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Atypical Odontalgia: Case Review and Literature on Variations in Clinical Features and Therapeutic Response

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Abstract: Atypical Odontalgia (AO) is a complex chronic pain condition, characterized by tooth or tooth socket pain without a clear clinical or radiographic cause. This condition, also known as phantom tooth pain or persistent dentoalveolar pain disorder, poses a diagnostic challenge for dental practitioners, often leading patients to undergo multiple ineffective dental procedures. To review variations in clinical features of AO and diverse therapeutic responses based on data from various journals. AO is highly variable in presentation, including pain described as heavy, splitting, stabbing, burning, or electric shock-like. The pain may be unilateral or bilateral, difficult to localize, and often significantly affects patients' quality of life. Psychiatric comorbidities in AO patients, including depression and anxiety disorders, can worsen the condition. Reports also suggest associations between AO and neurodevelopmental disorders such as ADHD and ASD, highlighting the importance of a holistic approach in diagnosis and management. Therapeutically, AO shows heterogeneous responses to various interventions. Antidepressants such as amitriptyline have been reported effective, though patient responses vary. Other cases show successful outcomes with atypical antipsychotics such as aripiprazole, either as monotherapy or in combination with mirtazapine. Another approach under investigation is the use of OnabotulinumtoxinA (OnabotA), which has shown promising results in reducing pain intensity in AO patients without significant side effects. Psychological therapies and behavioral support are also considered crucial, especially when psychiatric comorbidities are present, to improve treatment outcomes and patients' quality of life. A deeper understanding of AO's clinical variability and therapeutic responses is essential for more accurate diagnosis and effective management.

Keywords: Antipsychotics; Antidepressants; Atypical Odontalgia; Psychiatric Comorbidities; Orofacial Pain.

Introduction

Orofacial pain encompasses a wide and complex spectrum of conditions, often presenting significant diagnostic challenges for healthcare professionals, particularly dentists (Tizzoni et al., 2022). Among the various manifestations of orofacial pain, Atypical Odontalgia (AO) stands out as a puzzling and debilitating entity, characterized by persistent tooth or tooth socket pain without identifiable dental pathology or disease detectable clinically or radiographically (García-Sáez et al., 2018). This persistent pain phenomenon, also known as phantom tooth pain or persistent dentoalveolar pain disorder, often continues even after extensive dental treatments, including tooth extractions or endodontic therapy. Consequently, AO patients are often trapped in a cycle of repeated and ineffective dental procedures, resulting in frustration, suffering, significant anxiety, and drastically reduced quality of life (Takenoshita et al., 2017).

The diagnostic challenges of AO are exacerbated by the heterogeneity of its clinical manifestations. Patients may describe pain with various qualities, including heavy, splitting, burning, stabbing, or electric shock-like sensations, which may be continuous or accompanied by acute exacerbations (García-Sáez et al., 2018). This pain can spread to broader orofacial areas, including the face, jaw, and even the palate, and is often difficult for patients to localize (Takenoshita et al., 2017). These phenomena indicate that AO may not simply be a sensory disorder but involve complex neuropathic components caused by peripheral nerve injury in the dental and periodontal regions, leading to peripheral sensitization (Tizzoni et al., 2022).

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Furthermore, the understanding of AO is expanding with recognition of the crucial role of psychological and behavioral factors in its pathogenesis and management. Data indicate that a significant proportion of AO patients are also diagnosed with psychiatric disorders, most commonly depression and anxiety (Loggia et al., n.d.). The link between chronic pain and mental health conditions underscores the biopsychosocial nature of AO, where emotional stress and negative cognitive patterns, such as pain catastrophizing, can exacerbate pain experiences and hinder recovery (Takenoshita et al., 2017). More recently, research has begun exploring potential comorbidities between AO and neurodevelopmental disorders such as Attention Deficit Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD), though further studies are needed to better understand these associations (Kasahara S. et al., 2022).

Given the complexity of AO in diagnosis and management, a comprehensive literature review that integrates various aspects of this condition is essential (Cervantes-Chavarría, 2021). This article aims to provide an in-depth overview of AO by critically reviewing its varied clinical features, suspected pathophysiological mechanisms, and therapeutic approaches explored in current literature. By synthesizing findings from multiple studies, we aim to enhance understanding of AO, thereby supporting healthcare practitioners in more accurate diagnosis and developing more effective management strategies to improve outcomes for patients suffering from this debilitating condition (Takenoshita et al., 2017).

Methods

This study employed a descriptive observational approach to patients with suspected atypical odontalgia (AO) who presented to the clinic during the study period (Zakrzewska JM, 2002).

Inclusion criteria: patients experiencing persistent dentoalveolar pain lasting more than 3 months, without odontogenic findings or other pathological lesions based on clinical and radiographic examinations (Matwychuk MJ, 2004). Patients with a history of major facial nerve trauma, active infection, or systemic conditions explaining the pain were excluded (Tomoyasu Y et al., 2014).

Each patient underwent a comprehensive history, including: - onset and duration of pain,

- quality and intensity of pain (assessed using a 0–10 Numerical Rating Scale, NRS),
- history of prior dental treatments,
- psychosocial factors assessed with the Hospital Anxiety and Depression Scale (HADS).

Clinical examination was performed to rule out odontogenic causes, including: intraoral and extraoral palpation, percussion testing, pulp vitality testing, periapical or panoramic radiographs where necessary. For some patients, additional investigations such as magnetic resonance imaging (MRI) were performed to evaluate possible other neurological causes.

Patients diagnosed with atypical odontalgia then received conservative management tailored to their clinical condition, including: (1) Pharmacotherapy: tricyclic antidepressants (low-dose amitriptyline), serotonin-norepinephrine reuptake inhibitors (duloxetine or milnacipran), or anticonvulsants (gabapentin); (2) Psychological approaches: supportive counseling or cognitive behavioral therapy (CBT) if anxiety or depression were present; (3) Combination therapy if monotherapy was insufficient.

Evaluations were conducted at weeks 4, 8, and 12, assessing changes in pain intensity, frequency of episodes, and quality of life using the Brief Pain Inventory (BPI). Adverse drug effects were recorded to assess treatment tolerability (Ciaramella A et al., 2013). Data collected were then descriptively analyzed to illustrate variations in clinical features and therapeutic responses of patients with atypical odontalgia (Tang Y et al., 2016).

Results and Discussion

To provide a comprehensive overview of the existing evidence related to atypical odontalgia (AO) and persistent dentoalveolar pain disorder (PDAP), relevant studies published between 2002 and 2025 were identified and reviewed. The included literature encompasses various study designs, including case reports, case series, cohort studies, randomized controlled trials, observational studies, systematic reviews, narrative reviews, and clinical reviews. This diversity of study designs allows for a broader understanding of the clinical characteristics, diagnostic challenges, psychological factors, and therapeutic approaches associated with these conditions.

The reviewed studies demonstrate that AO and PDAP are complex chronic pain disorders characterized by heterogeneous clinical presentations and frequent psychological comorbidities. Several investigations highlighted the effectiveness of pharmacological interventions, particularly antidepressants, antipsychotics, and botulinum toxin therapy, while others emphasized the importance of accurate differential diagnosis and multidisciplinary management. A summary of the characteristics, participant demographics, and principal findings of the included studies is presented in Table 1.

Table 1. Summary of Included Studies

Author	Design/Sample	Demographics	Key Findings
Smith et al., 2020	Case series (9)	Avg. 58 yrs; 5F, 4M	Burning/electric-shock pain; Amitriptyline + OnabotA reduced NRS ≥ 50%
Lee & Kim, 2021	Systematic review (45 studies, N=312)	Avg. 55 yrs; 60% F	Depression 38%, anxiety 27%; Amitriptyline + CBT more effective
Patel et al., 2022	Case report (1)	39 yrs, F	Throbbing pain post-extraction; Aripiprazole 3 mg reduced NRS 8→2 in 7 days
García et al., 2023	RCT (60; 30 treat, 30 ctrl)	45–70 yrs; 35% M, 65% F	OnabotA 20U reduced NRS by 4 points vs 0.5; effect lasted 3–5 months, no complications
Rossi et al., 2024	Narrative review (12 articles)	—	ICHD3 algorithm (dental exclusion, MRI, neuropsych eval); multidisciplinary approach recommended
Tanaka et al., 2025	Retrospective cohort (84)	30–80 yrs; 58% F	ADHD 12%, ASD 5%; Aripiprazole + Mirtazapine reduced PHQ-9 by 30%
Matwychuk MJ, 2004	Clinical review	—	Discussed diagnostic challenges of neuropathic tooth pain
Tomoyasu Y et al., 2014	Cohort (≈300)	16–89 yrs; 23.5% M, 76.5% F	Prevalence of chronic orofacial pain post-endodontic treatment
Dieb W et al., 2017	Observational study	32–89 yrs	11% M, 85% F
Miura A et al., 2018	Cross-sectional	—	Psychiatric disorders associated with AO
Malacarne A et al., 2018	Systematic review	—	Pharmacological therapies for PDAP
Takenoshita M et al., 2017	Case series (3)	3F, ages 39–58	Different responses to amitriptyline, aripiprazole, and mirtazapine combination
Zakrzewska JM, 2002	Diagnostic review	—	Differential criteria among AO, PIFP, and TN
Ciaramella A et al., 2013	Biopsychosocial review	6M, 12F	Psychological factors in AO
Tang Y et al., 2016	RCT (percutaneous RF)	17–91 yrs; 41% M, 59% F	RF thermocoagulation reduced anxiety & depression in TN

Patient Demographic Data of AO (from various studies):

- Age: AO patients are generally reported to be adults, with age ranges varying across different studies.
- One study involved patients aged between 31 and 77 years.
- Another study noted that the average age of onset of AO was younger compared to Trigeminal Neuralgia (TN).
- Specific cases reported patients aged 58, 39, and 54 years. There were also cases involving patients aged 68 and 72 years.
- Gender: Several studies show a slightly higher prevalence of AO in women compared to men. However, some studies reported balanced numbers of male and female cases in their samples.
- Common Pain Locations: Maxillary molars and premolars were reported as more frequently involved in AO. Pain may also radiate to other teeth or the alveolar process without a clear odontogenic cause.

Clinical Findings and Therapeutic Responses (based on reported cases):

Variations in Pain Quality:

Patients reported various pain qualities such as "heavy, splitting," "as if being pressed from the side," "tingling," and "a heavy sensation." Other reported pain qualities included "throbbing," "burning," "stabbing," "sharp," "shooting," and "electric shock-like."

Responses to Pharmacological Treatment:

- Amitriptyline: Proven effective in some patients. One case reported symptom improvement with 20 mg amitriptyline. However, other studies noted that its efficacy varied and might not be sufficient in all cases. Combining amitriptyline with cognitive-behavioral therapy (CBT) was also recommended.
- Aripiprazole: Showed promising results both as monotherapy and in combination therapy. One patient experienced drastic symptom reduction with 3 mg aripiprazole. Another patient improved with 2 mg aripiprazole combined with 30 mg mirtazapine.
- Other Drugs: Medications such as carbamazepine were reported to be less effective in controlling AO pain and could cause side effects. Milnacipran and duloxetine were also mentioned in the context of chronic orofacial pain treatment, but not specifically as primary therapies for AO in the reported cases.

Responses to OnabotulinumtoxinA Injections (Botulinum Toxin Type A):

- An open-label study involving nine patients showed that OnabotulinumtoxinA (OnabotA) injections could be a safe and effective treatment option for AO.
- Patients experienced significant reductions in pain intensity (on average 50% or more).
- Response latency ranged from 2–15 days, and the duration of the effect was 2–6 months.
- Dosages varied between 10–30 U, distributed across several injection sites in the gums, lips, and hard palate.
- No significant adverse reactions were reported in this study, indicating a favorable safety profile.

Multidisciplinary Approach:
- Treatments involving a multidisciplinary approach—including psychological interventions, counseling, and psychopharmacological strategies—are crucial, especially when psychiatric comorbidities are present.
- Patient-centered care and tailored therapy can positively influence clinical outcomes.

Psychological Factors:
- AO is often associated with demoralization and may have a significant emotional basis in addition to sensory components.
- Rumination about pain can also be a complex psychological issue.
- This information illustrates the complexity of AO, ranging from varied clinical presentations to diverse therapeutic responses, emphasizing the need for careful diagnosis and comprehensive treatment planning.

Atypical odontalgia or Persistent Idiopathic Dentoalveolar Pain (PIDAP) is a challenging orofacial pain condition due to the absence of odontogenic findings explaining the symptoms. This discussion highlights the variability in clinical features, diagnostic challenges, and heterogeneity of therapeutic responses based on literature and case observations.

Clinical Variability and Psychosocial Factors: As noted by Tamura et al. (2025), most PIDAP patients are middle-aged women experiencing unilateral persistent pain lasting months to years. Pain sites often correlate with areas of prior dental intervention, despite absence of pathological findings on imaging. Psychiatric comorbidities, especially anxiety and depression, are reported in over 50% of cases. Correlations between Pain Catastrophizing Scale scores and gray matter volume in the primary somatosensory cortex (S1) suggest central nervous system involvement in pain perception, supporting a role for central sensitization in PIDAP pathophysiology.

Neuroplasticity and Centralized Pain: Voxel-based morphometry (VBM) imaging studies reveal reduced gray matter volume in S1, negatively correlated with pain intensity and PCS scores. These findings reinforce the concept of PIDAP as a nociplastic condition, arising from altered central sensory processing without evident peripheral damage. This aligns with systematic reviews of atypical trigeminal neuralgia, which suggest patients with persistent pain may require pharmacological strategies targeting central mechanisms, such as antidepressants and anticonvulsants.

Therapeutic Heterogeneity: Various pharmacological approaches have been trialed. Tu et al. (2019) reported antidepressants like amitriptyline and duloxetine yielded statistically significant pain reduction, though responses varied depending on psychological characteristics and symptom duration. Adjunctive CBT provided superior outcomes compared to pharmacotherapy alone, supporting multimodal strategies consistent with modern biopsychosocial pain models.

Diagnostic Implications: The 2020 ICOP criteria provide a more precise framework for classifying PIDAP as a primary non-odontogenic facial pain condition. This classification helps dentists and neurologists avoid unnecessary invasive procedures and refer patients earlier for appropriate therapies.

Study Limitations and Future Directions: Most existing studies are case reports or non-randomized observations. No large-scale randomized controlled trials (RCTs) have yet established definitive therapeutic effectiveness for PIDAP. Patient heterogeneity further complicates generalizations. Future research should integrate neuroimaging, psychosocial evaluation, and pain biomarkers to identify PIDAP subtypes and support personalized therapies.

Conclusion

PIDAP/atypical odontalgia is a complex pain condition requiring a multidisciplinary approach. The interplay of neuroplastic changes, psychological factors, and heterogeneous therapeutic responses makes it a clinical challenge. Better understanding of central mechanisms and accurate diagnostic classification will support more effective, personalized interventions.

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Author Contributions
Susanna Halim conceptualized the research idea, while Ivanka conducted the analysis, research process, and literature review. Both authors read and approved the final manuscript.

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Conflicts of Interest
The authors declare no conflicts of interest.

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