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Toxin-induced chemosensory dysfunction: A case series and review

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Abstract

Background—Toxic chemical exposures are estimated to account for 1–5% of all olfactory disorders. Both olfactory neurons and taste buds are in direct contact with environmental agents because of their relatively unprotected anatomic locations, thereby making them susceptible to damage from acute and chronic toxic exposures. The aim of this study was to illustrate different aspects of the diagnostic and therapeutic approach to this disorder using a series of case reports and review of the literature.

Methods—Cases were selected for inclusion based on a retrospective chart review of patients who presented to a university-based nasal dysfunction clinic with toxin-induced olfactory or gustatory dysfunction between January 1985 and December 2008. Workup included complete history, otolaryngologic examination, psychophysical testing, and imaging.

Results—Patient ages ranged from 31 to 67 years (mean, 49.3 years). Etiology of chemosensory impairment included exposure to ammonia, isodecanes, hairdressing chemicals, chemotherapy, gasoline, and intranasal zinc. Five of the seven patients (71%) presented with olfactory dysfunction alone, one patient (14%) presented with dysgeusia alone, and one patient (14%) presented with both smell and taste loss. Only one patient (14%) reported parosmias. Tests of olfaction revealed normosmia in one patient (14%), mild-to-moderate hyposmia in one patient (14%), and severe hyposmia to anosmia in five patients (72%). Both patients who reported taste disorders had hypogeusia on testing.

Conclusion—This case series illustrates the wide spectrum of this disorder and provides a framework for the workup and treatment of these patients.

Keywords

Ammonia; anosmia; dysgeusia; gasoline; hyposmia; olfaction; smell; taste disorders; zinc

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Both olfactory neurons and taste buds are in direct contact with environmental agents

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because of their relatively unprotected anatomic locations, thereby making them susceptible to damage from acute and chronic toxic exposures.

Toxin-induced olfactory and gustatory loss has been a relatively neglected topic in the medical literature, with most previous publications being limited to case reports or broad reviews. For excellent reviews on this topic, the reader is referred to Doty and Hastings,² Upudhyay and Holbrook,³ Gobba,⁴ and Dalton.⁵ Over 100 substances have been implicated in olfactory dysfunction, including ammonia,⁶ wood dust,⁷ chromium,⁸ and hydrocarbon solvent mixtures.^{9,10} Well-designed studies including standardized olfactory testing and either blood or urinary toxin levels have reported a positive association for some groups, such as welders¹¹ and workers exposed to airborne cadmium,^{12–14} whereas no association was found for workers exposed to styrene.¹⁵ Unfortunately, many other case reports have no or limited objective testing data.

OBJECTIVE

Here, we present seven cases from the University of California, San Diego Nasal Dysfunction Clinic that illustrate the diagnostic and therapeutic approach to patients with chemosensory dysfunction secondary to toxin exposure.

METHODS

Cases were selected for inclusion based on a retrospective chart review of patients who presented to our clinic with toxin-induced olfactory or gustatory dysfunction between January 1985 and December 2008. Workup included a thorough history and an otolaryngologic examination including nasal endoscopy, imaging, and psychophysical assessment, as detailed in Harris *et al.*¹⁶ Olfactory testing included symptom ratings, olfactory threshold, odor identification, and/or University of Pennsylvania Smell Identification Test (UPSIT). Suprathreshold taste discrimination and identification testing was performed in select cases.

Testing was performed in accordance with a protocol approved by the University of California, San Diego, Human Resources Protection Program. All persons gave informed consent before inclusion.

A MEDLINE database search was performed for the period of January 1950 to January 2009. Key words used include various combinations of “anosmia,” “hyposmia,” “olfaction,” “taste disorders,” “dysgeusia,” “ammonia,” “isodecanes,” “gasoline,” “hair permanent,” “chemotherapy,” and “zinc.” Selected article reference lists were also reviewed for relevant literature.

RESULTS

Patient ages ranged from 31 to 67 years (mean, 49.3 years). Unless otherwise stated, all patients denied a history of environmental allergies, sinus disease, head trauma, antecedent viral infection, or smoking. Etiology of chemosensory impairment included ammonia, isodecanes, hairdressing chemicals, chemotherapy, gasoline, and intranasal zinc. Five out of the seven patients (71%) presented with olfactory dysfunction alone, one patient (14%) presented with dysgeusia alone, and one patient (14%) presented with both. Only one patient (14%) reported parosmias. Olfactory testing revealed normosmia in one patient (14%), mild-to-moderate hyposmia in one patient (14%), and severe hyposmia to anosmia in five patients (72%). Both patients who reported taste disorders had hypogeusia on testing. Refer to Table 1 for detailed testing results.

Ammonia

Case 1—A 31-year-old man presented with hypogeusia 4 months after biting down on an ammonia capsule hidden in a store-bought sandwich. He sustained an intraoral chemical burn injury, immediate-onset ageusia, and decreased sensitivity to oral stimuli. His medical history was significant for environmental allergies. He smoked <1 pack of cigarettes per day for <5 years. Examination and olfactory testing was normal. The patient correctly identified stimuli of moderate and high concentrations on suprathreshold taste testing. Intensity estimates were consistent with hypogeusia.

Case 2—A 47-year-old woman presented with hyposmia 2 years after completing a home remodel to remove black mold. Each day of the remodel, she scrubbed her hardwood floors with an ammonia-based cleaning fluid. She developed a significant allergic reaction to the mold, including nasal congestion. This impaired olfactory function, and, as her nasal mucosa was further damaged by each day of exposure, she began diluting the cleaning fluid less and less because she mixed it by “smell.” Ultimately, the nasal allergies resolved, but her hyposmia persisted so she sought medical care. Examination and sinus CT were normal. Olfactory testing confirmed severe hyposmia. Prednisone, amoxicillin, and nasal steroid were ineffective.

Commentary—Previous research has indicated that ammonia is highly irritating to the mucosal lining of the upper respiratory tract.⁶ Experiments in pigs involving airborne ammonia exposure (0–100 ppm) have shown a dose–response increase in neutrophil cell content in nasal lavage contents.¹⁷ This inflammatory response may damage the olfactory epithelium, leading to olfactory loss.

Holness *et al.*¹⁸ examined 58 soda ash workers exposed to airborne ammonia (mean, 9.2 ± 1.4 ppm) and found no relation between the length or level of exposure and smell loss. However, the study period was limited to 1 week, and testing consisted solely of odor detection. Prudhomme *et al.*⁶ reported one case of persistent hyposmia after acute overexposure to an ammonia vapor leak. Smell loss was confirmed by UPSIT and Smell Test Kit results. The patient also reported a transient metallic taste. Although no other reports have linked ammonia to dysgeusia, Isenberg *et al.*¹⁹ did report one case of chemical burns of the oral mucosa.

Isodecanes (Photograph Toners)

Case 3—A 63-year-old woman presented with smell and taste loss after a 3-year exposure to isodecane (isoparaffin). She initially experienced welts on her tongue and lips, chest tightness, and a bitter taste when exposed to isodecanes 8 years prior. She reported gradual smell and taste loss, intraoral burning sensations, and periodic perioral dermatitis. No improvement occurred with cromolyn sodium, zinc chloride, or copper sulfate. Examination of the olfactory epithelium revealed a flat, yellow area with scarring. Sinus CT scan was normal. Olfactory testing indicated mild-to-moderate hyposmia. Suprathreshold taste testing showed depressed intensity ratings, poor taste identification, and no response to bitter stimuli. After topical anesthesia, taste responses were reduced to zero. Oral prednisone and be-clomethasone nasal inhaler were ineffective.

Commentary—Isodecanes are used in the manufacture of paint, imaging toners, and floor cleaners. They are believed to have a low level of acute toxicity from dermal, oral, and inhalational routes.²⁰ Although no previous reports have linked isodecanes to olfactory or gustatory loss, there is one reported case of respiratory distress and bilateral lung abscesses after isoparaffin ingestion.²¹

Hairdressing Chemicals

Case 4—A 67-year-old woman presented with smell loss initially noted after a hair permanent wave 2 years prior. She reported the immediate onset of anosmia, followed by a pleasant parosmia. Nasal endoscopy and sinus CT were normal. Olfactory testing showed severe hyposmia. Nasal steroids and prednisone resulted in minimal improvement.

Commentary—Modern hair permanents are typically performed using sodium thioglycolate and hydrogen peroxide, both of which are harsh chemicals. However, there is currently no evidence to link these chemicals to olfactory loss.

Chemotherapy

Case 5—A 58-year-old man presented with complete olfactory loss after chemotherapy with MOPP (mustargen, vincristine, procarbazine, prednisone) and ABVD (adriamycin, bleomycin, vinblastine, dacarbazine) for lymphoma 9 years previously. He did endorse a recent history of environmental allergies, as well as a 30-year history of tobacco use. Examination showed leftward septal deviation. Olfactory testing showed anosmia on the left and severe hyposmia on the right.

Commentary—Olfactory deficits have been associated with several antineoplastic agents, including cisplatin, doxorubicin, methotrexate, and vincristine.²² However, in a recent cross-sectional study of 518 chemotherapy patients, 43 subjects reported increased odor sensitivity to one or several odors with no participants reporting decreased olfaction.²³ However, these results are based on questionnaire and interview responses, with no objective testing.

Gasoline

Case 6—A 44-year-old man was filling the gasoline tank on his motorcycle when the hose broke free from the nozzle. Gasoline forcefully squirted into his nose, eliciting an immediate burning sensation. He presented 3 years later because of persistent smell loss. Examination was normal. Olfactory identification and threshold testing revealed anosmia, as confirmed by UPSIT testing.

Commentary—Although there have been no previous reports linking gasoline to smell disorders, exposure to this chemical typically occurs *via* inhalation. However, direct cutaneous exposure can cause full-thickness burn injury, with severe multisystemic complications secondary to the absorption of hydrocarbons through the skin.^{24,25} Therefore, it appears feasible that gasoline could cause a similar chemical burn injury to the olfactory epithelium, resulting in anosmia.

Zinc Cation

Case 7—A 35-year-old white woman presented with hyposmia after the use of zinc nasal spray for a presumed upper respiratory tract infection (URTI). The patient reported that 2 months earlier she had squirted the medication into her nasal cavity and then sniffed. She immediately felt a strong burning sensation that lasted 4 hours. The following day, the patient noted olfactory impairment. She did not develop signs or symptoms of an URTI. Examination and CT scan were normal. Olfactory testing confirmed severe hyposmia, with an UPSIT score of 18/40. Prednisone, amoxicillin, and nasal steroids were ineffective.

Commentary—The reader is referred to the article by Alexander and Davidson for a complete discussion of zinc-induced anosmia.²⁶ In their series, patients typically reported the following sequence: squirting of the medication, and then sniffing and an immediate burning sensation in the nasal cavity, followed by smell loss within 1–2 days. Of note, these

cases were associated with a different drug-delivery method than that currently used. This history is distinct from the one typically reported in viral-induced anosmia, in which there is persistent smell loss despite resolution of other URTI-related symptoms.

DISCUSSION

Acute toxin-induced smell or taste loss may be amenable to a straightforward diagnosis if associated with a history of immediate-onset hyposmia or hypogeusia and a discrete toxin exposure. In contrast, chronic exposures are typically more difficult to diagnose. Repeated chemical exposures may cause gradual damage to the olfactory system over months to years with few physical symptoms due to habituation.²⁷

The diagnosis of toxin-induced chemosensory dysfunction may be complicated by several factors, as evidenced in the aforementioned cases. Patients may present to specialty clinics months or even years after the alleged exposure with limited data regarding the level of exposure or previous olfactory function. Medications,²⁸ smoking,^{29,30} and alcohol³¹ may act as confounders. Additionally, the patient's history may include other possible sources of smell loss, such as a recent URTI or head trauma. In our clinic, for cases that present 6 weeks after symptom onset, a sinus CT and/or prednisone challenge is performed to exclude undiagnosed inflammatory disease.³²

The impact of tobacco smoking on toxin-induced olfactory loss is controversial. Vent *et al.*³³ showed that rats exposed to tobacco and/or ethanol had a decrease in the size of olfactory epithelium, as well as ciliary loss and metaplasia. Additionally, rats exposed to tobacco had a dramatic increase in the degree of apoptosis in the olfactory epithelium.³⁴ In humans, clinical studies have linked smoking to olfactory dysfunction^{29,30} and decreased odor identification ability.³⁵ However, there is also evidence that smoking may provide some protective benefit against toxin-induced olfactory loss. Several studies have indicated that nonsmoking workers exposed to paint manufacturing chemicals, acrylates, and methacrylates have lower UPSIT scores when compared with their smoker counterparts.^{36,37}

Prognosis for a given patient is difficult to provide, but likely will rest on the specific chemical, duration of exposure, and potential future exposures. Unfortunately, relatively limited data are available regarding outcomes. Potentially reversible chemosensory loss has been reported in workers with significant exposure to hydrocarbon solvent mixtures⁹ and acrylates.³⁷ In contrast, a permanent olfactory loss has been linked to other toxins.³⁸

Current data regarding possible treatments for toxin-induced anosmia is limited. Although some cases may improve with time and removal of the offending agent, others may result in irreversible damage. In our clinic, attempted remedies include nasal steroids, oral corticosteroids, and nasal irrigation, with limited success. The cornerstone of treatment should include reassurance and counseling regarding safety measures, including smoke/gas detectors and avoiding spoiled food.

Animal research has shown that the peripheral olfactory system has unique regenerative potential after injury, a capability that may persist well into old age.^{39,40} For instance, in rodents in which the olfactory epithelium has been damaged by inhaled methyl bromide, the majority of the epithelium appears morphologically normal within 8–10 weeks of injury, although some metaplasia does occur.^{41,42} In the future, this area of research may offer hope for possible therapeutic interventions for toxin-induced anosmia.

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Table 1

Detailed history and examination results by case

Case	Sex	Age (yr)	Toxin	Length of Exposure	Time (mo) Since Exposure	Butanol Threshold			Odor ID	UPSIT	Taste Testing	Imaging	Involved in Litigation
						L	R	R					
1	M	31	Ammonia	<1 day	4	50	50	50	50	—	Hypogeusia; suprathreshold ID correct for sweet, salty, and bitter stimuli at moderate/high concentration	—	Yes
2	F	47	Ammonia	1–2 yr	24	20	20	20	10	19/40	—	Mild ethmoid disease	No
3	F	63	Isodecanes	3 yr	96	50	50	10	30	—	—	WNL	—
4	F	67	Hairdressing chemicals	<1 day	24	0	10	20	10	—	—	WNL	No
5	M	58	Chemotx	<1 yr	108	0	20	0	10	—	—	—	No
6	M	44	Gasoline	<1 day	36	0	0	0	0	7/40	—	—	Yes
7	F	35	Zinc	<1 day	2	30	30	10	10	18/40	—	WNL	—

UPSIT = University of Pennsylvania Smell Identification Test; Chemotx = chemotherapy; WNL = within normal limits.