ORAL MANIFESTATIONS IN PRIMARY PEDIATRIC VASCULITIS

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ABSTRACT

Vasculitis are disorders characterized by the presence of an inflammatory process in the blood vessel wall, resulting in damage or necroses of certain tissues or organs. Numerous clinical symptoms, ranging from acute localized hypersensitivity reactions to severe auto-immune systemic disorders that are incurable and life-threatening, can be attributed to the types and locations of affected arteries as well as the level of inflammation. Typical oral or facial symptoms of several forms of vasculitis can help in an early diagnosis of vasculitis. IgA vasculitis and Kawasaki disease (KD) are the two predominant types of pediatric vasculitis that involve the mouth, followed by ANCA vasculitis. Furthermore, SLE, a connective tissue disease, is one of the most prevalent autoimmune illnesses in children and can proceed rapidly across multiple organs or start mildly and gradually. Numerous more systemic conditions, such as infection, autoinflammatory disorders and neoplasia, can also primary or secondary localize in the oral cavity, infections being more frequent. Many various professionals, including dentists, family physicians, pediatricians, rheumatologists, hematologists, gastroenterologists, and otorhinolaryngologists, examine and treat children with oral symptoms. In 87.7% of patients overall and over 90% of patients with KD and IgA vasculitis (formerly known as Henoch-Schönlein purpura), cutaneous involvement was observed. Recurrent oral aphthous ulcers were present in all Behçet syndrome patients (1).

Key words: pediatric vasculitis, oral symptoms, autoimmune illness

INTRODUCTION

Blood vessel inflammation, which can result in tissue damage with vascular stenosis, blockage, aneurysm, and/or rupture, is a hallmark of systemic vasculitis. The degree of inflammation is correlated with subsequent damage to the vessel wall and changes the vascular hemodynamics. Either an underlying disease or a primary process may be the cause of the inflammation. Fibrinoid necrosis in the blood vessel walls is the primary histological feature in vasculitis. The size and type of the affected blood vessels, the clinical signs, and the pathologic modification discovered within the vessel walls are used to categorize primary vasculitis (2).

SLE is another significant entity. It is an autoimmune illness in which the body attacks its own tissues, leading to tissue destruction and extensive inflammation in the organs that are impacted. Although oral mucosal lesions are common in the pediatric population and typically benign, the incidence of these lesions in children of all ages is unknown (3).

The parents may happen to notice them when they go for a dental or medical exam. Additionally, children with oral lesions also present fever, discomfort,

refusal of alimentation, or malaise that calls for an urgent visit to the emergency room.

The American Academy of Pediatric Dentistry (AAPD) states that children and adolescents with special needs and complex medical problems may have a lifelong increased risk of dental disorders. As a result, maintaining oral health in these people calls for specialized knowledge, increased awareness, and adaption strategies. In particular, vascular and renal disorders are among childhood diseases that are associated with specific clinical and functional manifestations in oral hard and soft tissues (4).

IgA VASCULITIS AND ORAL MANIFESTATIONS

IgA vasculitis (IgAV), also known as Henoch-Schönlein purpura (HSP), is an immune-mediated vasculitis linked to IgA deposition, and is the most frequent type of vasculitis in children.

The EULAR/PRINTO/PRES criteria for IgAV (HSP) require the presence of one or more of the following: purpura (commonly palpable and in crops) with lower limb predominance and petechiae (without thrombocytopenia), diffuse abdominal pain, arthritis or arthralgia, leukocytoclastic vasculitis or proliferative glomerulonephritis with predominant IgA deposition, kidney involvement: hematuria, red blood cell casts, or proteinuria (5).

The general course of treatment for IgAV is determined by its severity and organ involvement. For example, if there is no renal involvement, treatment is limited to symptomatic measures, but in cases of glomerulonephritis, corticosteroids or other immunosuppressive medications are recommended. IgA vasculitis's cutaneous symptoms include palpable purpuric rashes that primarily affect the buttocks and lower extremities but can also occur elsewhere. Skin necrosis can arise from a variety of lesions, including hemorrhagic bullae, ecchymoses, and petechiae. Mucosal lesions affecting the esophagus, stomach, and intestines can include erosions, hemorrhages, swelling, hyperemia, petechiae, purpuric lesions, and ulcers (6). Nonetheless, there are very few reports of mucosal involvement with purpura over the lips in kids with IgA vasculitis. The severity of glomerulonephritis has a significant impact on the prognosis of the disease because it is the primary cause of morbidity and mortality in children with renal impairment (7).

Appropriate management of any local or systemic infectious processes that may be present is also crucial. Hence, dental caries, pulp infection/inflammation, periapical infections, and periodontopathies are all very common in children with IgA glomerulonephritis. The oral involvement in these patients predispose them to infections that spread to other body organs. Consequently, one of the most crucial roles for the pediatric dentists is treating these oral infections appropriately, which improves the disease's overall prognosis. When treating this kind of patient, pediatric dentists should pay attention to dental treatments, such as exodontia procedures, root canal therapy, or periodontal therapies, which are recommended for treating severe or chronic oral infectious processes, may cause the disease to develop as a side effect (8). Also, oral diseases, in particular dental caries (70%) and apical periodontitis (5%), are more common in children with IgA glomerulonephritis (9). Oral active

infectious foci in children with immunosuppression, especially those with severe renal impairment, need to be completely eliminated in order to prevent the infection from spreading to other internal organs like the skin or kidney, which could have serious systemic consequences and worsen the prognosis of the illness (10).

In conclusion, dental illness and dental treatments should be taken into account by clinicians when treating pediatric patients as possible causes of IgA glomerulonephritis. To minimize the risk of streptococcal bacteremia following an invasive dental procedure, it is also essential to control oral infections in children during the course of the disease. Puspa-Pertiwi notes that oral active infectious lesions can harbor up to 300 different species of both aerobic and anaerobic bacteria. These pathogens generate a variety of inflammatory cytokines and cell-degradation derivatives that can enter the bloodstream during a brief episode of bacteremia. This can lead to damage to the blood vessel walls and the continuation of active immune responses (11). Consequently, children with IgA glomerulonephritis should be carefully considered as candidates for prophylactic antimicrobial therapy prior to any dental procedures, just like other patients (e.g., cardiovascular diseases). The AAPD has published various antibiotic prophylaxis regimens for dental procedures in children who are considered to be at risk (12).

KAWASAKI DISEASE AND ORAL MANIFESTATIONS

Kawasaki disease (KD), formerly known as mucocutaneous lymph node syndrome, is a prevalent childhood vasculitis and is very rare in adults. The majority of medium-sized muscular arteries are widely inflamed, as seen by the clinical characteristics of KD. The basis for the diagnosis is the presence of signs of mucocutaneous inflammation along with evidence of systemic inflammation (such as fever). The diagnostic criteria for KD are based on characteristic clinical signs, which typically appear after a brief nonspecific prodrome of respiratory or gastrointestinal symptoms. These signs include bilateral nonexudative conjunctivitis, erythema of the lips and oral mucosa, rash, extremity changes, and cervical lymphadenopathy (13).

The characteristics of clinical modifications in KD include a "strawberry tongue" and red, cracked lips. In the evolution of the disease appears the sloughing of the filiform papillae and denuding of the inflamed glossal tissue. The remnants of fungiform papillae are visible as bumps on the "strawberry".

These oral mucositis symptoms can appear alone, in very mild form, or not at all. Tonsillar exudate and discrete oral lesions like vesicles or ulcers are suggestive of a disease process other than KD (14).

ANTINEUTROPHIL CYTOPLASMIC AUTOANTIBODY (ANCA)-ASSOCIATED VASCULITIDES (AAV) AND ORAL MANIFESTATIONS

Antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitides (AAV) are a group of disorders affecting primarily small-sized arteries and are classified in: granulomatosis with polyangiitis (GPA),

previously known as Wegener granulomatosis, microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA), or Churg Strauss disease and renal-limited vasculitis. All have similar features on kidney histology, are linked to ANCA, and primarily affect small-sized arteries (15). Initially, GPA and MPA are often misinterpreted as infections, cancers, or inflammatory joint diseases. Other symptoms that may arise from lesions affecting the ear, nose, and throat (ENT) include hemoptysis, coughing, dyspnea, and rhinosinusitis. Patients with either an MPA or a GPA may exhibit ENT symptoms. On the other hand, patients with GPA experience them far more frequently (estimated frequency is 90% versus 35% in MPA). ENT symptoms can include bloody or purulent nasal discharge, oral and/or nasal ulcers, polychondritis, sinusitis, otitis media, earache, otorrhea, and persistent rhinorrhea. Patients often experience sensorineural or conductive hearing loss, either of which can result in profound long-term hearing loss (16).

Oral lesions affect 6–13% of patients with GPA. The initial GPA symptom, known as "strawberry gingivitis," is restricted to gingiva inflammation. The oral cavity can present with symptoms that are specific to the following areas: palate (ulcers, osteonecrosis, oronasal fistulas), gingiva (gingivitis, bleeding, ecchymosis, necrosis), tongue (ulceration, necrotic lesions), alveolar process (osteitis, resorption), teeth (toothache, tooth loss), nasopharynx (ulcers), lips (swelling, nodules, exfoliation). Parotitis, or inflammation of the submucosal or sublingual salivary glands, with its painful enlargement, is an uncommon sign of the GPA (17). The similar aspect can be associated with GERD, where the dental erosion. GERD can also cause changes in soft tissue and salivary flow, associated with burning sensation, dry mouth, halitosis, and erythema of the soft/hard mucosa and uvula (18). The American College of Gastroenterology guidelines define gastroesophageal reflux disease (GERD) as “symptoms or mucosal damage produced by the abnormal reflux of gastric contents into the esophagus” (19). In the same time, the GERD can be a consequence of vasculitis, and triggers a whole set of symptoms or complications (20-24).

Poland et al analyzed the disease's oral cavity manifestation in patients with MPA and GPA. Fungi-induced white coating of the tongue or filiform papillary hypertrophy of the tongue were the most common oral lesions, detected in 55.6% of the patients. In 66.7% of the patients, the infection was confirmed, and the most commonly cultured fungus was Candida albicans. Patients with GPA who experience recurring fungal infections may benefit from long-term systemic therapy, particularly when immunosuppressive medications like glucocorticosteroids are used. This could have significant clinical and therapeutic ramifications. Patients may experience large, recurring, or persistent lip and mucosal erosion ulcers. They commonly report having chronic stuffy noses, blocked sinuses with nose bleeds, and nasal crusting, among other nasal and sinus issues. This may worsen to the point where the nasal septum is destroyed, causing the nose's bridge to collapse and developing the recognizable saddle nose. Strawberry gingivitis and phantom toothache can be caused by blocked or restricted vessels supplying the teeth and periodontal tissues. Damage to the

periodontal tissues and pulpal necrosis without apparent cause could arise from this (25).

SYSTEMIC LUPUS ERYTHEMATOSUS AND ORAL MANIFESTATIONS

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune inflammatory disease with an unknown cause that can affect any organ system, most commonly the skin, joints, kidneys, nervous, hematologic, and cardiovascular systems. It is distinguished by the production of numerous autoantibodies. Although SLE in children is fundamentally the same as in adults, with the same etiology, pathogenesis, and laboratory findings, there are some differences in the frequency and severity of certain clinical manifestations. It is widely accepted that children with SLE have a more severe disease and accumulate disease damage sooner than adults with SLE (26,27). Mucocutaneous involvement is seen in 70 % of patients and is represented by: malar rash, photosensitivity, oral or nasal ulcers, and/or discoid rash (28).

Oral involvement was noted in 61.4% of cases, with erosion, hyperkeratosis, pigmentation, and ulcers being the most common, according to Zakeri et al. These lesions primarily affected the hard palate, with the soft palate and lower lip being the next most common (29). Another oral manifestation is gum hypertrophy, like primary manifestation of SLE, or secondary of cyclosporine treatment (30). As previously stated, oral ulceration is the most common manifestation that can occur at the oral level; in fact, it is one of the criteria to be taken into account when attempting to classify SLE (31). Furthermore, early ulcer detection is critical for faster diagnosis and treatment, as delayed detection is linked to worse prognosis and increased disease activity (32). A differential diagnosis should be made because some illnesses, like COVID-19, lichen planus, pemphigus, or syphilis, also depend on the development of ulcers for their diagnosis (23-36).

While oral ulcers are the most common oral manifestation, other conditions that may be present include hyposalivation, hyperpigmentation brought on by antimalarial medications, oral mucosal lesions, dental caries, and periodontal disease. More than 75% of SLE patients experience hyposalivation, or decreased salivary flow, which can also result in xerostomia or the feeling of having a dry mouth. As SLE activity increases with age, SLE patients' salivary gland production declines, according to information found in a study conducted by Leite et al. (37). The oral route of administration of some immunosuppressive therapy with the duration of administration are linked directly to renal impairment, in same time with oral manifestation (38). Oral health is integrated into general health and it is essential to well-being and quality of life, especially in the chronic diseases (39).

CONCLUSIONS

Oral manifestations are frequently encountered symptoms in primary pediatric vasculitis, sometimes representing the initial signs of these conditions. The full range of dental implications and oral manifestations and their consequences in pediatric vasculitis is not well researched and needs further

studies. Pediatricians and pediatric dentists find it challenging to reach a diagnosis and provide appropriate care in the majority of cases. In fact, in primary pediatric vasculitis, there are several clinical manifestations of oral ulcers, and some lesions occur when the disease is active, indicating that early management of the disease should be started.

AUTHOR CONTRIBUTIONS

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