Severe and Unrecognized Dental Abnormalities After Drug-Induced Epidermal Necrolysis

Toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS) are severe cutaneous reactions characterized by extensive apoptosis and detachment of the epithelium of skin and mucous membranes. Both conditions carry a high mortality rate (25%-30%) and high risk of sequelae. According to the French patients’ association Amalyste (http://www.amalyste.fr/), survivors of TEN and SJS often experience dental problems that are considered by their physicians to be unrelated to the disease. We organized an oral and dental checkup of 16 patients with a history of SJS or TEN. The study was approved by the ethics committee of the French Society of Dermatology.

Methods. Patients were aged 11 to 57 years (median age, 37 years) and were examined from 1 to 36 years (median, 11 years) after diagnosis of SJS and/or TEN. The clinical examination was performed with panoramic radiography, bacteriologic analysis of periodontal pocket samples (reverse transcriptase–polymerase chain reaction), and quantitative and qualitative analysis of the saliva (viscosity, pH, and buffering capacity), which was collected by having the patient spit after 5 minutes of chewing a special wax (Saliva-Check Buffer; GC Europe NV, Leuven, Belgium). We obtained reference values for normal saliva from 12 healthy adult volunteers (controls), aged 24 to 64 years (median age, 32 years).

Results. All patients complained of mouth discomfort. Nine had altered tongue mucosa (erythema and/or no lingual papilla) (Figure 1). Thirteen had inflammation of the gingiva; 14 had gingival recession; and 6 had gingival synechiae (Figure 2).

All patients had sicca syndrome (Table). Compared with controls, patients had reduced mean (SD) saliva volume (4.6 [0.8] vs 5.8 [0.5] mL), with more acid pH (6.53 [0.44] vs 7.26 [0.16]), and lower buffering capacity (8.9 [1.6] vs 11.5 [0.9] mmol/L) (Mann-Whitney P = .001 for all comparisons). Saliva viscosity was abnormal in 9 of 16 patients vs 2 of 12 controls.

Dental alterations were frequent among patients. Eleven patients had caries; 8 had at least 1 missing tooth; and 3 had severe periodontal disease. All 5 patients who contracted TEN during childhood (at ages 2.5, 5.0, 5.0, 11.0, and 11.0 years) had severe periodontal abnormalities (Table). The more severe abnormalities (dental agenesia, root dysmorphia, root-building abortion with incomplete root apex closure, shorter root, and microdontia) affected the 3 youngest patients, who each had at least 11 teeth involved (Figure 3).

Porphyromonas gingivalis and Tannerella forsythia, 2 bacteria strongly associated with periodontitis, were present in 5 and 9, respectively, of the 12 tested sulcular samples (Table). Severe periodontitis was observed in 3 patients, 2 of whom tested positive for both P gingivalis and T forsythia.

Comment. Because of an obvious selection bias, low numbers, and absence of an adequate control group, this preliminary study has no epidemiologic value. Nevertheless, the frequency and homogeneity of the alterations observed are impressive, especially in younger patients, and strongly suggest the existence of dental complications of drug-induced TEN. Actually, all 16 investigated patients had at least 2 oral problems.

Sicca syndrome has been reported after TEN and was present in all of our patients. Quantitative and qualitative saliva alterations were probably cofactors in the pathogenesis of caries, gingival inflammation, and periodontitis, specifically in so far as they promoted the growth of uncommon bacterial species (ie, T forsythia and P gingivalis). These findings would suggest that patients with SJS and/or TEN might have a higher risk of periodontal disease.

The severe tooth abnormalities observed in patients who had childhood TEN were similar to those observed after chemotherapy for cancer but with even more important...
damages. The most likely explanation is that the Hertwig epithelial root sheath, the epithelial proliferation zone of the enamel organ in a developing tooth, is affected by the acute process of apoptosis leading to the root-building abortion observed in the youngest patients.

We have to reinforce our vigilance against these severe and until recently unknown (or denied) dental consequences of SJS or TEN. Patients should be informed of the potential risk and instructed on preventive dentistry. Mouth and dental follow-up examinations should be recommended to all patients with SJS or TEN.

Frédéric Gaultier, DDS, PhD
Juliette Rochefort, DDS
Marguerite-Marie Landru, DDS
Laurence Allanore, MD
Adrien Naveau, DDS
Jean-Claude Roujeau, MD
Bruno Gogly, DDS, PhD

Accepted for Publication: June 11, 2009.
Author Affiliations: Department of Odontology, Hôpital Albert Chenevier (Drs Gaultier, Rochefort, Landru, Naveau, and Gogly), and Reference Center for Toxic and Autoimmune Blistering Diseases, Department of Dermatology, Hôpital Henri Mondor (Drs Allanore and Roujeau), Créteil France.
Correspondence: Dr Roujeau, Department of Dermatology, Hôpital Henri Mondor, LIC EA4393, Créteil, France (jean-claude.roujeau@hmm.aphp.fr).

Author Contributions: Drs Rochefort, Roujeau, and Gogly had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Roujeau and Gogly. Acquisition of data: Rochefort, Landru, and Gogly. Analysis and interpretation of data: Gaultier, Rochefort, Landru, Roujeau, and Gogly. Drafting of the manuscript: Gaultier, Rochefort, Naveau, Roujeau, and Gogly. Critical revision of the manuscript for important intellectual content: Landru, Allanore, and Gogly. Statistical analysis: Gaultier. Administrative, technical, and material support: Rochefort, Landru, Allanore, Naveau, Roujeau, and Gogly. Study supervision: Rochefort, Roujeau, and Gogly.

Financial Disclosure: Dr Roujeau serves as a consultant for Medimmune, Vertex, Servier, and OM-Pharma and has received research grants from Boehringer-Ingelheim, GlaxoSmithKline, Iris-Servier, Novartis, Pfizer, and Sanofi-Aventis.

Additional Contributions: Sophie Gaultier-Gaillard provided valuable help with statistical data analysis.