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Oral Surgical Considerations and Management of Patients with VEXAS Syndrome: A Narrative Review

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ABSTRACT

VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome is a rare, late-onset, X-linked, somatic disorder characterized by various systemic manifestations, including pancytopenia, airway chondritis, and altered bone marrow, among others. The oral surgical management of patients with VEXAS syndrome is an unexplored component of the comprehensive health plan for these patients. This narrative review aims to provide an overview of VEXAS syndrome, its symptoms, and implications for oral surgery and management.

Embase and OVID Medline were searched using terms including, but not limited to, "VEXAS syndrome, pathogenesis, oral surgery, dental, management, and oral health," for articles published in English, with no restrictions on date.

Extrapolation of potential risks, based on similar conditions, suggests that patients with VEXAS syndrome may be at an increased risk of bleeding, cardiovascular events, infections, and airway complications during oral surgical procedures. Similarly, extrapolating these findings to oral conditions, patients could have increased risk of temporomandibular disorders and periodontitis due to physiological disease processes, and higher risk of xerostomia and thereby caries, due to adverse effects of drugs used in the treatment of VEXAS syndrome.

When performing oral surgery on these patients, depending on their presentation and their individualized risk, it may warrant consideration of supplementary hemostatic measures, antibiotic or antifungal agents when appropriate, extra precautions during sedation, and taking breaks to relax the jaw during appointments. Extra preventive measures, like frequent scaling visits, fluoride application, and saliva substitutes, may be beneficial.

Given the complex systemic manifestations affecting patients with VEXAS syndrome, it is advised that oral surgical care is provided in the context of a multidisciplinary approach, in close communication with the patient's medical team and other relevant specialists. Oral surgeons ought to be aware of VEXAS syndrome, its oral and systemic manifestations, and oral surgical management considerations. Further research is required on the pathophysiology of this syndrome, its oral manifestations, and optimal surgical treatment modalities.

Keywords: VEXAS syndrome, Oral surgery, Oral manifestation, Oral and maxillofacial surgery, Perioperative management, Immunocompromised patients.

1. Introduction

VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome was first reported in December 2020. Its prevalence is estimated to be 1 in 14,000 individuals, with a higher prevalence in males (1). The prevalence rate in males older than 50 years is 1 in 4000, compared to 1 in 26,000 for females (1). VEXAS syndrome is named after its pathophysiological characteristics, which include vacuoles present in myeloid and erythroid progenitor cells in bone marrow aspirates. E1 enzyme refers to the ubiquitin-activating enzyme encoded by the X-linked gene UBA1. UBA1 mutations are restricted to myeloid cell lineages, and result in autoinflammatory processes, while somatic mutations are responsible for the late onset of this syndrome (1). See Figure 1 for an illustrated depiction of the pathogenesis of VEXAS syndrome.

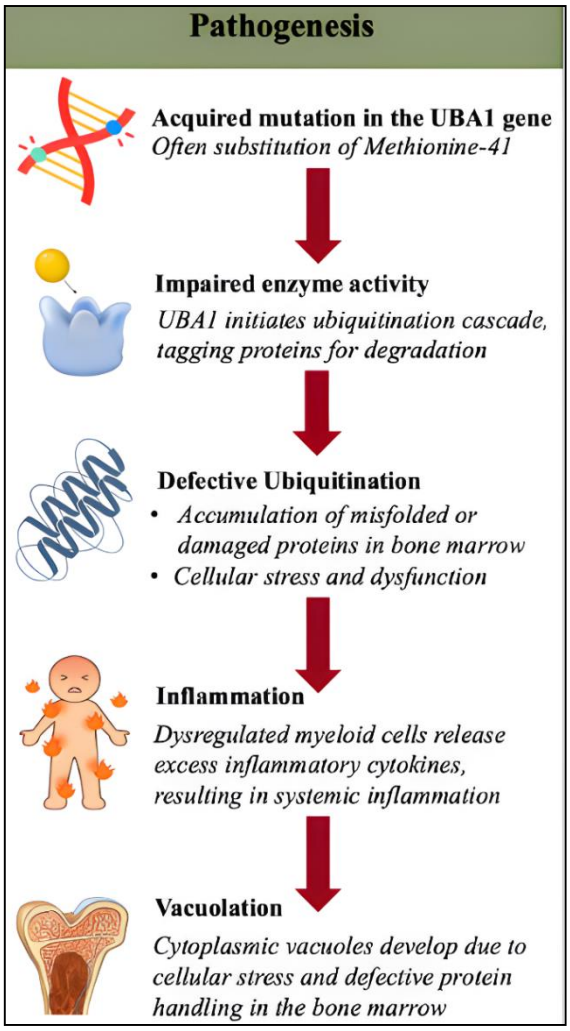


Figure 1: Overview of the molecular pathogenesis of VEXAS syndrome

The extensive influences of the syndrome's unique pathophysiology result in a variety of clinical manifestations, which include skin lesions, fever, weight loss, and blood abnormalities (1). While the systemic effects of VEXAS have been well-documented, its impact on oral health and surgical management is a largely unexplored area of interest. Patients with VEXAS may experience unique challenges related to oral surgery with the burden of oral disease having a significant impact on their quality of life. To our knowledge, this is the first work assessing the oral surgical management of these patients and exploring best practices for their surgical care.

The management of patients with VEXAS syndrome

requires a comprehensive and collaborative approach involving physicians, oral surgeons, and other healthcare professionals. Early recognition of oral manifestations, individualized surgical care strategies, and a thorough assessment of potential drug adverse effects and interactions are critical elements for optimizing care for individuals with VEXAS syndrome.

This narrative review aims to provide an overview of VEXAS syndrome, its symptoms, and implications for oral surgical management. By synthesizing existing literature and analyzing clinical considerations relating to similar syndromes, this paper seeks to enhance understanding and optimize surgical care and oral health outcomes for patients with VEXAS syndrome.

2. Search Strategy

A literature search was conducted using Ovid MEDLINE and Embase from database inception to January 31st, 2026, with no restrictions on publication date. Searches were limited to articles published in English. Search terms included, "VEXAS," "VEXAS syndrome," "vacuoles E1 enzyme X-linked autoinflammatory somatic," "UBA1," "oral," "oral health," "dentistry," "dental," "dental management," "oral surgery," "oral surgical procedures," "maxillofacial surgery," "dentoalveolar surgery," "extraction," "pathogenesis," "periodontitis," "periodontal disease," "gingivitis," "temporomandibular disorder," "TMD," "TMJ," "xerostomia," "dry mouth," "dental caries," "oral infection," "oral candidiasis," "wound healing," "bleeding," "hemorrhage," "hemostasis," "thrombocytopenia," "pancytopenia," "infection," "immunosuppression," "airway," "chondritis," "sedation," "anesthesia," "anaesthesia," "perioperative complications," and "postoperative complications."

Eligible publications included original research studies, observational studies, case reports, case series, systematic reviews, narrative reviews, clinical guidelines, and expert consensus or guidance relevant to the pathogenesis, clinical manifestations, oral manifestations, or dental and oral surgical management of VEXAS syndrome. Articles were excluded if they were not published in English or did not provide information relevant to the objectives of the review. Reference lists of relevant publications were also screened to identify additional articles.

3. Systemic Manifestations

3.1 Constitutional Symptoms

The widespread inflammatory nature of VEXAS syndrome results in a constellation of symptoms. Non-infectious and recurrent fever was reported in 74% of VEXAS patients as one of the most common presentations as well as weight loss which was reported in 62% of patients (1,2). Lymphadenopathy, most notably in the hilar and mediastinal regions, was present in 35% of patients (3).

Other constitutional symptoms include poor appetite, fatigue, and elevation of acute-phase reactants, such as C-Reactive Protein (CRP), which can be caused either primarily by the syndrome or secondarily after initiating immunosuppressive treatment (2).

3.2 Dermatological Manifestations

Cutaneous manifestations are among the most frequently reported features of VEXAS syndrome, occurring in up to 88% of patients and with a diverse array of symptoms (2) Presentations include neutrophilic dermatoses, erythema nodosum, erythematous papules, sweet's syndrome-like nodules, urticaria, periorbital edema, pressure plaques, injection site reactions, and leukocytoclastic vasculitis (2,3).

When presenting with VEXAS, some of these skin manifestations, such as neutrophilic dermatoses, have histologically shown mature neutrophils, myeloid, and lymphoid cells through skin biopsy, which carry the UBA1 mutation responsible for VEXAS (1) However, other skin conditions, such as leukocytoclastic vasculitis, when paired with VEXAS, do not show the UBA1 mutation, suggesting that some skin manifestations are clonal, or directly tied to the UBA1 mutation, while others are paraclonal (1).

3.3 Musculoskeletal/Rheumatological Manifestations

Arthralgia and myalgia were reported in 27%-58% of VEXAS patients (1). VEXAS syndrome also results in symptoms mimicking rheumatoid arthritis, seronegative spondyloarthropathies, small and medium vessel vasculitides, Sweet's syndrome, and Behçet's disease (3). More than a half of patients had already met the diagnostic criteria for relapsing polychondritis before receiving a confirmed diagnosis of VEXAS syndrome, reflecting the significant overlap in clinical features, including chronic cartilage inflammation and systemic involvement (2).

3.4 Pulmonary Manifestations

Pulmonary involvement is a frequent feature of VEXAS syndrome, affecting approximately a half of all patients. The most common manifestations include pulmonary infiltrates and pleural effusion. Other respiratory complications can include pulmonary fibrosis, neutrophilic inflammation of the alveoli (neutrophilic alveolitis), pneumonia, bronchiolitis obliterans, and vasculitis (2,3).

3.5 Hematological Manifestations

Cytopenias are very common in VEXAS patients, with presentations including macrocytic anaemia (100%), lymphopenia (80%), thrombocytopenia (50%) and monocytopenia (50%) (1). See Table 1 for detailed prevalences of hematologic abnormalities. Moreover, myelodysplastic syndrome (MDS) has been reported in 50% of VEXAS patients (2). A study concerning this issue found that pancytopenia and myelodysplasia in VEXAS syndrome are closely tied to severe systemic inflammation, as these conditions tend to worsen during flare-ups, but improve once the inflammation subsides (2). Furthermore, some patients with VEXAS have been found to carry mutations in the DNMT3A gene, which may contribute to the development of hematologic malignancies, such as myelodysplastic syndrome (MDS), commonly seen in this condition (2).

Table 1: Prevalence of hematologic abnormalities in VEXAS patients

Abnormality	Estimated Prevalence (%)
Macrocytic Anemia	100
Lymphopenia	80
Monocytopenia	50
Neutropenia	12.5
Thrombocytopenia	50
Myelodysplastic syndrome	45

3.6 Other Rare Systemic Manifestations

Less common manifestations include eye-related inflammation in 40.5% of patients, such as swelling around the eyes (periorbital edema), uveitis, and scleritis (2,3). In addition, gastrointestinal symptoms may involve abdominal pain, persistent diarrhea, or gastrointestinal bleeding in 14% of patients (2,3). Cardiovascular manifestations are present in 11% of patients and include pericarditis, myocarditis, and heart, arterial, or venous involvement, including venous thromboembolism, which has been reported in around 50% of patients (2,3). Kidney and urogenital involvement have also been reported in 9.5% of patients, presenting as proteinuria, hematuria, progressive renal disease, epididymitis, orchitis, and prostatitis (3). Neurological symptoms are extremely rare, but can include hearing loss, headache, sensory nerve damage, stroke, meningitis, and episodic flare-ups of chronic inflammatory demyelinating polyneuropathy (CIDP) (2,3). See Figure 2 for an illustrated depiction of the systemic and hematologic manifestations of VEXAS syndrome.

4. Oral Manifestations

The available literature on VEXAS syndrome has focused predominantly on its systemic manifestations and medical management, with limited description of oral and dental manifestations. Consequently, many of the potential oral manifestations and management considerations discussed in this review are extrapolated from the known systemic features of VEXAS syndrome, the adverse effects of therapies used in its management, and evidence from patients with comparable medical conditions or risk factors. Where direct evidence in patients with VEXAS syndrome is unavailable, these considerations should therefore be interpreted as biologically or clinically plausible rather than as established VEXAS-specific associations.

Dysregulation of inflammatory pathways caused by UBA1 mutations leads to systemic production of pro-inflammatory cytokines (2). In other disorders, these have been linked to the pathogenesis of gingivitis and periodontitis, increasing the risk of gingival bleeding, clinical attachment and alveolar bone loss, tooth mobility and potential tooth loss, although they have not been found to be directly associated with VEXAS syndrome (2,4).

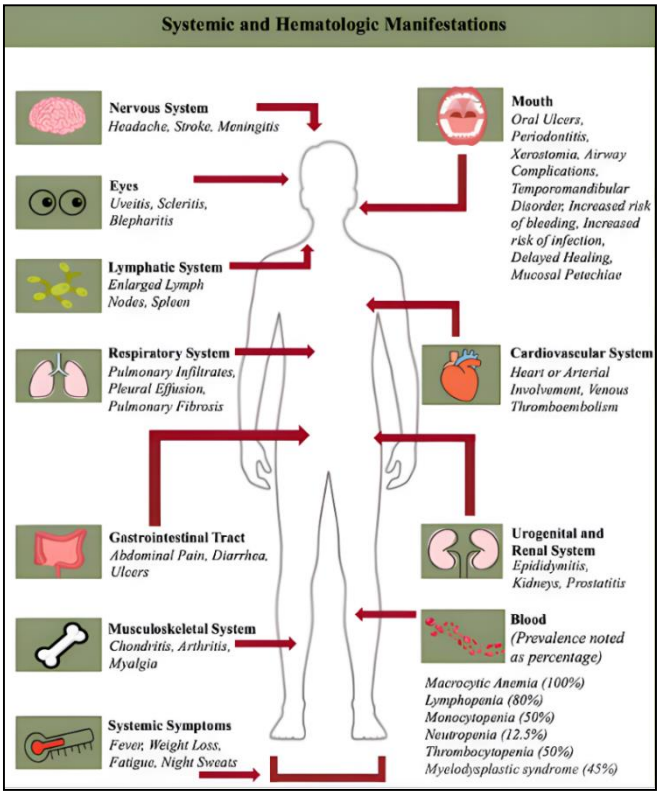


Figure 2: Multisystem and hematologic signs and symptoms of VEXAS syndrome

VEXAS-related thrombocytopenia can theoretically result in gingival bleeding and mucosal petechiae (1,5,6). In addition, the high prevalence of macrocytosis caused by VEXAS may potentially contribute to glossitis (7). Aphthous ulcers have also been attributed to VEXAS, albeit with lesser frequency compared to other manifestations (8). However, Sweet's syndrome, a common inflammatory phenotype observed in patients with VEXAS, promotes oral mucosal lesions (1).

Pain resulting from potential gingival inflammation or ulcerations could hinder proper toothbrushing, and compromise oral hygiene, elevating the risk of dental caries. Moreover, lymphopenia in patients with VEXAS syndrome may theoretically contribute to a higher caries risk. Neutrophils contain human neutrophil peptides 1-3, which are typically present in gingival crevicular fluid and help non-oxidatively combat microbial infections (9,10). When these peptides are absent, cariogenic bacteria may thrive, potentially increasing the risk of caries in VEXAS patients (9,10). Nevertheless, this connection is deemed plausible and not yet well-established, requiring additional research.

Many medications, such as antiemetics, gastric acid secretion inhibitors, and decongestants, used in the treatment of VEXAS syndrome have adverse effects, like xerostomia (11). Medication induced xerostomia has been found in other populations to increase the risk for various oral conditions, including caries, candidiasis, halitosis, burning mouth, dysgeusia, dysphagia, difficulty chewing and speaking (11). These symptoms together could theoretically act as risk factors for malnutrition, social isolation, care dependency, and frailty, having a significant effect on the overall well-being of VEXAS patients (11).

Another symptom of VEXAS is arthritis, which may have implications for potential temporomandibular joint disorder (TMD) involvement (12). Moreover, long-term use of corticosteroids in treating VEXAS syndrome may result in skeletal abnormalities within the jaw, which could also plausibly have conceivable effects on TMD (1) TMD has been found to have a significant impact on oral health-related quality of life (12). Although, TMD has not been directly associated with cases of VEXAS syndrome, it is biologically plausible that VEXAS patients could be at higher risk of TMD and further screening, and further research may be warranted (12).

The management of VEXAS syndrome often

involves immunosuppressive medications, which pose significant considerations for any surgery. These agents can theoretically impair postoperative wound healing and increase the risk of complications, such as infection (13). The use of biological therapies, which are also employed in managing the condition, may exacerbate immune suppression, and can be extrapolated to potentially further elevate risk of postoperative complications, like fungal infections (1,13).

Though there is no empirical data assessing the prevalence of dental or oral pathology in patients with VEXAS syndrome, in part due to its rarity and novelty, the systemic effects of the syndrome and medications used to treat it are likely to influence the oral cavity. This review outlines the plausible mechanisms and pathophysiologic processes extrapolated to be involved in the development of oral health conditions for patients with VEXAS syndrome.

5. Oral Surgical Management

The systemic nature of VEXAS syndrome may present unique challenges for oral surgical management, highlighting the benefit of a multidisciplinary approach and close communication with the patient's medical team. Although direct evidence regarding oral surgical management of VEXAS patients is limited, its hematological, immunological, and structural manifestations warrant careful consideration when planning and providing surgical treatment.

5.1 Surgical Considerations

The complex hematological profile of VEXAS patients requires prudent pre-surgical assessment and preparation. A platelet count is recommended prior to any surgical procedure to assess primary hemostasis; a complete blood count (CBC) is recommended to evaluate immunocompromised status; international normalized ratio (INR) and liver function tests are recommended to monitor secondary hemostasis and assess potential bleeding risks.

Extra-precautionary measures, such as supplementary hemostatic agents, may be necessary. Treatment in a hospital setting, with an oral and maxillofacial surgeon, or with replacement factors could be considered for high-risk patients. Postoperative care could include precautionary measures, like giving written and verbal postoperative instructions, extra gauze to control any further bleeding, a phone number which can be reached after working hours, like the surgeon's cell phone number, and regular follow-up visits to monitor healing progress.

5.2 Airway and Skeletal Abnormalities

Relapsing polychondritis, a manifestation of VEXAS, could theoretically cause airway compromise during surgical procedures (1-3). Oral surgeons must be vigilant for signs of breathing difficulty and take appropriate precautions during sedation.

Bone abnormalities, including osteolytic lesions, may be present in VEXAS patients (1-3). These lesions should be carefully evaluated with consideration given to cone beam computed tomography (CBCT) scans, and potential biopsy to avoid mistaking them for odontogenic pathology. If the patient presents with TMD or jaw discomfort, then frequent breaks during procedures could be implemented to minimize pain. Orthodontic consultation may be beneficial to assess and address skeletal abnormalities affecting occlusion and jaw alignment.

6. Management of Oral Lesions

VEXAS patients may experience major aphthous ulcers, which can be managed with short-term topical corticosteroids to reduce inflammation and topical analgesics for pain relief. Minor ulcers can be observed for a two-week period before intervention. Given the potentially heightened risk for fungal infections associated with VEXAS, topical antifungal treatments should be promptly initiated when needed (1-3).

7. Pain Management

Pain management in VEXAS patients requires careful consideration of the syndrome's complications. Avoiding opioids may be prudent when pleural inflammation is present, due to the theoretical risk of respiratory depression (1,2).

Depending on the patient’s bloodwork, non-steroidal anti-inflammatory drugs (NSAIDs) may be used, with consideration for potential increased bleeding risks and gastrointestinal upset. Acetaminophen remains the preferred choice for pain management due to its minimal bleeding risk. Liver function may be monitored during long-term acetaminophen use as a precaution against excessive NAPQI metabolism.

8. Medication Considerations and Perioperative Steroid Management

The long-term use of immunosuppressive and biologic

therapies in VEXAS patients can pose challenges for surgical management. These medications are associated with impaired wound healing and elevated risk of infection, thus consideration of the use of prophylactic antibiotics should be given when appropriate (1,2).

Corticosteroid use, common in VEXAS patients, increases the risk of secondary adrenal insufficiency (AI). For oral surgeries, corticosteroid supplementation may be beneficial through intravenous, oral, or intramuscular routes. Communication with the patient's medical team is critical to ensure overall safety.

9. Preventive Measures

Patients with VEXAS syndrome may be at elevated risk of oral disease, emphasizing the need for early and ongoing preventive measures. Routine recall visits, sealant applications, professional fluoride treatments, and comprehensive oral hygiene education should be prioritized. If xerostomia is reported or observed, saliva-stimulating or substitute measures, such as xylitol-containing gum or candies, can be recommended. Patients should be informed that excessive xylitol consumption may cause gastrointestinal discomfort (9).

Given the theoretically increased risk of periodontal disease, patients with VEXAS syndrome may benefit from more frequent periodontal maintenance and monitoring, including scaling and root planing when indicated, with adjunctive measures, such as chlorhexidine mouth rinse and antibiotic therapy considered on an individualized basis when clinically appropriate. Because many patients with VEXAS syndrome receive immunosuppressive therapy or have hematologic abnormalities, the need for perioperative antibiotic prophylaxis should be determined on an individual basis after considering the patient's immune status, current medications, neutrophil count, planned procedure, and consultation with the treating physician when appropriate (9).

10. Interdisciplinary Care and Monitoring

Given the complexity of VEXAS syndrome, effective oral surgical care may require interdisciplinary collaboration. Communication with periodontists, otolaryngologists, hematologists, and other specialists should be considered to provide comprehensive care. Regular monitoring for potential complications, including the long-term impacts of medications and signs of hematological or immune dysfunction, should be a standard part of surgical management.

11. Knowledge Gaps and Future Directions

Despite the growing recognition of VEXAS syndrome, evidence regarding its oral manifestations and optimal oral surgical management remains extremely limited. To date, there are no prospective studies evaluating the prevalence of oral disease, post-operative complications, wound healing outcomes, or long-term oral health-related quality of life in this patient population. Consequently, many of the recommendations presented in this review are extrapolated from the management of patients with comparable hematologic, rheumatologic, and immunosuppressive conditions. Future research should focus on multicentre registries, prospective observational studies, and detailed case series to better characterize the oral phenotype of VEXAS syndrome, validate perioperative management strategies, and establish evidence-based clinical guidelines for dental and oral surgical care.

12. Conclusions

VEXAS syndrome is a recently identified disorder with systemic and medication-related effects likely to lead to a disproportionately higher prevalence and severity of oral diseases, significantly impacting quality of life. This paper provides an initial framework for considerations in the oral surgical management of individuals with VEXAS by outlining the syndrome's characteristics, its plausible oral manifestations, and strategies for prevention and treatment, based on similar conditions. Given the complex medical considerations associated with VEXAS, a multidisciplinary approach involving close collaboration between oral surgeons and medical specialists can minimize morbidity and optimize long-term oral health outcomes. By implementing a tailored and proactive approach, oral surgeons can play a critical role in improving both the oral and overall health of affected individuals. As awareness of VEXAS syndrome continues to increase, oral surgeons will play an increasingly important role in the multidisciplinary care of these medically complex patients. Until disease-specific evidence becomes available, individualized treatment planning, careful medical collaboration, and meticulous perioperative management remain essential to optimizing patient outcomes.

Conflict of Interest

None.

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