

Systemic disease or periodontal disease? Distinguishing causes of gingival inflammation: a guide for dental practitioners. Part 1: immune-mediated, autoinflammatory, and hereditary lesions

Josefine Hirschfeld,^{*1} Jon Higham,² Despoina Chatzistavrianou,³ Fiona Blair,¹ Andrea Richards² and Iain L. C. Chapple¹

Key points

Provides dental practitioners with an understanding of the manifestation of systemic diseases to the periodontium.

Highlights elements in the clinical assessment which will aid in establishing a diagnosis.

Presents different conditions concisely and outlines these using clinical photographs.

Abstract

Periodontitis and gingivitis remain two of the most common diseases that affect the oral cavity. As they are caused by plaque, effective oral hygiene, elimination of plaque-retentive factors and successful periodontal treatment will result in resolution of gingival and periodontal inflammation. Certain systemic diseases can have a clinical appearance similar to periodontal diseases or exacerbate existing periodontitis/gingivitis and *vice versa*. This paper aims to provide the dental practitioner with an understanding of the manifestations of systemic diseases to the periodontium and highlights elements in the clinical assessment, which will aid in establishing a correct diagnosis. Additional anamnestic and clinical clues are important for distinguishing between plaque-induced and non-plaque-induced lesions. The first part of this compendium covers immune-mediated and hereditary conditions as causes of gingival lesions, which can resemble those caused by dental plaque. The different conditions are presented concisely and exemplified by clinical photographs. Dental practitioners should be aware of the various manifestations of systemic diseases to the periodontium in order to offer appropriate diagnosis and treatment, which can reduce both patient morbidity and mortality.

Introduction

Periodontitis is a complex inflammatory disease that affects the soft and hard periodontal structures (Fig. 1a). It is a plaque-related disease initiated by bacteria, and driven by the host response, genetic predisposition and environmental risk factors. Periodontitis, if left untreated, often leads to progressive destruction of the tooth supporting tissues and tooth loss.¹ Typical clinical findings are pocketing and/or gingival recession. Gingivitis on the other hand is characterised by redness and swelling of the keratinised gingiva adjacent to the

teeth (Fig. 1b). In plaque-induced gingivitis, these symptoms resolve after plaque control. Unlike periodontitis, gingivitis is therefore a reversible disease. There are, however, cases that do not respond to classic plaque control regimes, including establishment of appropriate oral hygiene, scale and polish, administration of chemical plaque control and elimination of plaque-retentive factors. In cases

of non-resolving gingival inflammation the underlying cause is often of a systemic nature and careful examination of the oral cavity for other mucosal changes may reveal findings indicative of an underlying systemic condition.²

Prompt and accurate diagnosis of underlying systemic disease facilitates appropriate referral, investigation and management. It is also important to acknowledge that

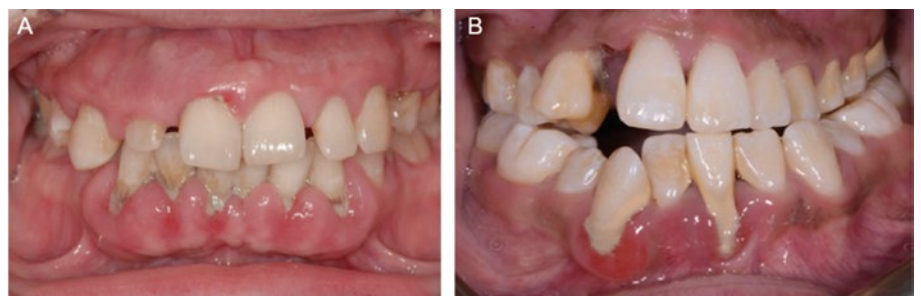


Fig. 1 Plaque-induced gingival/periodontal diseases. (A) Plaque-induced generalised gingivitis. (B) Generalised chronic periodontitis with localised gingival swelling, recession formation, tooth loss and pathologic tooth migration

¹Department of Periodontology; ²Department of Oral Medicine; ³Department of Restorative Dentistry, Birmingham Dental School and Hospital, 5 Mill Pool Way, B5 7EG, Birmingham, UK

*Correspondence to: Josefine Hirschfeld
Email: j.hirschfeld@bham.ac.uk

Refereed Paper.

Accepted 15 July 2019

<https://doi.org/10.1038/s41415-019-1050-8>

non-plaque-induced gingival lesions are often colonised and infected by oral bacteria whereby gingival and periodontal inflammation can additionally contribute to disease activity. Thus, plaque control measures may ameliorate such lesions but they do not resolve until the systemic cause is targeted. The National Health Service (NHS) UK recommends that patients are seen for dental check-ups between every 3 to 24 months, depending on their oral health and needs. Because of the regular frequency of dental check-ups dental practitioners are in a unique position to facilitate an early diagnosis of systemic diseases, which can manifest in the oral cavity.

This compendium focuses on non-plaque-induced and non-resolving lesions of the keratinised gingiva in dentate patients and aims to aid the practitioner to distinguish those systemic diseases that might be confused with plaque-induced gingival lesions. However, the authors have also included other systemic and related conditions, which commonly manifest to the gingivae, with the aim to provide the reader with a guide to establishing a differential diagnosis. The non-plaque-induced gingival/periodontal lesions described herein are also in accordance with the recently published Consensus Report of Workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions.³

The systemic underlying conditions along with oral clinical photographs, demographic data and clinical descriptions are presented in a summary table. In this article, part 1 of this compendium, we review immune mediated, autoinflammatory, and hereditary gingival lesions. In part 2 of the compendium we go on to review cancer related gingival lesions, infective and other causes of gingival inflammation.

1. Anatomy and terminology

1.1 Anatomy of the periodontium

The periodontium consists of five types of tissues:

1. Free gingiva, the tissue collar around the tooth, which forms the gingival crevice and is lined with epithelium, which is non-keratinised on the tooth-facing side and keratinised on the oral cavity-facing side. It is attached to the tooth at its base by the epithelial attachment, the junctional epithelium. The interdental free gingiva is referred to as the interdental papilla, which is knife-edged under healthy conditions
2. Attached gingiva, the tissue adjacent to the



Fig. 2 Drug-induced gingival enlargement. Photograph courtesy of Mr Mutahir Rahman, Department of Periodontology, Birmingham Dental School and Hospital, Birmingham, UK



Fig. 3 Desquamative gingivitis in a patient with lichen planus

3. Alveolar mucosa, the area beyond the mucogingival junction, which is less firmly attached and non-keratinised. The mucogingival junction, a scalloped line, divides attached gingiva and alveolar mucosa
4. Alveolar bone consisting of dense cortical plates and cancellous bone as well as of the lamina dura, the wall of the socket
5. Periodontal ligament, which is attached to the lamina dura as well as to the cementum of the tooth, consists of apical, oblique, horizontal, alveolar crest and interradicular fibres as well as of blood and lymphatic vessels and nerves.

1.2 Plaque-induced gingival lesions

The oral cavity is habitat to several hundred microbial species including bacteria, viruses and fungi. The periodontium is a unique point of challenge in the body, as the tooth-bone interface constitutes a potential port of entry for microorganisms, whereas all other surfaces of the

gastro-intestinal tract provide a closed epithelial layer, which eliminates colonising bacteria by epithelial shedding. Thus, if microorganisms on tooth surfaces are allowed to overgrow in the form of a biofilm (plaque), or calculus, an inflammatory response of the periodontal and gingival tissues is initiated. Plaque-induced gingivitis is characterised by redness and swelling, but is fully reversible by eliminating biofilms from the tooth surfaces. Periodontitis is accompanied by pocket formation in the area of the junctional epithelium, in an attempt by the host immune cells to eliminate the biofilm by releasing toxic enzymes, proteins and reactive oxygen species. Nevertheless, the pocket environment provides excellent growth conditions for anaerobic bacteria, thereby driving inflammation and host-mediated tissue destruction. Only if biofilms and calculus are effectively removed from the pockets can tissue repair take place. An important distinguishing feature of plaque-induced gingival lesions is that, with the exception of necrotising and ulcerative forms, they are usually painless

whereas non-plaque-induced gingival lesions are often symptomatic.

1.3 Gingival enlargement

Gingival enlargement or overgrowth (Fig. 2) is encountered in a variety of systemic and related conditions including orofacial granulomatosis (see section 2.3.1), granulomatosis with polyangiitis (see section 2.4), neutropenia (see section 2.6), plasma cell gingivitis (see section 2.7), hereditary gingival fibromatosis and idiopathic gingival enlargement (see section 3.1), drug-induced gingival enlargement (see Part 2 of this series, section 3.1), scurvy (see Part 2: section 3.2) and mouth breathing (see Part 2: section 4.1). It can also occur in plaque-induced gingivitis and periodontitis, especially in adolescents, during pregnancy, and in necrotising/ulcerative forms of these diseases. Distinguishing the cause can therefore be challenging but the medical history, extent of gingival swelling, presence of inflammation, and response to periodontal intervention can help in differentiating a diagnosis. An important distinguishing feature of some but not all of the systemic conditions in which gingival enlargement occurs is involvement of both the attached and unattached gingivae sometimes termed a 'full-width' or 'full-thickness' gingivitis. Involvement of the unattached gingivae can be seen in orofacial granulomatosis, plasma cell gingivitis, and polyangiitis with granulomatosis.

1.4 Desquamative gingivitis

Desquamative gingivitis (DG) (Fig. 3) is a clinical descriptor rather than a diagnosis. Several mucocutaneous pathologies, including pemphigus vulgaris (see section 2.1), pemphigoid and erythema multiforme (see section 2.2), lichen planus and lupus erythematosus (see section 2.5), allergic reactions (see section 2.7) and drug-induced lesions (see Part 2: section 3.1), can result in desquamative gingivitis. Widespread desquamation and/or erosion of the attached gingiva of the teeth is considered the chief characteristic feature of desquamative gingivitis, it often affects the buccal and labial gingivae but can also occur in the palatal and lingual gingivae. Similarly to full-thickness gingival enlargement, DG is often but not always contiguous with involvement of the adjacent unattached gingivae and sulcus mucosa, which should alert the practitioner to the possibility of an alternative diagnosis. In addition to the underlying immune-inflammatory condition driving the desquamative gingivitis dental

plaque is an important aggravating factor. It is often difficult to distinguish the cause of DG on purely clinical grounds and histology and immunologic testing are usually necessary to establish a diagnosis.⁴

2. Immune-mediated and autoinflammatory gingival lesions

2.1 Pemphigus vulgaris

Pemphigus vulgaris (PV) is an autoimmune blistering disease affecting the skin and mucous membranes (Fig. 4, Table 1). Oral lesions usually appear before skin lesions, and in many cases the oral cavity remains the only site affected. Autoantibodies are directed against desmosomes (epithelial adhesion proteins) that bind stratified squamous epithelial cells together.⁵ In common with other vesiculobullous diseases oral PV presents as shallow oral ulceration, preceded by fluid-filled blisters, which are rarely seen clinically due to their fragility. PV can affect any mucosal surfaces and desquamative gingivitis is a common feature. The preliminary diagnosis is based on the clinical presentation and confirmed by histology. PV can be life threatening, particularly in cases with extensive cutaneous involvement, by means of secondary infection leading to septicæmia. Early diagnosis and management can prevent this complication.⁶ However, treatment particularly with high dose corticosteroids can lead to significant and potentially life-threatening complications including diabetes, cardiovascular disease, peptic ulcers, adrenal insufficiency and infection.⁷

2.2 Pemphigoid

Pemphigoid is a group of vesiculobullous diseases and is a type of immune-mediated sub-epithelial blistering disease (IMSEBD). These diseases are mediated by a variety of autoantibodies that target the extracellular components that link the basement membrane to basal epithelial cells or to the lamina propria.⁸ A number of IMSEBD can affect the oral cavity including dermatitis herpetiformis, toxic epidermal necrolysis/erythema multiforme, chronic bullous dermatosis of childhood, and pemphigoid variants. Pemphigoid variants include gestational pemphigoid, bullous pemphigoid, and mucous membrane pemphigoid (MMP). Additionally, acquired epidermolysis bullosa and linear IgA disease are now thought to be variants of MMP.^{9,10} Of the pemphigoid variants, mucous membrane

pemphigoid (MMP) most commonly affects the oral cavity, with approximately 85 percent of affected patients having oral involvement (Fig. 5, Table 1). When affecting the gingiva, mucous membrane pemphigoid commonly presents as desquamative gingivitis.¹¹ Additionally MMP can affect a variety of extraoral sites including the ocular, nasal, nasopharyngeal, anogenital, laryngeal and oesophageal mucosa, and can also rarely involve the skin. Ocular involvement is of particular concern as this results in scarring which can eventually lead to blindness in the affected eye.¹² Although this disorder has an unclear aetiology, pemphigoid-like lesions can occasionally be drug-induced. There is no standard treatment protocol for the management of patients with MMP. The treatment strategies depend on the age of the patient, comorbidities, severity of the disease and the site involved, and may include the administration of corticosteroids, antimetabolites or antibiotics. Plaque control measures can play an important role in controlling oral inflammation in this condition.¹³










2.3 Orofacial granulomatosis and related conditions

Orofacial granulomatous inflammation can occur in a variety of disparate conditions including inflammatory bowel disease, particularly Crohn's disease, sarcoidosis, Melkersson-Rosenthal syndrome, tuberculosis and other mycobacterial infections. Cases can also occur without any apparent association with an underlying systemic disease in which case it might be thought of as idiopathic orofacial granulomatosis.¹⁴ Although the aetiopathogenesis of these conditions is varied or indeed unknown, we have grouped these disorders together based on their common clinical presentation to facilitate discussion.

2.3.1 (Idiopathic) orofacial granulomatosis

Orofacial granulomatosis (OFG) is a rare, granulomatous inflammatory disorder that is characterised by persistent enlargement of the soft oral and perioral tissues and has an unknown aetiology. Importantly, an onset of OFG during childhood may predict future development of Crohn's disease.¹⁵ Affected patients typically present with persistent painless swelling of the lips (cheilitis granulomatosa), indurated tag-like lesions, cobblestoning, linear ulceration and mucogingivitis. One of the characteristic features of the hyperplastic gingivitis seen in OFG is that it affects the attached and unattached gingivae (full-thickness gingivitis). The mechanism of the enlargement is granulomatous inflammation.

Table 1 Overview of systemic and conditions and non-plaque related causes of gingival and periodontal lesions. All data are derived from the references indicated in the main text as well as from the Orphanet Rare Disease Collection: <http://www.orphadata.org>. Orphanet Report Series (Rare Disease Collection), Prevalence and incidence of rare diseases: Bibliographic data. Orphanet, 2018

Figure	Condition	Demographics and incidence	Image	Clinical description
Fig. 4	Pemphigus vulgaris	Prevalence: 18/100,000 (in Europe) Age group: usually in the 5th-7th decades, although childhood onset forms have been described. Gender: F>M		Main clinical presentation: ulcers, vesicles/bullae, mucosal erosions. Commonly presents as desquamative gingivitis Pain: moderate to severe Oral tissues involved: palate, buccal mucosae, lips
Fig. 5	Mucous membrane pemphigoid	Prevalence: unknown Age group: usually in the 5th-7th decades Gender: F>M		Main clinical presentation: ulcers, vesicles/bullae, mucosal erosions. Commonly presents as desquamative gingivitis Pain: mild to severe depending on extent of involvement and disease activity Involvement of other oral tissues: palate, buccal mucosae, tongue (less common)
Fig. 6	Oral manifestations of inflammatory bowel diseases	Prevalence: 10-60% of those affected by IBD Age group: any Gender: M>F		Main clinical presentation: indurated tag-like lesions, cobblestoning, mucogingivitis, edema, aphthous stomatitis, ulceration, pyostomatitis vegetans, hyperplasia Pain: orofacial granulomatosis: no; pyostomatitis vegetans: variable; oral ulceration: moderate to severe Involvement of other oral tissues: buccal mucosa, lips (swelling and vertical fissuring), perioral tissues (dermatitis), floor of mouth (stag-horning)
Fig. 7	Sarcoidosis	Prevalence: 12.5/100,000 (worldwide) Age group: any, but more prevalent in the 3rd to 6th decade Gender: M=F		Main clinical presentation: firm swelling or nodular lesions Pain: no Involvement of other oral tissues: lips, hard and soft palate, buccal mucosa, tongue, tonsils, salivary glands
Fig. 8	Granulomatosis with polyangiitis	Prevalence: 0.85/100,000 (in Europe) Age group: any Gender: F=M		Main clinical presentation: granulomatous/papillary hyperplasia, erosion, ulceration, strawberry gingivitis Pain: no Involvement of other oral tissues: no
Fig. 9	Oral lichen planus	Prevalence: 1,300/100,000 (worldwide) Age group: between the 4th and 5th decade Gender: F>M		Main clinical presentation: reticular white patterns (striae), keratotic plaques, atrophy, erosions/ulceration, papules, bullae (rare) Pain: mild to severe depending on extent and disease activity Involvement of other oral tissues: every area of the oral mucosa
Fig. 10	Neutropenia	Prevalence: variable, depending on cause Age group: variable, depending on cause Gender: variable, depending on cause		Main clinical presentation: pronounced gingivitis, often without visible plaque deposits. Recurrent aphthous stomatitis. Pain: variable – usually no Involvement of other oral tissues: all oral mucosal sites
Fig. 11	Plasma cell gingivitis	Prevalence: unknown Age group: unknown Gender: unknown		Main clinical presentation: erythema, edema, loss of stippling, papillary enlargement Pain: sometimes, occasionally accompanied by other sensations Involvement of other oral tissues: palate and buccal mucosa (occasionally)
Fig. 12	Hereditary gingival fibromatosis	Prevalence: unknown Age group: any Gender: F=M		Main clinical presentation: gingival enlargement Pain: no Involvement of other oral tissues: no Photograph courtesy of Mr Mutahir Rahman, Department of Periodontology, Birmingham Dental School and Hospital, Birmingham (UK)

The best treatment of this condition and its prognosis are uncertain.

Melkersson-Rosenthal syndrome, a neurological disorder, is characterised by orofacial swelling analogous to OFG, lower motor neurone facial palsy, and less commonly, fissured tongue. The facial palsy tends to be unilateral and may be indistinguishable from Bell's palsy.¹⁶

2.3.2 Inflammatory bowel diseases

Oral manifestations of the inflammatory bowel diseases Crohn's disease (CD) and ulcerative colitis (UC) have been reported to affect up to 60% of the affected patients.^{17,18} Crohn's disease is a polygenic autoinflammatory syndrome and which can affect any part of the gastrointestinal tract, including the mouth, although a majority of cases involve the terminal ileum. Orofacial granulomatosis is the commonest orofacial manifestation of this disease, but aphthous stomatitis is also occasionally seen in both CD and UC; however, this is a non-specific finding.

Pyostomatitis vegetans is most commonly encountered in patients with UC but has occasionally been reported in patients with CD. It is a chronic mucocutaneous ulcerative disorder consisting of multiple miliary white or yellow pustules with an erythematous and oedematous mucosal base (Fig. 6, Table 1). The pustules can rupture and coalesce to form linear or 'snail-track' ulcers. The most frequently involved regions of the oral cavity are the labial gingiva and the labial and buccal mucosa, the tongue and floor of the mouth are rarely involved but it can affect almost all parts of the oral cavity.^{18,19}

2.3.3 Sarcoidosis

Sarcoidosis is a chronic systemic disease of unknown aetiology and is characterised by an accumulation of epithelioid granulomas. Sarcoidosis affects multiple organs, especially the lungs, lymph nodes, skin and eyes. The salivary glands are frequently involved, sometimes resulting in xerostomia or bilateral parotid swelling, the combination of parotid swelling, fever, and anterior uveitis is known as uveoparotid fever or Heerfordt syndrome. Oral sarcoidosis is rare and the prevalence is unknown, while the treatment remains controversial and may range from oral glucocorticoids to surgical excision.²⁰ Oral mucosal presentations are varied but include orofacial granulomatosis and localised erythematous swelling which can affect any oral mucosal site including the gingivae (Fig. 7, Table 1).²¹

2.4 Granulomatosis with polyangiitis

Granulomatosis with polyangiitis, previously known as Wegener's granulomatosis, is a rare systemic disorder that can affect all areas of the body, including the oral cavity. It is a form of vasculitis that affects small- and medium-size vessels in many organs. Those with the disease require long-term immunosuppression, as otherwise this condition is lethal. The typical oral manifestations occur as gingival erosions and ulcerations, which often appear hyperplastic, leading to the typical clinical presentation of a 'strawberry gingivitis'. Oral involvement in granulomatosis with polyangiitis has been reported in 10–62% of cases, but oral involvement as the first sign of the disease is found in only 2% of cases (Fig. 8, Table 1).²²

2.5 Oral lichen planus

Lichen planus is a mucocutaneous disorder, which commonly affects the skin and skin appendages (including scalp and nails), oral mucosa, and genitalia. Oesophageal, ocular, laryngeal, nasal, and urinary tract mucosa involvement have also rarely been reported. The epithelial damage is immunologically mediated by cytotoxic T-cells directed against basilar keratinocytes and results in vacuolar degeneration and lysis of basal cells. It is not a classical autoimmune disorder and is probably best typified as an inflammatory disease. Its aetiology is poorly understood but a variety of factors have been suggested including genetic, physiological, systemic disease, and hypersensitivity but there is currently no consensus.²³ Oral lichen planus (OLP) is one of the most common oral mucosal diseases.²⁴ Gingival involvement (desquamative gingivitis) is very frequently observed, and the disease is characterised by a high variability in clinical appearance and symptoms (Fig. 9, Table 1). There are several recognised clinical types including reticular, papular, plaque-like, atrophic, erosive/ulcerative and, rarely, bullous variants. Additionally, oral lichenoid lesions including lichenoid contact lesions, lichenoid drug reactions, lichenoid lesions of graft versus host disease and lichenoid interface mucositis, seen in certain forms of lupus, can confuse the diagnosis. In common with many immune-inflammatory oral mucosal diseases, a synergy with periodontal inflammation exists, which can influence disease activity. Therefore, patients with OLP require appropriate periodontal management, in combination with systemic evaluation, and topical or systemic immunosuppression/modulation.²⁵

2.6 Neutropenia

The neutrophil is a polymorphonuclear immune defence cell and is the principal cell of the innate immune system. It therefore plays an important role in responding to infection through a diverse array of killing mechanisms including degranulation, respiratory burst resulting in the release of reactive oxygen species, and extrusion of their cytosol and nuclear chromatin as neutrophil extracellular traps. Additionally, as the first responder to microbial ingress the neutrophil helps orchestrate the immune-inflammatory response to infection.²⁶

As stated in section 1.2, the oral cavity is a unique environment in the body as there is a break in the integument at the tooth-bone/mucosa-tooth interface, which constitutes a potential direct entry port for microorganisms. As such the oral cavity has long been recognised as a site of particular relevance in individuals with immune defects, and this is commonly the case in those with neutropenia. Neutropenia is defined as a paucity or defective function of neutrophils, and there are several causes of neutropenia including primary forms (chronic benign neutropenia, cyclical neutropenia, and other congenital and familial neutropenias) and secondary forms (iatrogenic, aplastic anaemia, leukaemia, connective tissue disease, malignancies and infections) all of which result in underproduction of neutrophils in the bone marrow. Neutropenia can also result from increased destruction of neutrophils (hypersplenism and immune neutropenia) and is rarely due to congenital immune defects (leukocyte adhesion deficiency, Chediak-Higashi syndrome, hyper-IgE syndrome, recurrent infection syndrome, and chronic granulomatous disease).^{27,28} All forms of neutropenia can result in oral mucosal pathology, primarily aphthous stomatitis and aggressive forms of gingivitis, which can be hyperplastic in nature (Fig. 10, Table 1).^{29,30}

Treatment is varied and depends on the cause of the neutropenia but can include granulocyte-colony stimulating factor (G-CSF), prophylactic use of antibiotics and antifungals, interferon-gamma, allogeneic bone marrow transplantation, gene therapy, intravenous immunoglobulins, corticosteroids and other immunomodulatory or immunosuppressive therapies.

2.7 Plasma cell gingivitis

Plasma cell gingivitis (Fig. 11, Table 1) is a rare and benign condition, which is sometimes accompanied by cheilitis or glossitis ('plasma-cell gingivostomatitis'). It may represent a sub-type

of plasma cell orofacial mucositis, which can be life threatening when it affects the airway and includes diverse entities such as Zoon's balanitis/vulvitis, which affect the genital mucosa, but may also be a separate disease entity. Other terms that have been used to describe this condition are idiopathic gingivostomatitis, atypical gingivostomatitis, allergic gingivostomatitis and plasmacytosis. The clinical presentation is that of erythematous mucosa with papillomatous, cobblestone, nodular, or granulomatous enlargement and it is histologically characterised by a dense plasma cell infiltrate.³¹ It may or may not involve the free gingival margin and can also be a localised lesion. Its aetiology is poorly understood but plasma cell gingivitis has been reported to be associated with hypersensitivity reactions to substances such as toothpaste and chewing gum ingredients, mint, pepper and cinnamon and in these cases resolution follows cessation of the offending allergen.³² However, beyond this there is currently no consensus on management of the disease.

3. Hereditary conditions

3.1 Hereditary gingival fibromatosis and idiopathic gingival hyperplasia

Hereditary gingival fibromatosis is a rare, mostly autosomal dominant disease, which can develop as an isolated disorder or a feature of a syndrome. It is a benign oral condition characterised by slow and progressive enlargement of both maxillary and mandibular attached gingiva. It is commonly associated with hypertrichosis (excess hair growth) as well as with epilepsy and intellectual disability.³³ A progressive fibrous enlargement of the gingiva is a feature of idiopathic hyperplasia/fibromatosis of the gingiva (Fig. 12, Table 1). Gingival fibromatosis may exist as an isolated abnormality or as part of a syndrome such as Laband syndrome.³⁴ The exact cause of the disease is unknown; however, involvement of platelet-derived growth factor isoforms and its receptor as well as qualitative and quantitative differences in tumour growth factor-beta isoforms and receptor expression by fibroblasts have been suggested.^{35,36}

Conclusion

In this article, the first part of this series of two papers, we have reviewed immune-mediated, autoinflammatory and hereditary gingival lesions, supported by epidemiological data, clinical descriptions and photographs. Several of these systemic conditions can have a similar clinical

presentation to periodontitis and gingivitis or exacerbate existing disease. On the other hand, plaque-induced inflammation often worsens non plaque-induced conditions, which can make it more difficult to distinguish both. At the same time, dental practitioners need to be aware that oral manifestations of systemic diseases can impair oral hygiene abilities in affected patients. Those lesions which are accompanied by pain, are non-resolving or show a morphology atypical of classic plaque-induced gingival inflammation, should encourage dental practitioners to refer their patient to a specialist unit. A full discussion is included in part 2: cancer related, infective, and other causes of gingival pathology. Readers are therefore referred to this paper.³⁷

Acknowledgements

The authors would like to thank Mr Mutahir Rahman at the Department of Periodontology of the Birmingham Dental School and Hospital for his permission to use clinical photographs. We further thank our patients for their consent to utilise their clinical photographs for this publication.

Author Contributions

JH (Josefine Hirschfeld) took the lead in writing and finalising the manuscript. JH (Jon Higham), DC and JH drafted the manuscript and gathered demographic data for the table; FB, AR and ILC provided guidance and clinical photographs. All authors provided critical feedback.

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