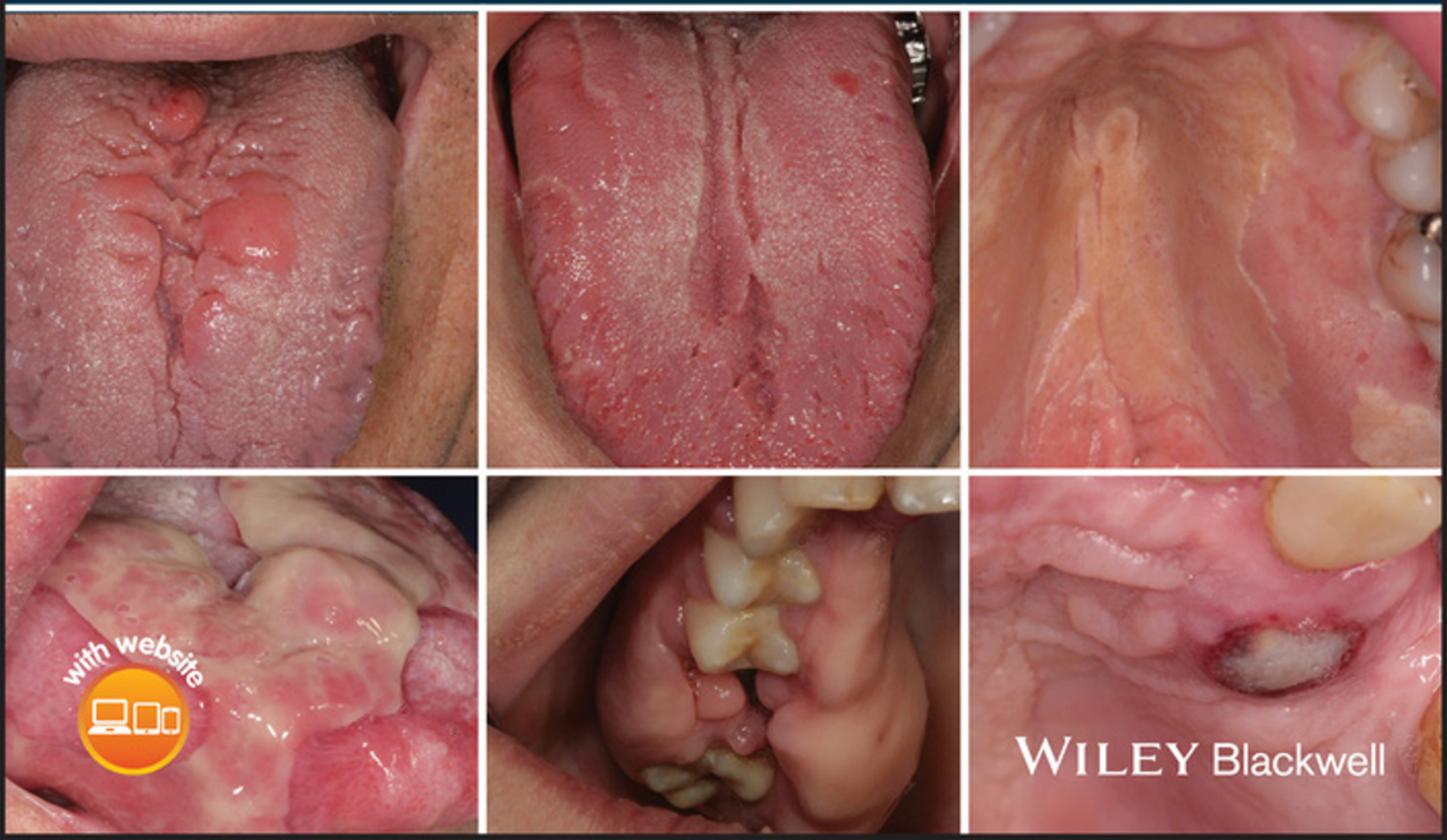
CLINICAL GUIDE TO ORAL DISEASES

DIMITRIS MALAMOS | CRISPIAN SCULLY



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Clinical Guide to Oral Diseases

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This edition first published 2021

Registered Offices
John Wiley & Sons, Inc., 111 River Street, Hoboken, NJ 07030, USA
John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK

Editorial Office
9600 Garsington Road, Oxford, OX4 2DQ, UK

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Library of Congress Cataloging-in-Publication Data

Names: Malamos, Dimitris, author. | Scully, Crispian, author.
Title: Clinical guide to oral diseases / Dimitris Malamos, Crispian Scully.
Description: Hoboken, NJ : Wiley-Blackwell, 2021. | Includes index.
Identifiers: LCCN 2020032170 (print) | LCCN 2020032171 (ebook) | ISBN 9781119328117 (paperback) | ISBN 9781119328131 (adobe pdf) | ISBN 9781119328155 (epub)
Subjects: MESH: Mouth Diseases–diagnosis | Diagnosis, Oral | Case Reports
Classification: LCC RK60.7 (print) | LCC RK60.7 (ebook) | NLM WU 140 | DDC 617.6/01–dc23
LC record available at https://lccn.loc.gov/2020032170
LC ebook record available at https://lccn.loc.gov/2020032171

Cover Design: Wiley
Cover Image: courtesy of Dimitris Malamos

Set in 9.5/12.5pt STIXTwoText by SPi Global, Pondicherry, India

10 9 8 7 6 5 4 3 2 1

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Preface

The idea of writing this book was born one Sunday afternoon three years ago, when Professor Scully and I discussed some interesting and intriguing clinical cases for diagnosis. We thought it would be a good idea to provide various clinical photos, and respond to relevant questions in a way that the readers could be led to the proper diagnosis. Professor Scully wanted this new book to be reader-friendly and hoped to approach the common oral diseases in a different way. This book would not be compared to any of the other outstanding and well-written textbooks on oral medicine, as it would not be a complete review of oral diseases or rare syndromes.

This guide aims to present a large selection of clinical cases that are representative of the majority of oral common diseases that are seen in a daily clinical practice, and it is recommended to all physicians and oral health providers, including dental and medical undergraduate and postgraduate students, dentists and medical practitioners, especially dermatologists, as well as ear, nose and throat specialists, internists, and oncologists.

Despite Professor Scully's sudden death, the composition of the book writing took place as an effort to follow his idea. The book is designed to provide a short revision of oral medicine by using three different groups of multiple choice questions (MCQs) and answers based on clinical colored photos. Each group of questions has different degrees of difficulty in answering. The first group of questions is adequate for undergraduate students and is related to diagnosis; the second is addressed to medical and dental practitioners; while the last and more difficult is for postgraduate students.

This book is divided into three parts. The first part includes Chapters 1–14 and refers to the classification of oral lesions by appearance and symptomatology; the second part comprises Chapters 15–24 and encompasses the most common oral lesions by location; while the third part consists of Chapters 25–27 and refers to the oral lesions that are normal variations, or have an age predilection, or are part of various clinical phenomena. Parts I and III are composed of 10 cases in each chapter, while the Part II has five cases in each chapter. Additionally, a concise table and a short text relevant to each chapter and containing a list of the common oral lesions/conditions is provided before cases presentation.

This book is based on more than 260 good quality, colored clinical photos, making this guide a brief practical atlas of common oral diseases. These clinical images come from my personal records, and I am deeply grateful to my patients who gave their permission, and to my publication team for plotting these images carefully. Their help was unique, and without it, this book would not be feasible.

Dimitris Malamos
Athens, 2020

Foreword

It is an honor and an immense satisfaction for me to provide the prologue for this book for two main reasons: the experience of its authors and the originality of this proposed editorial. When reviewing this ''Clinical Guide to Oral Diseases", one is surprised by the practical perspective with which its authors have imbued it, combining basic principles of problem-based learning with excellent images and an accurate and essential critical overview for arguing the differential diagnosis of each injury. Throughout the 27 chapters, the authors conduct an exhaustive review of the most common oral injuries based on the discussion of case studies. This approach perfectly combines Dimitris Malamos' clinical experience and Crispian Scully's academic rigor.

All of these features make this book a cross-sectional work, which can be useful both for undergraduate students, general dentists and specialists in the setting of medical-surgical dentistry. In the end, the success of the clinical activity is not based on academic titles but rather on the knowledge and expertise of the observer. In some manner, Professor Scully had already promulgated this idea during his final years, because he tended to end his emails with a phrase attributed to Goethe, "One only sees what one looks for. One only looks for what one knows."

Pedro Diz Dios
MD, DDS, PHD, EDOM, FRCSEd ad hominem
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Acknowledgment

I would like to thank the individuals whose help made this Clinical Guide possible; particularly Mrs J. Saiprasad for being so helpful and co-operative in determination to overcome delays in publication Mrs Carolyn Holleyman for checking the flowcharts and webcases, Mrs Susan Engelken for the cover of the book and especially Mr Vincent Rajan as Production Editor organizing and resolving problems before the publication and Mrs A. Argyropouloy for revising the text. I am grateful to my mentors Professor G. Laskaris (Greece) and Professor C. Scully (United Kingdom) as I truly appreciated their teaching and encouragement to me, to become seriously involved in Oral Medicine. Professor Scully's friendship, advice and expertise is still a part that I miss, and this book was written in his memory.

I wish also to express my sincere gratitude to Dr Pedro Diz Dios and to Dr Marcio Diniz Freitas for their help and advice throughout the preparation of this book. The participation of Dr Marcio Diniz Freitas as Content editor is precious.

Finally, I am especially indebted to my wife Vasiliki and my children Panagiotis and Katerina for their continuous love and support for all those years of my involvement in Oral Medicine, and during the preparation of this guide.

About the Companion Website

Don’t forget to visit the companion website for this book:

www.wiley.com/go/malamos/clinical_guide

There you will find valuable material designed to enhance your learning, including:

- Clinical cases
- Further reading

Scan this QR code to visit the companion website

Section I

1

Bleeding

Bleeding in the mouth may be a sign of various conditions related to the structure of blood vessels, the number or function of white blood cells and especially platelets, the deficiency or dysfunction of clotting factors or even interaction of various drugs. Some of these bleeding disorders appear at a very young age; some are also found among close relatives (inherited) while others are noticed later with a negative family history (acquired). The severity of the bleeding ranges from minor hemorrhages from gingivae and other parts of the oral mucosa with the formation of petechiae or ecchymosis (Figure 1.0), to extensive bleeding in other parts of the body, causing severe blood loss, even jeopardizing the patient's life.

The more important causes of oral bleeding are seen in Table 1.

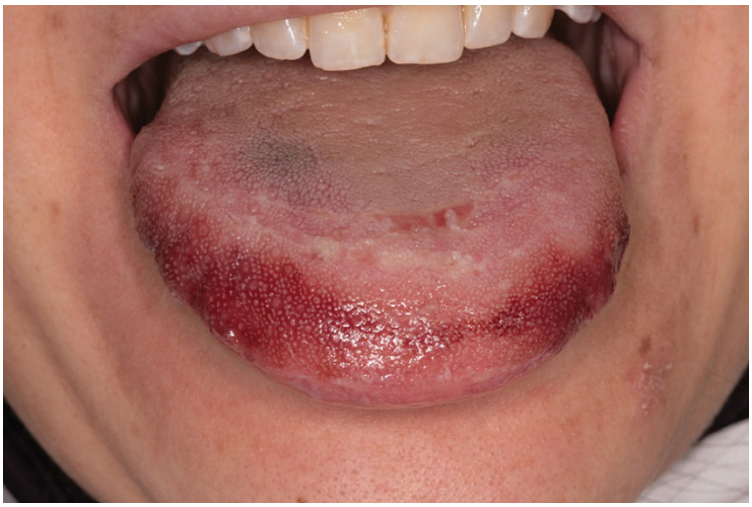

Figure 1.0 Tongue hematoma in a woman with seizures.

Clinical Guide to Oral Diseases, First Edition. Dimitris Malamos and Crispian Scully.

Companion website: www.wiley.com/go/malamos/clinical_guide

Table 1 Conditions related to oral bleeding.

Common and important conditions
• Local conditions
▪ Gingivitis/periodontitis
▪ Granuloma pyogenic/giant cell
▪ Jaw fracture
▪ Trauma
▪ Tumors invading blood vessels
• Systemic conditions
○ Congenital
▪ Hemophilia A or B
▪ Von Willebrand's disease
▪ Other factor deficiencies
▪ Glanzman thrombasthenia
○ Acquired
– related to coagulation
▪ Liver disease
▪ Vit. K deficiency, warfarin drug use
▪ Disseminated intravascular coagulation
– related to thrombocytopenia
▪ Idiopathic
▪ Drug-induced
▪ Collagen vascular disease
▪ Sarcoidosis
▪ Hemolytic anemia
▪ Leukemia
▪ Myeloma
▪ Waldestmom
– related to platelet dysregulation
▪ Alcoholism
▪ Chronic renal failure
▪ Drugs
▪ Liver disease
– related to vascular disorders
▪ Angina bullosa hemorrhagica
▪ Angiomas
▪ Ehrler-Danlos syndrome
▪ Hereditary hemorrhagic telangiectasia
▪ Infections from Ebola, HIV, HSV; EBV, Rubella
▪ Marfan syndrome
▪ Purpura
▪ Scurvy
– related to fibrinolysis
▪ Amyloidosis
▪ Streptokinase treatment

Table 1 (Continued)

Case 1.1

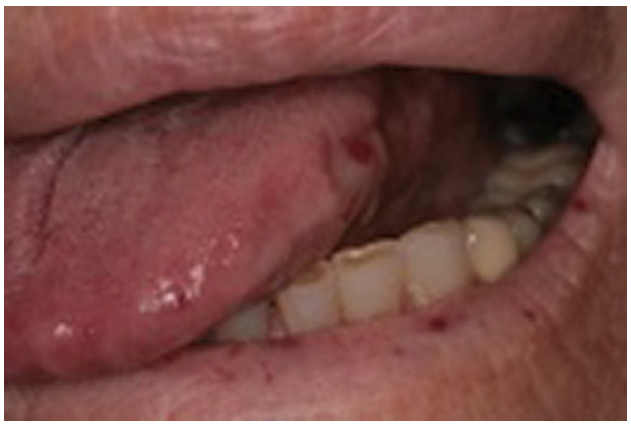

Figure 1.1a

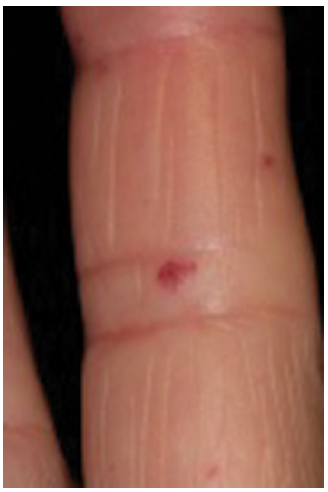

Figure 1.1b

CO: A 62-year-old woman was referred by her family doctor for evaluation of several red spots on her lips, mouth, and the skin of her fingers.

HPC: The red spots had been present since childhood, but had become greater on the surface of her face over the last five years causing cosmetic problems and patient's concern.

PMH: Her medical history revealed a chronic iron deficiency anemia which still remained despite the fact that

The following abbreviations are used throughout the book – CO: Complains of; HPC: History of present complaint; PMH: Past medical history; OE: oral examination.

the patient was in the post-menopause phase and had been treated occasionally with iron tablets. No other serious medical problems were recorded except for a few episodes of nose and gut bleeding which had caused her to ask for medical advice. She was a non-smoker and non-drinker.

OE: The examination revealed numerous red vascular papules, variable in size, ranging from pin head-like lesions to small red plaques at the vermilion border of her lips, and on the tongue and buccal mucosae (Figure 1.1a). A few asteroid-like red lesions, were also seen on the skin of her fingers (Figure 1.1b) and inside her nose which were responsible for her episodes of epistaxis.

Q1 Which is the possible cause of her red spots?

- **A** Crest syndrome
- **B** Sjogren syndrome
- **C** Rendu-Osler-Weber syndrome
- **D** Rosacea
- **E** Ataxia-telangiectasia

Answers:

- **A** No
- **B** No
- **C** Rendu-Osler-Weber syndrome or hereditary hemorrhagic telangiectasia (HHT) is a rare autosomal dominant condition that affects blood vessels throughout the body (telangiectasia; arteriovenous malformations) with a tendency for bleeding. This vascular dysplasia is commonly seen in oral, nasopharynx, lung, liver, spleen, gastrointestinal and urinary tracts, conjunctiva and the skin of arms and fingers.
- **D** No
- **E** No

Comments: Skin telangiectasias are also seen in patients with ataxia telangiectasia, Crest and Sjogren syndromes. In rosacea, main vascular lesions are the broken vessels that are located exclusively on the skin predominantly on the middle of the face, as in ataxia telangiectasia. In ataxia telangectasia, the vascular lesions are associated with poor coordination, and in Crest syndrome with calcinosis and sclerodactyly and Raynaud phenomenon. Sjogren's syndrome affects the mouth, eyes, nose and other organs causing dryness, swelling of the salivary glands and facial telangiectases.

Q2 Which are the main complications of this condition?

- **A** Anemia
- **B** Pulmonary hemorrhage
- **C** Ischemic stroke
- **D** Skin photosensitivity
- **E** Mental retardation

Answers:

- **A** Iron deficiency anemia is a very common complication induced by a series of episodes of blood loss through the nose (epistaxis) and gastrointestinal tract (melena stools) from telangiectic lesions.
- **B** Pulmonary hemorrhage is mainly found in patients older than 40 years old and with multiple visceral involvements, causing breathing problems, portal hypertension and liver cirrhosis.
- **C** Ischemic stroke is a rare yet serious complication in patients with HHT, and requires special care.
- **D** No
- **E** No

Comments: The vascular lesions on facial skin sometimes cause cosmetic problems, but never skin photosensitivity, while the brain lesions of HHT may cause neuro-psychiatric complications with various pathways which have not been related to mental illness before.

Q3 Which genes are linked with this condition?

- **A** Endoglin gene (ENG)
- **B** Fibroblast growth factor receptor 3 (FGFR3)
- **C** Activin receptor like kinase (ALK-1)
- **D** Collagen type I alpha 1 chain(COL1A1)
- **E** Dentin sialophosphoprotein (DSPP)

Answers:

- **A** Engoglin gene mutations have been isolated in HHT families (type 1)
- **B** No
- **C** Activin receptor like kinase (ALK-1)mutations have been found in HHT (type 2)

Comments: Mutations in the COL1A1 and COL1A2 genes are related to the development of the majority of osteogenesis imperfecta (>90%), while FGFR3 is associated with fibrous dysplasia and DSPP with dentinogenesis imperfecta.

Case 1.2

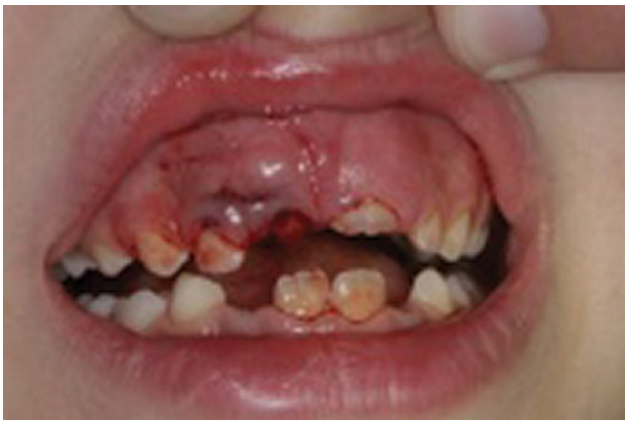

Figure 1.2

CO: A six-year-old boy was admitted with bleeding of his mouth.

HPC: The patient sustained a facial injury during a football match half an hour before the bleeding.

PMH: He was a healthy child with no serious medical problems. He was very sociable, and used to take part in all activities at his kindergarten.

OE: He is a very young child, feeling stress and fear because of the bleeding in his mouth, especially from the area of deciduous central right incisor. This tooth had been pushed into its hemorrhagic and swollen gingivae (Figure 1.2). No other problems with the rest of his teeth, jaws, and oral mucosa were noticed.

Q1 What is the possible cause of the hemorrhage of this child?

- **A** Trauma
- **B** Self-induced
- **C** Infections
- **D** Children abuse
- **E** Bleeding disorders

Answers:

- **A** Facial trauma is commonly noticed among children and characterized by soft tissue injuries (lips, oral mucosae, face) or deep ones into the maxilla or mandibular bone and their associated teeth. Facial trauma is responsible for the "impressive" bleeding due to the high vascularity of this area.
- **B** No
- **C** No
- **D** No
- **E** No

Comments: The absence of multiple bruises and hematomas alone, or with the different ages of lesions combined with the history of the accident and type of injuries in a child's body is an easy way to exclude bleeding disorders or child abuse from the diagnosis. The absence of fever, swelling and erythema in the lesion rules out infections (bacterial, viral, or fungal). In addition to this, the lack of similar lesions in the past together with the child's good healthy social life reinforces the idea that the lesion was not self-induced.

Q2 Which is/are the difference(s) of facial trauma between children and adolescents?

- **A** Etiology
- **B** Bone involvement
- **C** Symptomatology
- **D** Complications
- **E** Recovery rate

Answers:

- **A** Facial trauma is caused by falling in children and by assault or altercation in adolescents.
- **B** Fractures of nose bones or jaws are more common in adolescents rather than in children.
- **C** The symptomatology in children does not fit with the severity of the lesions and is more remarkable than in adolescents.
- **D** The facial trauma in children is more superficial than in adolescents and their complications seem to be minimal.
- **E** The younger the children, the easier their recovery.

Q3 Which is the clinician's first priority when faced with a patient with facial injury?

- **A** Calm patient and his parents
- **B** Retain the airway open
- **C** Check for broken or dislocated teeth
- **D** Stop bleeding
- **E** Treat facial wound (cleaning and suturing)

Answers:

- **A** No
- **B** Retaining child's airway open is the first priority as the mucosal edema is disproportional with the patient's airway tract. The clinician should remove obstacles like debris, clots and foreign bodies

from the oropharynx, control the location of patient's tongue while in severe cases an orotracheal intubation could be mandatory.

C No
D No
E No

Comments: The second priority for the clinicians is to control bleeding by putting direct pressure on the facial injury. Having bleeding under control, clinicians are then able to properly examine the soft tissue injury, investigate for possible teeth and jaws fractures and then go further to cleanse and suture the wound, as well as reassuring the patient and his parents.

Case 1.3

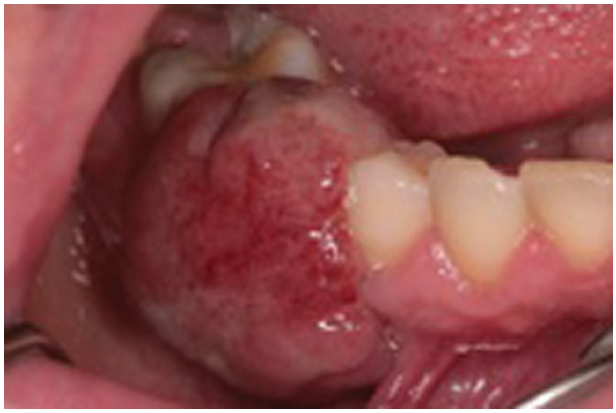

Figure 1.3

CO: A 32-year-old woman presented with a soft hemorrhagic lump on her lower left gingivae.

HPC: The lump appeared three months ago and became gradually bigger, covering the whole crown of the second premolar, thus causing eating difficulties and phobias to the patient of being a malignant neoplasm.

PMH: A healthy woman at the third month after baby delivery, with no serious medical problems and drug use apart from iron and calcium tablets prescribed by her gynecologist during her pregnancy. Smoking or drinking habits were plentiful.

OE: A very soft penduculated mass on the gingivae from the distal part of the 1st lower right premolar to the 1st molar. It was very soft, vascular and sensitive, and was bleeding easily with slight probing and caused eating problems (Figure 1.3). The lesion developed gradually and reaching its biggest site at the last month of pregnancy and began to decrease slowly within the next three months after her delivery. No other similar lesions were found within her mouth, other mucosae or skin. Regional or systemic lymphadenopathy was not recorded.

Q1 What is this lesion?

A Kaposi's sarcoma
B Pregnancy epulis
C Peripheral giant cell granuloma
D Gingival hemangioma
E Peripheral ossifying fibroma

Answers:

A No
B Pregnancy epulis is a localized hyperplastic hemorrhagic soft lesion on the upper and lower gingivae of pregnant women with decayed teeth and poor oral hygiene. The lesion grows slowly and reaches its largest size during the last trimester of pregnancy.
C No
D No
E No

Comments: In contrary to pregnancy epulis the gingival hemangiomas are found earlier (at childhood); sarcoma Kaposi are usually associated with lymphadenopathy and have an aggressive course. The peripheral odontogenic fibroma has a firmer feel on palpation, while the peripheral giant cell epulis does not improve with the baby's birth and is associated with endocrinopathies.

Q2 Which are the other oral conditions seen during pregnancy?

A Melasma
B Pregnancy gingivitis
C Increased risk of caries
D Erosions of teeth
E Sialorrhea

Answers:

A No
B Pregnancy gingivitis is the commonest complication of pregnancy and can start even from the second month, reaching its peak on the eight

month of pregnancy. This type of gingivitis is due rather to the action of increased female hormones on their gingival receptors rather than to microbial plaque.

C Pregnant women tend to be at increased risk of caries as the number of cariogenic bacteria in the mouth, and the frequency of eating, especially sweet food as a means of coping with nausea, are increased.

D Erosions on the palatal tooth surface and especially on the upper anterior teeth are common and are also attributed to the acidity of gastric juice that reaches the mouth during vomiting.

E Sialorrhea is a common finding in pregnant women and caused by the increased nausea and vomiting recorded during their pregnancy.

Comments: Melasma or pregnancy mask as it is known, is characterized by a brown discoloration of the facial skin and lips, but is never seen within the mouth of pregnant women and those taking contraceptives or hormone replacement medications.

Q3 Which conditions have been detected in babies, related to the periodontal status of their mothers?

A Premature birth
B Low weight
C Vision or hearing deficits
D Mental retardation
E Dental anomalies

Answers:

A Women with chronic inflammation of their gingivae seem to produce a number of inflammatory cytokines, some of which are responsible for the uterine muscle contractions which finally induce early labor.

B Premature babies show incomplete growth and low weight.

C Vision or hearing deficits are commonly seen in premature babies whose early birth may be associated with the periodontal problems of their mother.

D No

E No

Comments: The mental status of pregnant women may worsen their periodontal problems by increased secretion of cortisol and refusal of tooth brushing, while the periodontitis per se does not affect the mental status or dentition of their children.

Case 1.4

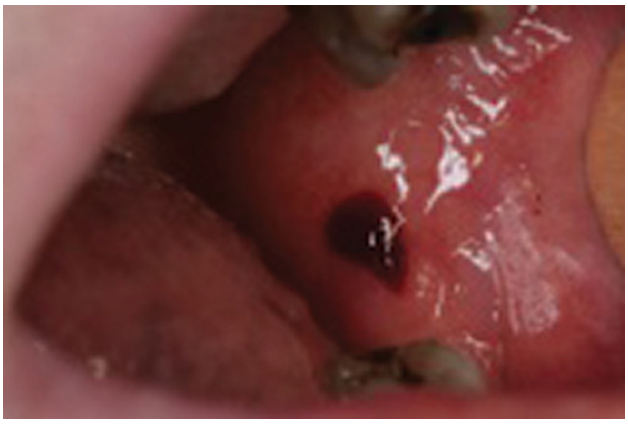

Figure 1.4

CO: A 42-year-old woman came in with a hemorrhagic bulla inside her cheek.

HPC: The bulla appeared three hours ago after eating a sandwich. No similar bullae were recorded in her or her close relatives in the past.

PMH: From her medical records a few episodes of allergic rhinitis controlled with antihistamine and steroids in crisis were recorded. No blood and other systemic diseases, other allergies or drug uptakes were recorded.

OE: Examination revealed a large bulla with hemorrhagic content on the left buccal mucosa at the occlusion level (Figure 1.4). The bulla appeared during mastication and was easily broken during the examination's manipulations, leaving a painful superficial ulceration. No other bullae, ulcerations or petechiae and ecchymoses were seen on the oral and other mucosae or skin. Cervical lymphadenopathy was not seen.

Q1 Which is the disease responsible for this bulla?

A Thrombocytopenia
B Burns
C Mucous membrane pemphigoid
D Angina bullosa hemorrhagica
E Hemorrhagic mucocele

Answers:

- **A** No
- **B** No
- **C** No
- **D** Angina bullosa hemorrhagica (ABH) is an acute, benign condition characterized by the development of subepithelial bullae filled with blood that are not attributed to any systemic disorders. A chronic trauma, consumption of hot and spicy or abrasive foods, or difficulties in restorative or periodontal treatment are considered to be the commonest causes.
- **E** No

Comments: Hemorrhagic bullae are often seen in other conditions such as thrombocytopenia, mucous pemphigoids and burns, but the presence of specific elements indicated the diagnosis. The appearance of low platelets and ecchymoses, epistaxis, and gingival bleeding in thrombocytopenia, the presence of numerous bullae with clear fluid in mucous pemphigoid, and the lack of close contact with thermal, chemical, or electrical elements in burns help to exclude these conditions from the diagnosis. Mucoceles are thicker and more resistant, while the bullae in angina are thinner and more easily break.

Q2 Which of the drugs below are usually related to the development of this condition?

- **A** NSAIDs
- **B** Antibiotics
- **C** Steroids
- **D** Anti-diabetics
- **E** Bronchodilators

Answers:

- **A** No
- **B** No
- **C** Chronic use of steroids, especially inhalers, causes oral mucosa atrophy and decreases the submucosa's elastic fiber content, resulting in capillary breakdown locally, finally forming the characteristic hemorrhagic bullae.
- **D** No
- **E** No

Comments: Diabetes mellitus has also been associated with hemorrhagic bulla formation due to increased vascular fragility in these patients, and not to the drug for blood sugar reduction. Similar bullae could also be seen in patients who take antibiotics or bronchodilators and have various autoimmune diseases. As for NSAIDs, these drugs are responsible for peptic ulcers and bleeding from the intestine, but more rarely for skin bullous rash and fever.

Q3 Which of the histopathological finding(s) is/or are characteristics of this condition?

- **A** Subepithelial bulla
- **B** Intra-epithelial abscess of neutrophils
- **C** Mononuclear inflammatory infiltration of submucosa deep to the muscles
- **D** Direct immunofluorescence negative
- **E** Eosinophils accumulation in the corium

Answers:

- **A** The breakage of the epithelial–connective tissue junction due to topical agents leads to local capillary hemorrhage and subepithelial bulla formation.
- **B** No
- **C** No
- **D** Direct immune-fluorescence is always negative. DI is always positivein pemphigus and other intra-epithelial blistering diseases.
- **E** No

Comments: The inflammatory response in ABH is intense and located only at the superficial parts of submucosa, often containing neutrophils but not eosinophils and mast cells.

Case 1.5

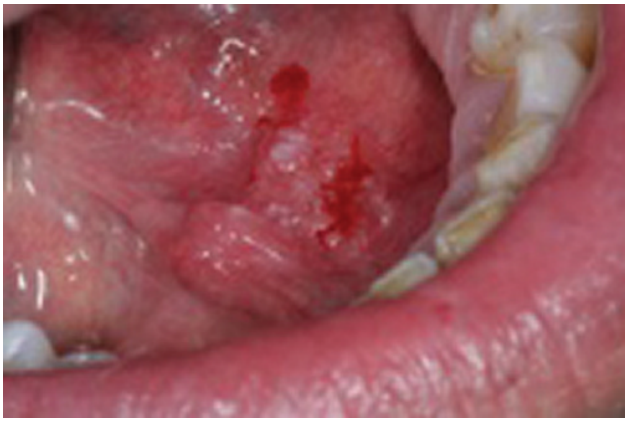

Figure 1.5

CO: A 48-year old man was presented with a hemorrhagic lesion on the floor of his mouth.

HPC: The lesion appeared six months ago while the bleeding was noticed during eating three days ago.

PMH: No serious medical problems were recorded apart from an episode of severe pneumonia which was diagnosed last December and was treated with a strong course of antibiotics. No other drugs were taken, but the patient was a smoker (>40 cigarettes, daily) and a drinker (4–5 glasses of wine or relevant spirit per meal).

OE: The examination revealed an asymptomatic white lesion on the floor of mouth extended from the left lower premolar to the molar region. The lesion was fixed in palpation and had a warty-like surface with two to three bleeding areas (Figure 1.5). Smoking-induced lesions such as increased gingival pigmentation, nicotinic stomatitis and brown teeth discoloration were also found, together with ipsilateral, fixed, enlarged cervical lymph nodes where oral or skin petechiae and ecchymoses were not seen.

Q1 What is the cause of bleeding?

- **A** Traumatic ulceration
- **B** Pemphigus vegetans
- **C** Verrucous leukoplakia
- **D** Giant verruca vulgaris
- **E** Squamous carcinoma

Answers:

- **A** No
- **B** No
- **C** No
- **D** No
- **E** Squamous cell carcinoma is the cause of his oral bleeding. This tumor is a locally aggressive, tumor which appears as an indurated swelling , ulceration or plaque of various cellular differentiation and risk of metastasis. This lesion grows either slowly and superficially, but in majority of cases grows fast and invades deep tissues such as muscles and blood vessels causing muscle dysfunction and bleeding.

Comments: This tumor differs from other vegetating oral lesions such as hyperplastic traumatic ulcerations, pemphigus vegetans, verrucous leucoplakia, and verrucous vulgaris. The lack of local trauma or other vegetating lesions in the flexures of the patient rules out traumatic ulceration and pemphigus vegetans from the diagnosis, while the hard consistency and strong fixation of the lesion with the underling tissues is not an indication of verrucous vulgaris and leukoplakia where biopsy is required.

Q2 Although the verrucous carcinoma is a variation of oral carcinomas, it differs from the other types in the following histological characteristics:

- **A** Evidence of dysplasia in adjacent epithelium
- **B** Shape of the rete pegs
- **C** Absence of keratinization
- **D** Location of mitosis
- **E** Basal basement membrane status

Answers:

- **A** Dysplastic epithelium is often seen close to the oral squamous, but not to verrucous carcinomas.
- **B** The shape of rete pegs entering the corium is variable in the majority of oral carcinomas, but is bulbous, like elephant feet in verrucous carcinoma.
- **C** No
- **D** In oral carcinomas, the mitoses are scattered in the basal and spinous layer, while in verrucous carcinoma they are located mainly in the basal layer.
- **E** In oral carcinomas the basal membrane is invaded by tumor islands, but in verrucous carcinoma it is intact and the tumor grows superficially as well.

Comments: Keratinization is commonly seen in both tumors; however keratin pearls are mainly found in squamous carcinoma, while keratin plugs are found in verrucous carcinomas.

Q3 Which of the measures below is/are not amenable to control bleeding from an oral carcinoma?

- **A** Identification of the underlying cause of oral bleeding
- **B** Blood investigations
- **C** Packing-dressing
- **D** Suturing
- **E** Radiotherapy

Answers:

- **A** No
- **B** No
- **C** No
- **D** No
- **E** Radiotherapy is sometimes useful to the control of excessive bleeding that may arise from lung but not oral carcinomas. Patients with oral carcinomas and other head and neck tumors have already received the maximum dose of radiotherapy when bleeding begins, and therefore other aggressive measures such as arterial embolization should be undertaken.

Comments: Clinicians must control oral bleeding by following some basic steps such as the identification of the causative factor by taking a comprehensive history and careful clinical examination; excluding bleeding diseases by checking white blood count and clotting profiles as well as packing or dressing with hemostatic agents, while in more severe cases with cauterization, suturing, or embolization should be used.

Case 1.6

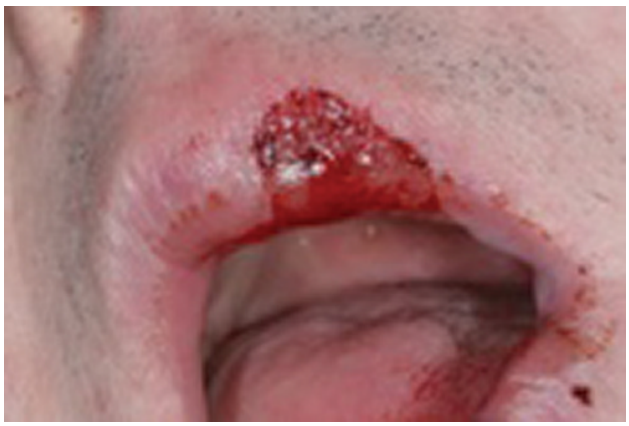

Figure 1.6a

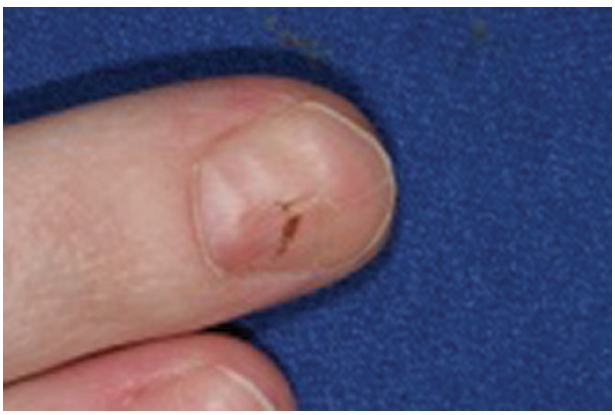

Figure 1.6b

CO: A 24-year-old male was referred for an evaluation of bleeding from his upper lip.

HPC: The hemorrhage appeared on his upper lip during eating from a broken bulla three hours ago.

PMH: This young man suffers from Down syndrome and over the last two years he has been complaining about multiple bullae on the skin of his legs, mouth, and genitals. He had a short course of steroid cream for skin bullae which was not effective, causing him to refuse any other medications since then.

OE: An anxious young man, showing numerous ulcerations inside his mouth, lips, and legs as a result of ruptured bullae due to friction. A hemorrhagic ulceration on his upper lip (Figure 1.6a) together with a tiny hemorrhage of the nail bed of his middle finger was found (Figure 1.6b). No other hemorrhagic lesions (petechiae or ecchymoses) were seen inside his mouth, skin or other mucosae. On the other hand, epistaxis was not referred and general symptomatology was absent. The patient was admitted to an examination, and blood results revealed no clotting

disorders while biopsy of the skin revealed a subepithelial bulla with positive immunofluorescence of IgG and C3 along the basement membrane zone (BMZ).

Q1 What is the cause of his lip bleeding?

- **A** Self-induced lip trauma
- **B** Pemphigoid disorders
- **C** Clotting disorder
- **D** Erythema multiforme
- **E** Herpetic stomatitis

Answers:

- **A** No
- **B** Pemphigoid bullous diseases (mucous and bullous) are a group of subepithelial bullous disorders which affect mainly the mouth (mucous type; or less frequently bullous type) or the skin. They have a characteristic immunofluorescence profile. Their bullae break easily and leave painful hemorrhagic ulcerations covered with hemorrhagic crusts as seen in this patient.
- **C** No
- **D** No
- **E** No

Comments: Clotting disorders are easily excluded from the diagnosis as the blood tests were negative. Herpetic stomatitis causes similar hemorrhagic oral lesions but is ruled out as this condition lacks chronic skin lesions and its severe mouth lesions occur only once and not constantly, as seen in this patient. Erythema multiforme shows similar findings with the patient's lesions, but is also excluded due to the short duration of its lesions and presence of fibrin instead of IgG and C_3 with BMZ. Factitious illness is a problem in the disabled but not in Down syndrome patients, as these are less likely to develop maladaptive behavior and the patient did not show any aggressive behavior capable of causing self-induced lesions in his body.

Q2 Which of the bullous disorders is/or are initiated with urticarial skin lesions?

- **A** Pemphigus vulgaris
- **B** Bullous pemphigoid
- **C** Cicatricial pemphigoid
- **D** Paraneoplastic pemphigus
- **E** Dermatitis herpetiformis

Answers:

- **A** No
- **B** Bullous pemphigoid is a chronic subepithelial blistering disease that starts as an urticarial eruption which develops large firm bullae, especially in flexor skin areas over a course of weeks to months.
- **C** No
- **D** No
- **E** Dermatitis herpetiformis is a chronic pruritic papulovesicular eruption which is associated with urticarial wheals and located symmetrically on the extensor surfaces of skin.

Comments: Although paraneoplastic pemphigus and cicatricial pemphigoid are chronic bullous disorders affecting oral and other mucosae and appear either as fragile intra-epithelial bullae associated with a neoplasm (leukemia or lymphoma) or subepithelial bullae, they are never associated with pruritic rash and scarring.

Q3 Which lip conditions are presented with lip bleeding?

- **A** Exfoliate cheilitis
- **B** Erythema multiforme
- **C** Actinic prurigo
- **D** Granulomatous cheilitis
- **E** Perioral dermatitis

Answers:

- **A** Exfoliate cheilitis is a common cheilitis characterized by the production of keratin scales in the vermilion border of lips in young women with anxiety, who have the habit of removing the scales by rubbing them against their teeth thus leaving ulcerated hemorrhagic lesions.
- **B** Erythema multiforme is an acute mucocutaneous reaction characterized by erythematous plaques, painful hemorrhagic bullae and erosions in the skin (target like lesions), in the mouth and other mucosae. The presence of hemorrhagic crusts on the lips is pathognomonic for this condition.
- **C** Chronic exposure to solar radiation causes actinic prurigo, a photodermatosis affecting the skin, lips and conjunctiva. Lips are usually erythematous, scaly and in places bleed while the skin lesions appear as itchy, red papillae or nodules on cheeks, nose, forehead or arms, and eyes showing hyperemia, photophobia and pseudopterygium.
- **D** No
- **E** No

Comments: Perioral dermatitis is a chronic itchy papulopustular rash affecting the skin around the mouth while granulomatous cheilitis is a chronic, persistent swelling of lips due to granulomatous inflammations. Neither of them have a bleeding tendency.

Case 1.7

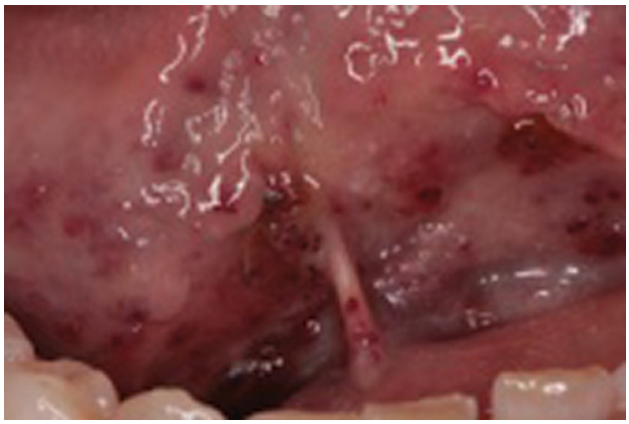

Figure 1.7

CO: A 36-year-old woman was presented with hemorrhage from her tongue.

HPC: Her tongue bleeding appeared one month ago when she gave birth to a baby girl. The bleeding had arisen from a superficial strawberry-like soft mass on the dorsum and inferior part of her tongue while it deteriorated with mastication movements.

PMH: Her medical history revealed no serious diseases such as bleeding disorders. A case of iron deficiency anemia was only recorded since puberty which was treated with iron supplements as well as a few tongue surgeries for the elimination of a vascular lesion of her tongue in the past. The patient was not a supporter of smoking or drinking habits, while she used to spend her free time painting.

OE. The oral examination revealed multiple small hemorrhagic dots on the dorsum and inferior part of tongue (Figure 1.7) which were similar to a mature strawberry. These dots are superficial and could easily bleed with touching, and were overlying a soft vascular mass. This mass was detected when she was one year old, and became larger during puberty, requiring surgery. It remained stable until her pregnancy when it became bigger and was occasionally bleeding. No other similar lesions, petechiae, or ecchymoses were found on her body.

Q1 What is the cause of bleeding?

- **A** Hemangioma
- **B** Vascular malformation
- **C** Kaposi sarcoma
- **D** Pregnancy pyogenic granuloma
- **E** Wegener granulomatosis

Answers:

- **A** No
- **B** Vascular malformations are characterized by abnormalities of the capillary, venous or arteriovenous vascular bed which appear at birth or a few months later, and grow gradually. Contrary to other vascular lesions though, they do not resolve; instead they can be exacerbated with various conditions such as pregnancy.
- **C** No
- **D** No
- **E** No

Comments: Based on the early onset and long duration of this single lesion,without resolution throughout the coming years hemangiomas are easily excluded while the long duration and slow progress without other similar lesions in patient's body or general symptomatolog rules out extensive pyogenic grannulomas or Wegener granulomatatosis from the diagnosis.

Q2 What are the differences between hemangiomas and vascular malformations?

- **A** Location
- **B** Course
- **C** Symptomatology
- **D** Pathogenesis
- **E** Complications

Answers:

- **A** No
- **B** Hemangiomas appear mostly at birth, grow rapidly and resolve during puberty while vascular malformation remain or even worsen.
- **C** No
- **D** Hemangiomas are characterized by endothelial hyperplasia while in vascular malformations the endothelial cell turnover is normal.
- **E** Both hemangiomas and vascular malformations cause a variety of complications from mild esthetic disfiguration to severe possibility of jeopardizing the patient's life dependent on the size and location of the lesion closely to vital organs.

Q3 Which of the syndromes below is/or are not associated with this condition?

- **A** Sturge-Weber syndrome
- **B** PHACE syndrome
- **C** Proteus syndrome
- **D** Maffucci syndrome
- **E** Blue rubber bleb nevus syndrome (BRBNS)

Answers:

A No
B PHACE syndrome is characterized by multi-organ lesions such as posterior fossa anomalies; facial hemangiomas, arterial and cardiac anomalies as well as eye problems
C No
D No
E No

Comments: Abnormal vascular malformations are often seen in a number of syndromes like Sturge-Weber; Maffucci, Proteus and blue rubber belb but all of them have different clinical presentation. Sturge-Weber syndrome is characterized by numerous facial (port-wine stain) and cerebral angiomas, glaucoma, seizures and mental retardation while in Maffucci syndrome, angioma is associated with numerous endochondromas. Proteus syndrome has characteristic skin, bone, muscle and vascular abnormal growths, while venous malformations of the gastrointestinal tract and skin are seen in blue rubber bleb nevus syndrome.

Case 1.8

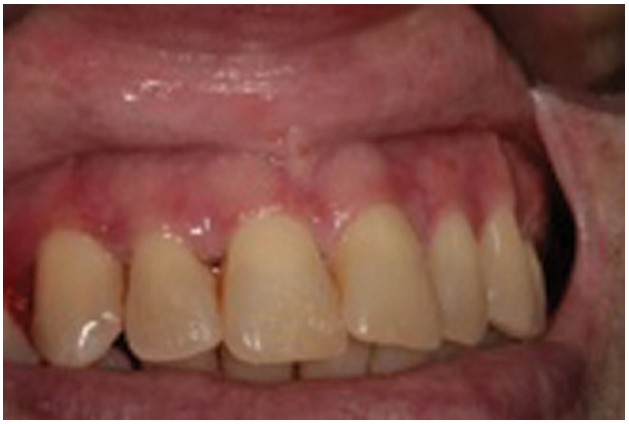

Figure 1.8

CO: A 68-year-old woman was presented with hemorrhagic gingivae over the last three months.

HPC: Her gingivae showed areas of hemorrhage over the last three months and was associated with generalized lymphadenopathy, fever, weight loss and sweating at night.

PMH: Hyperlipidemia and diabetes mellitus were the only serious diseases reported. A recent blood check-up revealed an increased number of eosinophils and lymphocytes as well as chronic sideropenic anemia, despite her proper diet. No smoking or drinking habits, but a chronic exposure to chemicals because of her job at a painting industry was reported.

OE: The examination revealed swollen, soft, edematous and hemorrhagic gingivae that were associated with a few scattered petechiae on buccal mucosae. The gingivae were pale and easily bled from the interdental papillae (Figure 1.8). A few ecchymoses were also found on her legs and associated with a generalized lymph node enlargement.

Q1 What is the cause of her gingival bleeding?

A Acute ulcerative gingivitis
B Scurvy
C Leukemia
D Plasma cell gingivitis
E Wegener disease

Answers:

A No
B No
C Leukemia is the cause. Leukemia is a malignant neoplasm of white blood cells characterized by an abnormal growth of a certain type of white cells, anemia, easy bruising or bleeding, susceptibility to infections, swollen lymph nodes, together with weight loss and night sweating, as was also observed in this patient who was finally diagnosed of having chronic lymphocytic leukemia
D No
E No

Comments: Gingival bleeding is a common finding in other local conditions such as in acute ulcerative and plasma cell gingivitis, or systemic diseases such as Wegener disease and scurvy. The lack of necrosis of interdental papillae (seen in acute ulcerative gingivitis) and the erythematous and edematous red attached gingivae (in plasma cell gingivitis) or the erythematous swollen-like-strawberries gingivae (in Wegener disease) and the ulcerated, swollen gingivae with deep pocketing (in scurvy) exclude the above diseases from the diagnosis.

Q2 Which laboratory tests are routinely used for the diagnosis of this condition?

A White blood count
B Immunophenotypic analysis with flow cytometry
C Bone marrow biopsy
D Urine analysis
E Cerebral fluid biochemical analysis