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LETTER TO THE EDITOR

Halitosis as a rare adverse effect of atomoxetine in a child with attention-deficit/hyperactivity disorder

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Dear Editor,

Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder in childhood that often requires pharmacological treatment (1). Atomoxetine, a selective norepinephrine reuptake inhibitor, is widely used as a non-stimulant medication for ADHD, particularly in patients who cannot tolerate stimulants or have contraindications (1, 2). Although atomoxetine's safety profile is generally well established, rare and atypical adverse effects may go unrecognized, especially in pediatric populations (3). This report presents a case of halitosis as a rare adverse effect occurring during atomoxetine treatment in a child with ADHD, highlighting an uncommon but clinically relevant side effect that may affect treatment adherence and quality of life.

A 6-year-old boy was referred to a child psychiatry clinic due to hyperactivity and poor school adjustment. His prenatal, perinatal, and postnatal histories were unremarkable, and his developmental milestones were age appropriate. He had no prior medical or psychiatric diagnoses. During the evaluation, he was constantly moving, had difficulty remaining seated, was easily distracted during structured activities, and demonstrated a tendency to interrupt others or act impulsively. Based on clinical interviews, teacher feedback, and parent and teacher ratings on the Turgay DSM-IV–Based Disruptive Behavior Disorders Rating Scale, he was diagnosed with ADHD according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria.

Pharmacological treatment was initiated with atomoxetine at 0.5 mg/kg/day and gradually titrated up to 1.2 mg/kg/day. Two weeks after reaching the target dose, his parents reported the emergence of persistent halitosis, which had not been present previously and was subsequently confirmed by the clinician during follow-up. The halitosis significantly interfered with the child's functioning, limiting daily social participation, including peer interactions and involvement in classroom activities.

To rule out organic causes, the patient underwent comprehensive dental and pediatric evaluations. The dental examination revealed no pathological findings. Moreover, other potential contributors—including dietary habits, hydration status, and oral hygiene factors—were considered and deemed unlikely. Physical examination and laboratory investigations, including a metabolic panel, were unremarkable. In the absence of an identifiable organic cause and given the clear temporal relationship between atomoxetine initiation and dose escalation, the medication was discontinued. The halitosis resolved within a few days of discontinuation. Given the therapeutic importance of atomoxetine and the need to confirm causality, a cautious re-challenge was performed under close clinical supervision with informed parental consent.

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Upon reinitiation of atomoxetine at the same dose, the halitosis promptly recurred. The medication was then permanently discontinued, and the symptom again resolved completely within days. This re-challenge strongly supports a causal association between atomoxetine and halitosis. Informed consent for publication was obtained from the patient's parents.

Following this clinical observation, a comprehensive literature search was conducted in the PubMed, Scopus, and Google Scholar databases using the keywords "atomoxetine," "halitosis," "oral malodor," "bad breath," "adverse effect," and "side effect," without time restrictions. No previous reports of atomoxetine-induced halitosis were identified in either pediatric or adult populations. To the best of our knowledge, this is the first documented case of atomoxetine-associated halitosis.

The Naranjo Adverse Drug Reaction Probability Scale yielded a score of 8, indicating a probable adverse drug reaction (4). Although halitosis is not listed among the known side effects of atomoxetine, this case suggests that it may represent a rare but clinically significant adverse effect. Because halitosis is not an immediately observable side effect and typically develops gradually after treatment initiation, it may be recognized some time after onset rather than during initial clinical observation. Such delayed recognition is consistent with the clinical course of the symptom and does not weaken the causal inference when temporal consistency is evident. In this case, the clinician directly observed the symptom during follow-up, and its prompt recurrence upon re-challenge further strengthened the causal association. Given the social and functional impact of halitosis in a child, as well as the importance of treatment adherence in long-term ADHD management, clinicians should remain alert to such atypical adverse events. Early recognition may prevent unnecessary investigations, facilitate timely intervention, and support individualized treatment decisions.

Atomoxetine was the first non-stimulant medication approved for the treatment of ADHD and remains an important option for patients who cannot tolerate stimulants, have contraindications, or are at risk of misuse (2). Although atomoxetine is widely used for ADHD and generally well tolerated, awareness of rare side effects such as halitosis is essential to maintain adherence and avoid unnecessary diagnostic procedures. Heightened recognition of atypical but clinically relevant adverse effects may enhance pharmacovigilance and assist clinicians in evaluating new-onset symptoms in children treated with psychotropic medications. Atomoxetine should be considered a potential cause of new-onset halitosis during treatment, particularly when no dental or metabolic abnormalities are identified and the symptom emerges shortly after treatment initiation.

Halitosis has previously been reported as a side effect of various medications. Among psychotropic agents, it has been described with imipramine and duloxetine (5). Both cases were reported in adult patients, and no additional contributing factors were identified. Interestingly, atomoxetine, imipramine, and duloxetine share two notable pharmacological properties. Firstly, they all function as norepinephrine reuptake inhibitors. Noradrenergic stimulation may contribute to halitosis by reducing salivary flow through increased sympathetic tone, altering salivary composition, inducing mucosal vasoconstriction, or affecting gastrointestinal motility. Moreover, xerostomia—a relatively common side effect of atomoxetine—may serve as an intermediary mechanism contributing to halitosis through reduced salivary secretion and oral dryness. However, in the present case, neither subjective complaints nor clinical signs of xerostomia were reported or observed during follow-up, suggesting that halitosis may occur independently of dry mouth. Secondly, all three medications are metabolized via cytochrome P450 2D6 (CYP2D6). In individuals with reduced CYP2D6 metabolic activity, accumulation of the drug or its metabolites may alter salivary composition, impair mucosal hydration, or affect gastrointestinal function—factors known to contribute to oral malodor (6,7). Given that duloxetine and imipramine—sometimes prescribed when ADHD is accompanied by comorbid mood or anxiety disorders—share pharmacodynamic and pharmacokinetic properties with atomoxetine, clinicians should remain alert to the possibility of similar adverse effects, such as halitosis, when prescribing these agents (2, 8).

This case highlights the importance of recognizing atypical adverse effects, such as halitosis, in children treated with atomoxetine for ADHD. Although rare, such reactions may negatively affect social functioning and treatment adherence, underscoring the need for careful pharmacovigilance in pediatric psychopharmacology. Clinicians should remain vigilant for unusual symptoms and consider drug-induced etiologies even in the absence of well-established side effect profiles. Further research is warranted to determine the prevalence and underlying mechanisms of this association.

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