M, 55	Septicaemia	Diabetes, Steroids, Metotrexate
Decleire, 2004, Belgium[20]	F, 81	Septic arthritis due to steroid infiltration	–
Sarma, 2004, India[21]	F, 19	Tropical pyomyositis	–
Neff, 2005, Switzerland[22]	F, 65	Septic arthritis due to steroid infiltration	–

The only case of SSSS reported in Italy in the last ten years in an adult patient was in actual fact a case of Lyell's syndrome, of which SSSS - together with graft-versus-host disease - was for years considered a form.[23] Even today SSSS is hard to distinguish in non-paediatric patients.

We present two patients sent to us in the last few years with a diagnosis of Lyell's syndrome.

Clinical cases

The two patients, both female, presented not dissimilar features (*Table II*).

Table II - Case histories and epidemiological features

	Patient 1	Patient 2
Age (yr)/sex	62/F	64/F
Disease	Diabetes Craniopharyngioma Bronchopneumonia	Meningioma
Drugs administered	Phenobarbital Steroids, Antibiotics	Phenobarbital Steroids
Hospitalization in burns unit	After 12 days	After 7 days

These features (age, pathologies, the taking of Lyell-inducing drugs) and the hospitalization in a burns centre some days after the onset of exfoliation were certainly misleading. However, certain clinical, haematological, microbiological, and histological criteria made it possible to reach the correct diagnosis and initiate effective therapy (*Table III*).

Table III - Criteria for diagnosis of toxinfection

	Patient 1	Patient 2
Clinical picture	Mucosae intact	Mucosae intact
Lymphocyte subpopulations	Within normal limits	Within normal limits
Rhinopharyngeal, conjunctival, and blood culture swabs	Positive	–
Biopsy	Intraepidermal cleavage	Intraepidermal cleavage
Antibiotic therapy	Effective	Effective
	(Vancomycin)	(Meropenem)

Discussion

The clinical picture. The typical features of SSSS are periorificial face scabs, de-epithelialization of friction zones, e.g. flexor folds, conspicuous desquamation after initial erythroderma - these conditions are generally all present together. However, the main sign is the absence of mucosal involvement, which in Lyell's syndrome may be serious, affecting not only the visible mucosae but also the respiratory, gastrointestinal, and urinary mucosae.

In SSSS, the mucosae cannot be affected because Desmoglein 3, a protein present in all strata of the epithelium, compensates for the lysis of Desmoglein 1 (which is present only in the stratum granulosum of the epidermis), maintaining cellular adhesion.[5]

Cellular immunity. For the purposes of differential diagnosis between Lyell's syndrome and SSSS, a study of cellular immunity, which should be routine, will highlight (*Table IV*) totally different pictures.[24-26]

Table IV - Cellular immunity in Lyell's syndrome and SSSS

	Lyell's syndrome	SSSS
Lymphopenia	Yes	No
CD4+ (T helper)	Reduced	Normal
CD8+ (T suppressor)	Normal or increased	Normal
CD4+/CD8+	Reduced	Normal

The literature reports two cases of SSSS presenting impairment of cellular immunity. As one patient, an adult, had AIDS[27] and the other, a pre-term neonate, had post-operative chilothorax,[28] this condition was not part of the general SSSS picture.

Histology. The histological pictures are also totally different. The characteristic feature of Lyell's syndrome is epidermal apoptosis with detachment at the junction between epidermis and dermis. In SSSS the detachment is subcorneal and is caused by the loss of adhesion of cells without apoptosis.[22] However, pending biopsy results, a rapid differentiation can be made between the two diseases using the Amon and Dimond test, i.e. examining a frozen section of the roof of a bulla and subjecting the base to the Tzanck cytodiagnostic test.[29]

Microbiology. The case is presented of a 43-yr-old schizophrenic whose skin swabs contained *Staphylococcus aureus* of phage group II, type 71. The patient was treated for SSSS until skin biopsy revealed Lyell's syndrome.[30] *Staphylococcus aureus* is in fact the germ that nearly always infects skin lesions in Lyell's syndrome. Should SSSS be suspected, the focus of infection - considering that the damage to the skin is caused by circulating exotoxins - should be looked for elsewhere. Phage typing, if indeed performed in every laboratory, is not currently acceptable for confirmation of a diagnosis of SSSS.[2,8]

Another reason why this is so is that there have been reports of cases caused either by germs belonging to phage groups other than those classically considered responsible[31] or even by *Staphylococci* producing enterotoxins or tox-

ins responsible for the toxic shock syndrome (MRSA) which generally behave like superantigens.[14,18,21,32]

Once the focus of infection has been found, which in many cases - despite Koch's postulates - is not apparent,[33] and once the germ has been isolated, it has to be investigated (polymerase chain reaction) in order to establish its toxigenic capacity.[11,34] These investigations have however only limited use in clinical practice and are mainly utilized for research purposes.

Conclusions

Clinical observation, lymphocyte typing, and histology make it possible to reach a differential diagnosis between Lyell's syndrome and staphylococcal scalded skin syndrome. Anamnestic and epidemiological criteria and microbiology are useful only if correctly interpreted. Differential diagnosis is of extreme practical importance, for recovery is possible only following specific treatment.[35,36]

Steroids being totally contraindicated, treatment for SSSS consists of:

- antistaphylococcal antibiotic therapy;
- surgical restoration of the area of the focus of infection;
- administration of fresh frozen plasma, also - when necessary - for resuscitation purposes;
- administration of intravenous human immunoglobulin.

RÉSUMÉ. Les Auteurs, après avoir considéré la littérature internationale relative des dix derniers ans, décrivent deux cas du syndrome de la peau ébouillantée staphylococcique chez des adultes. Puisque le diagnostic au moment de l'hospitalisation a été celui du syndrome de Lyell dans tous les deux cas, les Auteurs discutent les critères principaux de diagnostic différentiel entre les deux pathologies pour permettre un traitement spécifique et efficace.

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