

TABLE OF CONTENTS

1. Dental management of patients taking Warfarin <i>Amrutha KP</i>	<i>pg 5</i>
2. Dental management of patient taking Aspirin <i>Sidharth Manoj</i>	<i>pg 14</i>
3. Changing trends of Lichen Planus: Is stress the real culprit in early onset of Lichen Planus in adolescent age group? <i>Dr. Anlin Anto</i>	<i>pg 22</i>
4. Peripheral presentation of Central Schwannoma in the floor of the mouth: Perplexing entity <i>Dr. Saranya Raj P</i>	<i>pg 27</i>
5. Oral melanotic macule <i>Dr. Thulasi Raj</i>	<i>pg 36</i>

Literature Review

DENTAL MANAGEMENT OF PATIENTS TAKING WARFARIN

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Abstract

The possibility of postoperative bleeding in patients taking warfarin is a concern for dentists. However, before deciding if warfarin therapy should be interrupted the risk of preoperative or postoperative bleeding must be balanced against the risk of thromboembolism. Before dental treatment a thorough medical history should be obtained including details of any condition likely to be treated with warfarin. The dentist should also consider possible drug interactions with warfarin. Medications including antibiotics such as Metronidazole, herbal remedies and alcohol may unpredictably alter the INR. If an interaction is considered likely or if the effect of any prescribed medication is not known, the dentist should consult the doctor supervising the patient's anticoagulant therapy. The INR should be checked before surgery. The purpose of this article is to discuss about the dental and surgical management of the patients who are on warfarin therapy.

Key Words: warfarin, management, anticoagulant

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Introduction

Warfarin is an anticoagulant which helps in reducing the formation of blood clots. Warfarin is used to treat or prevent blood clots in veins or arteries, which can reduce the risk of stroke, heart attack, or other serious health conditions.¹

Warfarin is an anticoagulant which inhibits synthesis of the vitamin K-dependent coagulation factors II, VII, IX and X.

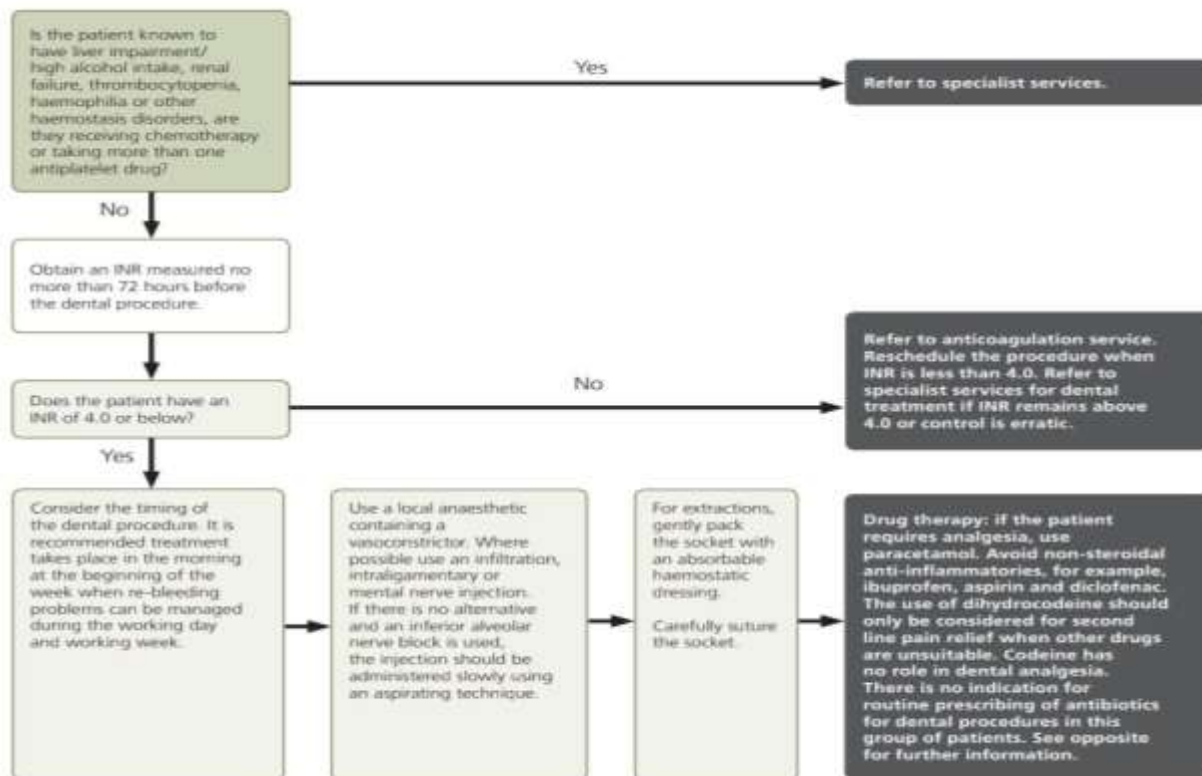
Indications for anticoagulation are increasing, and dentists will be consulted by patients taking warfarin.²

The activity of warfarin is expressed using the international normalised ratio (INR).³ A normal coagulation profile has an INR of 1.0. The desirable INR range for patients depends on the condition being treated. Patients receiving treatment for deep vein thrombosis have a lower target range than

those with prosthetic heart valves.⁴ The risk of bleeding increases exponentially as the INR rises. Gingival bleeding can indicate a raised INR. Oral surgery can be completed safely with an INR from 1.5 to 2.5.⁵ Teeth may be removed by simple extraction with

an INR of 2-4.⁶ However dentists should still be cautious before they remove teeth where the INR exceeds 3. In this article we are going to discuss about how to manage the patients who is on warfarin therapy.

Table 1: Dental management of patients on warfarin treatment



Dental management of patients on warfarin treatment

Patients who receive warfarin management and undergo surgical procedure may be at risk of bleeding, and as a result, a range of guidelines exist relating to the management of such patients prior to surgical intervention. The American College of Chest Physicians suggests that patients

should stop warfarin 5 days before any surgical intervention, and also that warfarin

should be temporarily replaced with low molecular weight heparin as a bridge therapy.⁷ The American Heart Association, in contrast, suggests reducing the INR to a range between 2.0 and 2.5, with strict INR monitoring.⁸

Teeth extraction is a procedure where bleeding can be encountered. The difficulty of the extraction itself or complications related to the procedure may affect the risk of bleeding in at-risk patients. Simple tooth extraction involves gentle forceps manipulation of the tooth with minimal trauma to the tissue. A patient undergoing warfarin treatment should be carefully evaluated prior to such a dental procedure.^{9,10} There is always controversy related to the modification of warfarin treatment prior to dental procedure. The rebound hypercoagulability after suddenly stopping warfarin treatment has been reported in the literature.¹¹

Bacci et al¹² have shown that teeth extraction can be done safely in patients taking anticoagulants without any modification of the anticoagulation therapy. It has been shown that patients who have comorbidities such as diabetes, liver disease, and chronic renal failure need to bring their INR within a narrower safety range, with upper limit of between 2.5 and 2.8 to avoid serious bleeding complications during oral surgical procedures.¹³

The INR reading should be obtained at the same day of surgical procedure. This was obtained by the help of the CoaguChek system, which can give the value of INR within seconds. Since the presence of underlying disease such as liver or coagulopathies can increase the risk of bleeding in patients on warfarin treatment,¹³ it is advisable that any patient with complicated medical history and warfarin treatment should be treated under special conditions.

The risk of bleeding in medically compromised patients who are taking

warfarin could be due to changes in the physiologic process of hemostasis, epithelialization, and maturation of wounds following dental surgery.¹⁴

What is the normal INR range?

The activity of warfarin is expressed using the international normalised ratio (INR). For an individual not taking warfarin a normal coagulation profile is an INR of 1.0.¹⁵

Are patients at risk of thromboembolic events if warfarin is stopped?

Stopping warfarin for two days increases the risk of thromboembolic events. This risk is difficult to estimate but is probably between 0.02% and 1%.

It has been common in primary care dental practice to discontinue warfarin treatment for a few days prior to dental surgery in order to limit bleeding problems. It has been assumed that stopping warfarin for a short period presents a negligible risk to the patient. The majority of patients had no adverse effects. This gives an incidence of serious thromboembolic complications of 1%.

The risk of thromboembolic events associated with the perioperative withdrawal of oral anticoagulants is also relevant to non-dental procedures. One survey among American dermatologists estimated that following withdrawal of warfarin for between two and seven days, one thromboembolic event occurred for every

6,219 cutaneous excisions (0.02%) conducted.¹⁵

Which patients taking warfarin should not undergo surgical procedures in primary care?

Patients who have an INR greater than 4.0 should not undergo any form of surgical procedure without consultation with the clinician who is responsible for maintaining their anticoagulation (this may be a physician or pharmacist in primary care or the hospital anticoagulant clinic). The warfarin dose will need to be adjusted prior to the procedure. Patients who are maintained with an INR >4.0 or who have very erratic control may need to be referred to a dental hospital or hospital based oral/maxillofacial surgeon.

The following medical problems may affect coagulation and clotting:

- Liver impairment and/or alcoholism
- Renal failure
- Thrombocytopenia, haemophilia or other disorder of haemostasis
- Those currently receiving a course of cytotoxic medication. Patients with any of these conditions who also take warfarin should not be treated in primary care but referred to a dental hospital or hospital-based dental clinic. Patients requiring major surgery are unlikely to be treated in the primary care setting.^{16 17}

For what procedures can warfarin be continued safely?

• Minor surgical procedures

Minor surgical procedures can be safely carried out without altering the warfarin dose. Those likely to be carried out in primary care will be classified as minor e.g. simple extraction of up to 3 teeth, gingival surgery, crown and bridge procedures, dental scaling and the surgical removal of teeth.¹⁸

When more than 3 teeth need to be extracted then multiple visits will be required. The extractions may be planned to remove 2-3 teeth at a time, by quadrants, or singly at separate visits.¹⁹

• Periodontal procedures

Periodontal examinations and supragingival scaling are considered to be low risk for bleeding. However, subgingival debridement may cause significant bleeding especially if the gums are inflamed.²⁰ Good plaque control is important before performing periodontal procedures in anticoagulated patients. Scaling and root planing should initially be restricted to a limited area e.g. one quadrant, to assess if the bleeding is problematic.

How should the risk of bleeding be managed?

Timing

Think about the timing of the surgery. Planned surgery should ideally be:

- At the beginning of the day - this allows more time to deal with immediate re-bleeding problems.
- Early in the week- this allows for delayed re-bleeding episodes occurring after 24–48 hours to be dealt with during the working week.^{21 22}

Local anaesthetic

A local anaesthetic containing a vasoconstrictor should be administered by infiltration or by intraligamentary injection wherever practical. The use of a short 27-gauge needle will minimise tissue damage. Regional nerve blocks should be avoided when possible. However, if there is no alternative, local anaesthetic should be administered cautiously using an aspirating syringe. Local vasoconstriction may be encouraged by infiltrating a small amount of local anaesthetic containing adrenaline (epinephrine) close to the site of surgery.²¹

Local haemostasis

Sockets should be gently packed with an absorbable haemostatic dressing²³ e.g. oxidised cellulose (Surgicel®), collagen sponge (Haemocollagen®) or resorbable gelatin sponge (Spongostan®), then carefully sutured. Haemostatic dressings promote and stabilise clot formation by providing a mechanical matrix. Trials in patients who have continued anticoagulant therapy throughout the perioperative period have used resorbable (catgut or synthetic (polyglactin, Vicryl®) or non-resorbable (silk, polyamide, polypropylene) sutures.

Resorbable sutures are preferable as they attract less plaque.

If non-resorbable sutures are used they should be removed after 4-7 days. Following closure, pressure should be applied to the socket(s) by using a gauze pad that the patient bites down on for 20 minutes.

Surgical management of patients taking warfarin

Key Recommendations

Warfarin discontinuation prior to invasive procedures is necessary for all interventional procedures except for minor skin procedures, routine dental work, cataract surgery, endoscopies without biopsy, and percutaneous venous access.

For elective procedures, warfarin should be stopped for 5 to 6 days prior to the procedure to allow gradual normalization of the international normalized ratio (INR).

For urgent procedures, use of prothrombin complex concentrate is highly effective in rapidly reversing warfarin anticoagulant activity and has a duration of action of ~ 6 hours.

The use of bridging heparin therapy is dependent on the risk of thrombosis.

Discuss the risk of bleeding with the surgeon and anesthesiologist to determine optimal timing for resuming warfarin and bridging heparin therapy after surgery.

Management

Therapeutic Measures for Reversal of Warfarin Therapy

Vitamin K

- Intravenous (IV) delivery is the fastest and most reliable way to obtain the effect of vitamin K.
- Intramuscular (IM) or subcutaneous delivery should be avoided..
- Effect on INR is observed after 8 - 12 hours, depending on route of administration.
- Recommended doses:
 - o Oral 1 - 2 mg, or
 - o IV 5 mg in 50cc normal saline infused over 30 minutes.²⁴

Management of Perioperative Anticoagulation

1. Acceptable INR for surgery

Discuss with surgeon and anesthesiologist what the goal INR should be before surgery.

Baseline INR is recommended in every case and this will guide further therapy.

An INR < 1.5 is generally acceptable except for neurosurgery, ocular surgery and procedures requiring spinal anesthesia or epidural analgesia.²⁵

2. Risk of bleeding

In general, the type of procedure determines the risk of bleeding and how long anticoagulation must be withheld post-operatively.

Discontinuation of warfarin is essential for procedures associated with a high risk of bleeding.

Discontinuation of warfarin is usually not necessary for procedures associated with a low risk of bleeding.

Assess with surgeon and anesthesiologist what the risk of bleeding from the procedure

3. Management based on risk of thrombosis

For low risk of thrombosis (including risk associated with preoperative and postoperative):

Discontinue warfarin 5 days prior to surgery. Therefore, give last dose on day 6, to achieve 5 warfarin-free days if day of surgery = day 0.

Check INR the day before procedure to ensure it is lower than the goal INR (< 1.5 for most procedures). If INR is higher than goal INR, discuss with physician performing procedure.

Restart warfarin at preoperative dose as soon as hemostasis is assured and only after epidural catheters are removed post-surgery.

Recheck INR within one week after starting warfarin at the last stable dose and resume regular monitoring and dose adjustment. Warfarin doses may change postoperatively if there were significant changes in

medication (especially use of antibiotics) or nutrition.

Patients can receive prophylactic doses of unfractionated heparin or LMWH for thromboprophylaxis until the INR is therapeutic.

For high risk of thrombosis (including risk associated with preoperative and postoperative):

Discontinue warfarin at least 5 days prior to surgery. Therefore, give last dose on day 6 to achieve 5 warfarin-free days if day of surgery = day 0. Unless target INR is 3.0 (range 2.5 to 3.5) stop 6 days prior. Therefore, give last dose on day 7 to achieve 6 warfarin-free days if day of surgery = day 0.24

Conclusion

Since warfarin carries the risk of bleeding, it is very important to evaluate the need for dose modification during any surgical intervention when all patients should be assessed carefully. In the present study, we have shown that simple teeth extraction in patients on warfarin treatment can be performed safely without high risk of bleeding but providing that the INR is equal or less than 3.5 at the day of extraction. A close follow-up and monitoring of patients taking warfarin is mandatory after dental extraction.

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Literature Review

DENTAL MANAGEMENT OF PATIENT TAKING ASPIRIN

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Abstract

The number of geriatric patients seeking dental service is ever-rising because of increased life expectancy, also with problem of increased chronic medical conditions. One of them are patients on anti-thrombotic medication. Bleeding complication after minor oral surgery by anti-thrombotic agents is of concerns to dentists on dental management of these patients. Risk and benefit of the anti-thrombotic agents must be weighed before initiating dental procedures, which should be established as a treatment guideline. Purpose of the paper is to optimize the management of the dental patients on anti-thrombotic medication via standardization of treatment protocol of such a patient.

Key Words: anti-thrombotic, anti-coagulant, anti-platelet, minor oral surgery

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Introduction

Thromboembolism in acute coronary syndrome or atrial fibrillation is largely prevented by anti-thrombotic agents.^{1,2} However, bleeding complications related to these agents after minor oral surgery is of concern to dentists for dental management of these patients. Risks and benefits of the anti-thrombotic agents must be weighed before initiating dental procedures, which should be established as treatment guidelines.

The purpose of this paper is to optimize the management of dental patients on anti-

thrombotic medication via standardized treatment protocols. The target readership of the paper is undergraduate and postgraduate dental students, and general dental practitioners.

Hemostasis occurs as a result of the interaction of the components of Virchow's triad, namely endothelial cells, blood composition and vascular flow. Interplay of these three factors determines the chance of thrombotic accident. Arterial thrombosis is related to platelet-rich white clots, whereas venous thrombosis is related to fibrin-rich

red clots.³ Anti-thrombotic agents (Table 1) are classified into two categories, anti-platelets and anti-coagulants. While anti-platelet agents inhibit platelet aggregation, anti-coagulant agents block the coagulation cascade after platelet aggregation. Anti-platelet agents are useful for the prevention and treatment of platelet-rich white clot formation, whereas anti-coagulant agents prevent and treat venous thromboembolism.

Anti platelet agents

1) Aspirin (Astrix)

Aspirin is an anti-inflammatory drug that inhibits the cyclooxygenase pathway of arachidonic acid, which is mobilized in the inner cellular membrane.^{4,5} In inhibiting this pathway, aspirin also inhibits the production of thromboxane, making it a standard for treatment of ischemic heart diseases. It can be used as a single load or used in combination with clopidogrel in dual antiplatelet therapy (DAPT).^{6,7}

There are more thromboembolic complications after discontinuation when aspirin is used for secondary prevention than when used for primary prevention,^{8,9} which necessitates careful consideration of aspirin discontinuation, especially when it is used in secondary prevention of thromboembolic complication.

2) Clopidogrel (Plavix)

In contrast to aspirin, which impairs thromboxane-mediated platelet activation, clopidogrel is a purinergic receptor

antagonist that inhibits binding of P2Y₁₂ receptors on the platelet surface with adenosine diphosphate (ADP).¹⁰

It can be administered at a rate of 75 mg once a day for primary prevention. In cases of acute coronary syndrome, the initial loading dose is 300 mg, followed by a daily maintenance dose of 75 mg. In cases of secondary prevention, it is more effective in preventing thromboembolism when used concomitant with aspirin (DAPT).

3) New anti-platelet agents

(1) Prasugrel (Effient)/ticagrelor (Brilinta)

Clopidogrel is a prodrug whose bioactive form is created through enzymatic cleavage in the liver. Metabolism of clopidogrel through hepatic enzyme CYP2C19 into its active form is a time-consuming process, and clinical efficacy of clopidogrel is largely dependent on inter-individual differences caused by genetic variability of expression of the enzyme CYP2C19.¹¹

Prasugrel is the same type of prodrug as clopidogrel, but is less subject to genetic variability and rapidly becomes biologically active because of differences in the metabolic pathways.^{12,13}

Ticagrelor is different from clopidogrel or prasugrel, which are thienopyridines; it has a reversible inhibitory action against P2Y₁₂ receptor. Ticagrelor exerts its action via binding to the P2Y₁₂ receptor in a manner

different from ADP, resulting in an allosteric antagonist.¹⁴

(2) Vorapaxar (Zontivity)

Thrombin is a serine protease that exhibits the most potent platelet activation at sub nano molar concentrations, in contrast to ADP, which requires micro molar concentration to exhibit its action.^{15,16} Thrombin action on platelets is mediated via platelet protease-activated receptors (PARs). Vorapaxar is a reversible PAR-1 inhibitor that directly inhibits thrombin action. Large phase III trials resulted in clinical effect for reducing atherothrombotic event in addition to current standard anti-platelet therapy.¹⁷ However, with clinical data still being accumulated, a cardiology consult is recommended before dental procedures.

Mechanism of action of aspirin

The pathological basis related to arterial thrombosis involves atherosclerotic vascular disease mediated by platelet thrombi. Thrombin is a principle mediator in this type of thrombosis. Treatment modality against the arterial thrombosis involves drugs with antiplatelet and antithrombin activity. The antithrombotic effect of aspirin is mediated by irreversible inhibition of cyclooxygenase activity in platelets. On activation, phospholipase-A2 acts on the cell membrane to release arachidonic acid. Cyclooxygenase acts on arachidonic acid to produce thromboxane A2. Thromboxane A2 is a potent platelet stimulant leading to

degranulation of platelet and platelet aggregation. Aspirin inhibits cyclooxygenase enzyme and thus decreases the level of platelet stimulant thromboxane A2.

Why aspirin is used as prophylactic agent against thromboembolic events

Aspirin was developed in 1897 and is one of the world's safest and cheaper drugs with proven efficiency for over 100 years. A general practitioner in Glendale, California, named Lawrence Craven reported that daily low-dose aspirin has preventive role against myocardial infarction and stroke. He prescribed his 400 patients low-dose aspirin. None of his patients developed myocardial infarction for a period of 2 years (1948–1950). This was probably the first attempt to use aspirin to prevent myocardial infarction.

The prophylactic role of aspirin and other non aspirin antiplatelet drugs has been confirmed by Anti-Platelet Trialists Collaboration after previous thromboembolic events. Vascular events were reduced by 20–25% in the first few years. The overall mortality rate was reduced by 12%. These results were based on a meta-analysis of 287 studies which involve a total of 135,000 patients.

Other studies and publications reported that antiplatelet treatment has reduced the overall mortality of vascular disease by 15% and nonfatal vascular complications by 30%.

Antiplatelet dose of aspirin

Aspirin is effective as antiplatelet drug at much lower doses than that required for analgesic and anti-inflammatory functions. Antiplatelet activity of aspirin has been seen even at dose as low as 40mg/day. The antiplatelet properties are effective up to 320mg daily dose. In fact, doses of aspirin >320mg/day may even decrease the effectiveness as antiplatelet agent due to inhibition of prostacyclin production.

Various evidence based studies recommended aspirin in the range of 75–100mg/day for the prophylaxis against serious vascular events in high risk patients. However, recent randomized clinical trial indicates that 160mg/day is the optimal dose of aspirin to prevent myocardial infarction and stroke. In clinical situations where immediate antithrombotic effect is required (such as unstable angina, acute myocardial infarction, or stroke), a loading dose of 300mg is recommended.

Most frequently recommended doses of aspirin for prevention of myocardial infarction and stroke are 81, 160, and 325mg/day in the United States, whereas, in Europe and other countries, these doses are 75, 150 and 300mg/day.

Bleeding risk management

General dental management principles for patients on anti-thrombotic agents recommend following standard procedures to avoid causing bleeding.

If the anti-thrombotic medication is not prescribed as a life-long medication, dental treatment may be delayed until after discontinuation of the medication. For patients with prosthetic metal heart valves or coronary stents, direct written instructions from the cardiologist are required to alter their anti-thrombotic medications. Analgesic medications such as aspirin, ibuprofen and diclofenac can exacerbate the bleeding risk of the patient and should be prescribed carefully.

The most useful hemostasis is local mechanical arrest, such as packing of open sockets with hemostatic material and suture. There is no reason to interrupt anti-thrombotic medication if the patient is taking aspirin alone, because there is no evidence of higher bleeding risk in these patients than in non antithrombotic patients. Scheduling elective procedures early in the day and week is recommended for patients on anti-thrombotic agents to allow time for bleeding control, in case of bleeding episodes.

1. Dental management of patients on anti-platelet agents

When contemplating dental procedures for a patient taking antiplatelet drugs, several important factors must be considered: Is the surgery urgent or elective? Is the patient at high or low risk of thromboembolism if the drug is discontinued? Can the procedure be done safely without discontinuing the drug? Does the patient understand the nature of the

dental procedure and the risks associated with continuing or discontinuing the drug? What degree of risk are the patient and the provider willing to accept? Finally, is the patient on a single antiplatelet drug or on combination therapy with another drug.¹⁸

With no suitable test for measuring antiplatelet effects causing bleeding, it is common belief that dual antiplatelet medication tends to prolong bleeding compared to aspirin alone. However, it is recommended that dental management be given without altering antiplatelet medication for patients on aspirin alone or on DAPT. Patients who undergo a coronary artery stent surgery must keep their antiplatelet prescription for up to 12 months.

If the patient is on aspirin alone, it is recommended that the initial treatment site be limited, that is, extract only a single tooth or limit the subgingival scaling to three teeth, so that bleeding can be assessed before further procedures. For procedures with anticipated higher bleeding complications, staged treatment with active engagement of local hemostatic measures such as suturing and packing should be considered.

Although the Ivy bleeding time has been used to assess platelet function, it is not suitable for estimating the hemorrhagic risk of a patient taking antiplatelet medication. Patients taking aspirin or other platelet-inhibiting drugs may have prolonged

bleeding times, although these may not be clinically relevant for procedures such as the removal of one or two teeth, the placement of implants, or other minor procedures, as postoperative bleeding can be controlled using local measures. Significant bleeding usually does not result unless the bleeding time is greater than 20 minutes.

However, its ability to determine the likelihood that a patient will bleed excessively during surgery has yet to be established detecting platelet dysfunction due to aspirin ingestion. Patients who have had previous thrombotic events are considered to be at risk for other thrombotic events.¹⁹

Patients who are at high risk of perioperative thromboembolic events include those with mechanical heart valves who have atrial fibrillation, older aortic valve prostheses, recent deep venous thromboses (DVT), hypercoagulable states, or a history of recent life-threatening thromboembolic events.

Patients at moderate risk include those with mechanical valves and a normal sinus rhythm, DVT more than three months prior to planned dental treatment, and atrial fibrillation with coexisting coronary artery disease, diabetes or hypertension.

Patients at low risk include those with atrial fibrillation without a history of stroke, a hypercoagulable state without recent or life-

threatening thrombosis, or a history of DVT treated remotely.

A patient who has had a previous thrombotic event should be considered to be at risk for thromboembolism, if the ongoing antiplatelet therapy is discontinued. A provider who is uncomfortable making the decision concerning treatment while the patient is taking antiplatelet drugs may consult with the patient's primary care physician or specialist.²⁰

Bleeding that lasts for more than 12 hours after surgery, causes the patient to return to an emergency room. It can result in a large hematoma or ecchymosis of the oral soft tissues.

2. Local measures to use in the event of a bleeding episode

Merits a blood transfusion may be defined as a significant bleeding event in the postoperative period.²¹ Less than 20 mL of blood loss is considered mild; between 20 mL and 50 mL is considered moderate; and more than 50 mL is considered severe.²²

Postoperative bleeding after minor dental procedures usually can be controlled using local measures.²³ For patients taking low-dose aspirin, most cases of postoperative bleeding require only suturing for hemostasis. An absorbable hemostatic dressing (such as oxidized cellulose, collagen sponge, microfibrillar collagen flour, or resorbable gelatin sponge) can be

packed gently in sockets and sutured, followed with gauze pressure for at least 30 minutes. Resorbable sutures are thought to attract less plaque than other materials. Non-resorbable sutures should be removed after 4-7 days.¹⁸ Extensive dental surgeries (such as a total odontectomy, periodontal surgery, or extensive deep scaling) may require sutures, superficial laser, oxidized cellulose, microfibrillar collagen, or absorbable gelatin sponge to control hemostasis.

Blood clots in extraction sites and postoperative oozing also can be stabilized by 10% tranexamic acid, which neutralizes oral fibrinolytic activators and can be added to local packing, applied topically, or used as a rinse for two minutes, four times a day.²⁴ Tranexamic acid both inhibits bleeding and re bleeding.²⁵ Epsilon aminocaproic acid (250 mg/mL) is another hemostatic agent that can be added to local packing or applied topically to inhibit or block fibrinolysis of the clot.²⁶

Patients who are taking combinations of antiplatelet drugs or higher doses of aspirin especially those with bleeding times of more than 20 minutes should consult with their treating physician.

Emergency surgery for patients taking high doses of aspirin with prolonged bleeding times may be treated with desmopressin acetate.²³ It can be given parenterally (0.3 µg/kg of body weight) or by nasal spray (300 mg/kg). Consultation with the patient's

physician or hematologist is recommended prior to this therapy, especially among older patients.

Epilogue

The number of geriatric patients seeking dental service is ever rising because of increased life expectancy in conjunction with increased chronic medical conditions. Patients on anti-thrombotic medication fall into this category; treatment guidelines of such patients were described in this review.

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Case Report

CHANGING TRENDS OF LICHEN PLANUS: IS STRESS THE REAL CULPRIT IN EARLY ONSET OF LICHEN PLANUS IN ADOLESCENT AGE GROUP?

* Dr. Anlin Anto, * Dr. Shanima Sherin KC, ** Dr. Prejith Sampath

Abstract

Lichen planus is an immune mediated mucocutaneous disorder which is most common in 4th decade of life. But nowadays most teens experience more stress when they perceive a situation as dangerous, difficult, or painful and they do not have the resources to cope. This stress can induce autoimmune or inflammatory skin disorders through neuroendocrine and neuroimmune dysregulations. The prevalence of oral lichen planus in adolescence is rare. This paper is about a 17-year-old girl who reported to the department of Oral Medicine & Radiology with lichen planus. Early referral to the psychiatrist would not only result in the improvement of the mood but also help to cope with the lichen planus.

Key Words: lichen planus, stress, adolescence, desquamative gingivitis, gingival veneers

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Introduction

Oral Lichen Planus (OLP) is a common chronic immunological inflammatory mucocutaneous disorder, that varies in appearance from keratotic to erythematous and ulcerative. The sites involved over the skin include the flexor surfaces of the legs and arms, especially the wrists and elbows and Scalp. The Prevalence rate of oral lichen planus is 0.5% to 2.2%.¹

Women are more frequently affected as compared to men and is found rarely in children. The typical age of presentation of

this lesion is between 30 to 60 years. Although the precise etiology of

OLP is unknown, in most cases, a multifactorial process is considered to be involved. Some of these factors could act as causal agents, while others may trigger the process.^{2,3}

Exacerbation of OLP has been linked to periods of psychological stress and anxiety, a predictable correlation with any condition that is related to an immune system imbalance. These factors can either trigger onset of the disease or cause existing disease to worsen.

Case Report

A 17-year-old female presented to Department of Oral Medicine and Radiology with a chief complaint of burning sensation and swollen gums for the past 6 months. She was referred from a general dentist for diagnosis and management of the same. She was also prescribed multivitamins and antibiotics for a month, but burning sensation on gingiva did not subside. She appeared to be depressed and sad on general examination.



Figure 1: Desquamation and erythema in relation to maxillary and mandibular anterior region. Fine white linear striae with areas of erosion

On clinical examination gingiva was bright red and edematous. Desquamation and erythema were present on labial gingiva with respect to upper and lower anterior teeth. Bleeding was noticed on slightest provocation. White linear striae with areas of erosion were seen on the interdental papilla in relation to lower anterior region. Nikolsky sign was positive and stippling was absent. Associated teeth were non tender. No local or systemic factors were

detectable which could contribute to bleeding of gingiva.

Incisional biopsy was done to rule out other vesiculo bullous lesions such as pemphigus vulgaris, mucous membrane pemphigoid which also show features of desquamative gingivitis.

Histopathological examination revealed epithelium with acanthosis and hyperkeratosis and basal cell degeneration with formation of subepidermal cleft. Sub epithelium shows band like infiltrate of lymphocytes and melanophages.

Based on all above features a final diagnosis of lichen planus was given. Patient and parent counselling were given.



Figure 2: After 3 weeks of therapy

2 tablets of 1 mg betamethasone for three consecutive days at morning for 3 days in a week was prescribed for 15 days along with clobetasol gel 0.05% for topical application and montelukast 10 mg once daily for 1

month with 40 mg pantoprazole once daily for a week. Patient reported thereafter 3 weeks for follow up.

Discussion

Adolescence is a time of many psychosocial and physiological changes. One such change is how an individual responds to stressors. Specifically, adolescence is marked by significant shifts in hypothalamic-pituitary-adrenal (HPA) axis reactivity, resulting in heightened stress-induced hormonal responses. It is presently unclear what mediates these changes in stress reactivity and what impacts they may have on an adolescent individual. However, stress-sensitive limbic and cortical brain areas that continue to mature during adolescence may be particularly vulnerable to these shifts in responsiveness. Consequently, perturbations of the maturing adolescent brain may contribute to the increase in stress-related psychological dysfunctions.⁴

Erasmus Wilson in 1869 characterized the patients as anxious, high strung, and sensitive with a tendency to worry excessively and with periods of undue emotional stress. Approximately, two-third of OLP patients report oral discomfort.

Most cases of symptomatic OLP are associated with atrophic (erythematous) or erosive (ulcerative) lesions. Symptoms vary from mucosal sensitivity to continuous debilitating pain. OLP lesions usually persist for many years with periods of exacerbation

and quiescence. During the periods of exacerbation, erythema or ulceration increases with increased pain and sensitivity which decreases during periods of quiescence. Patients are often unaware of quiescent OLP that presents typically as faint white striations, papules or plaques. Exacerbation of OLP has been linked to periods of psychological stress and anxiety.⁵

Sometimes lichen planus may be confined to gingiva and present as desquamative gingivitis. Clinician should be able to identify the primary cause meticulously behind such presentations. Desquamation of epithelial tissue is generally seen in free and keratinized gingiva. Generally, the lesions that affect the buccal/labial surfaces of the gingiva, although not formed due to bacterial plaque, are exacerbated with plaque accumulation.⁶ Although they are generally observed in the anterior region, they can be seen in any gingival area.^{7,8,9}

Similar lesions can be seen in the edentulous alveolar ridge. While only desquamations can be observed in the patients, there can also be associated vesicular-bullous lesions, in addition to ulcerative and lichenoid lesions. In severe cases, it can be seen generalized at the oral mucosa, and the alveolar mucosa can be affected together with the gingiva. The patient can either have no complaints or there can be a burning sensation or severe pain.

A positive response to medium-potency corticosteroid treatment, such as triamcinolone acetate 0.1%, powerful fluorinated steroids as fluocinolone acetonide 0.05% and 0.1%, and more high-potency halogenated corticosteroids, like clobetasol propionate 0.05%, has been reported in most treated patients.⁶ Surgical excision, cryotherapy, CO2 laser, and ND: YAG laser have all been used in the treatment of OLP. Photo chemotherapy is also used. Relaxation, meditation and hypnosis have positive impact on many cutaneous diseases and help to calm and rebalance the inflammatory response which can ameliorate inflammatory skin disorders. Due to excessive saliva and tongue movement the effectiveness of treatment is limited.

Acrylic labial veneers were advocated by Emslie in 1955 to improve the aesthetics in patients with chronic periodontitis. They were subsequently used by LX & Range and Strahar in 1970 to carry periodontal dressings postoperatively. This can be used for the effective delivery of drug in desquamative gingivitis.^{10,11} Acrylic veneers were constructed in heat-cured pink acrylic usually to a thickness of 1 mm, thus conferring appropriate flexibility.¹⁰

Conclusion

Vocalization and the process of bringing out into the consciousness the troubling issues and realization that a caring individual is lending a concerned ear can often alleviate

the patient's concerns, tensions, anxiety, and stress. We can improve the quality of care provided to patients through use of such measures and by referring patients with psychological risk factors to a psychologist or psychiatrist skilled in assessing and treating such patients. The reasons of referral should be explained carefully to the patients in order to reduce possible defensiveness and increase receptivity.

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Case Report

PERIPHERAL PRESENTATION OF CENTRAL SCHWANNOMA IN THE FLOOR OF THE MOUTH: PERPLEXING ENTITY

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Abstract

Schwannoma (Neurilemmoma) is a benign tumour of neuroectodermal origin. It usually occurs as a asymptomatic, solitary, smooth- surfaced and slow growing lesion, emerging at any age, with as such, no gender predilection. Occurring as a common tumour in the head and neck region, its intraoral presentation is very rare and has a wide variety of morphologic and radiologic features. This makes differential diagnosis difficult, and only histopathological features can lead to a definitive neurilemmoma diagnosis. Here, we present a rare case of intraoral schwannoma in the floor of the mouth in a 65-year-old female, thereby highlighting the consideration of this rare entity as one of the differential diagnosis in cases who present to us with swelling of the floor of the mouth.

Key Words: benign neoplasm, soft tissue tumour, schwannoma, floor of the mouth, neurogenic neoplasm

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Introduction

Schwannoma or neurilemmoma is a rare, benign neurogenic neoplasm composed of Schwann cells (nerve sheath). They are described as epineurium-encapsulated neoplasms arising from any cranial, peripheral, or autonomic nerve that contains Schwann cells.¹ They originate more frequently from sensory nerves and can affect all cranial nerves, except the olfactory and optic, which are extensions of white matter from the brain. About between 25 and 45% of all schwannomas are found in the head and neck region, and only between 1 and 12% of them have an intraoral origin.²

Most of the intraoral cases are found on the upper and lower side of the tongue and vestibule, being rare on the palate. Intraosseous schwannomas are rare, but when they occur, the mandible is the most common site, particularly in the posterior areas of the body and ramus.³

Case Report

A 65 year -old female was referred to the Department of Oral Medicine and Radiology by a General practitioner for diagnosis and management of a painless swelling in the floor of the mouth. She had noticed a marked swelling for the past two years. She also had

a history of similar swelling in the floor of the mouth 11 years back that was surgically excised. The intraoral lesion was noticed 2 years before, which according to her was initially small in size and gradually progressed to its present size. She had difficulty in speech, mastication and spitting since 6 months. She did not report any pain or dyspnea, bleeding, pus discharge or fever. FNAC and MRI were advised by the general practitioner and were done one week back. She was otherwise healthy and had history of diabetes and hypertension since 10 years for which she is under medication. Her family history was unremarkable; however she had a history of uneventful multiple extraction few years back.



Figure 1: Intraoral view showing the extent and surface characteristics of the lesion

Intra oral examination showed a diffuse swelling of diameter 3.5 cm on the anterior part of the floor of the mouth. The swelling extends medio-laterally from 35 region to 44, antero-posteriorly it extends from the lingual surface of the mandible to the base of the tongue. The swelling was sessile and

lobulated in appearance. The overlying mucosa was normal in color. Tongue movement was marginally restricted by the physical presence of the swelling which affected speech, however swallowing was unaffected. Pathologic migration of 31 and 41 was noticed. No bleeding or pus discharge was associated with the swelling.

On palpation, the non-tender mass was soft and fluctuant in consistency. Swelling was compressible but non-reducible. The labial vestibule was slightly obliterated in relation to the 31 and 41 region. Salivary flow and consistency was found to be normal. No bleeding or pus discharge was noticed during palpation. There was no sensory neural deficit. There was no enlarged and palpable cervical lymph node.

Based on clinical findings and anatomic location, differential diagnosis of salivary gland tumour, ranula, epidermoid cyst were considered.

Fine Needle Aspiration Cytology (FNAC) report revealed presence of single cells as well as cells arranged in sheets and loose clusters. Individual cells are spindle/oval with moderate amount of cytoplasm and ovoid nuclei with fine chromatin. The background showed fibrillary myxoid matrix and few giant cells which indicated a diagnosis of a spindle cell lesion with cystic change.



Figure 2: Panoramic radiographic showing the extent of radiolucent lesion

Magnetic Resonance Imaging (MRI) showed well-defined multicystic lesion arising from the mandible at the level of midline/symphseal region causing expansion and thinning of cortex which is preserved. Few loculations are noted within the lesion. The borders were well demarcated and there was no evidence of calcification noted. No periosteal reactions were present. The bone marrow was normal and there was no infiltration adjacent to the soft tissue.

Panoramic radiography revealed a multilocular radiolucency with corticated margin extending from 31 to 43 with presence of root resorption in relation to 41, 42 and pathologic migration of 31 and 41.

Based on these findings radiographic diagnosis of ameloblastoma in lower anterior region was made.

The CBCT image revealed a well-defined, expansile, osteolytic lesion with scalloped margin situated within the mandibular anterior region. Antero-posteriorly lesion extends from the mesial aspect of 33 to mesial aspect of 44, and superiorly 2mm below the alveolar ridge. Inferiorly lesion extends 7mm superior to the inferior border of mandible. Internal structure is homogeneously hypodense except in the areas of 31 & 32, where small locules resembling a honey comb pattern is seen. Distal and superior displacement of roots of 31, 32, and 33, 41, 42, 43 were noticed. Resorption of roots of 31, 41, 42, 43 was

present. Epicenter of the lesion appears to be in the periapical region of 42, 41 region causing buccal and lingual expansion and perforation of the cortical plates.

CBCT findings were suggestive of benign aggressive neoplasm of anterior mandible and ameloblastoma and central giant cell granuloma were considered as differential diagnoses.

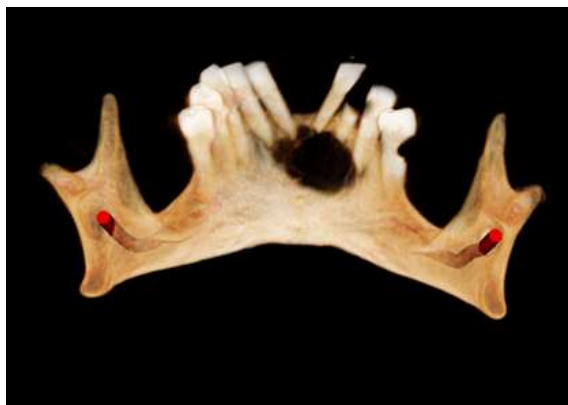
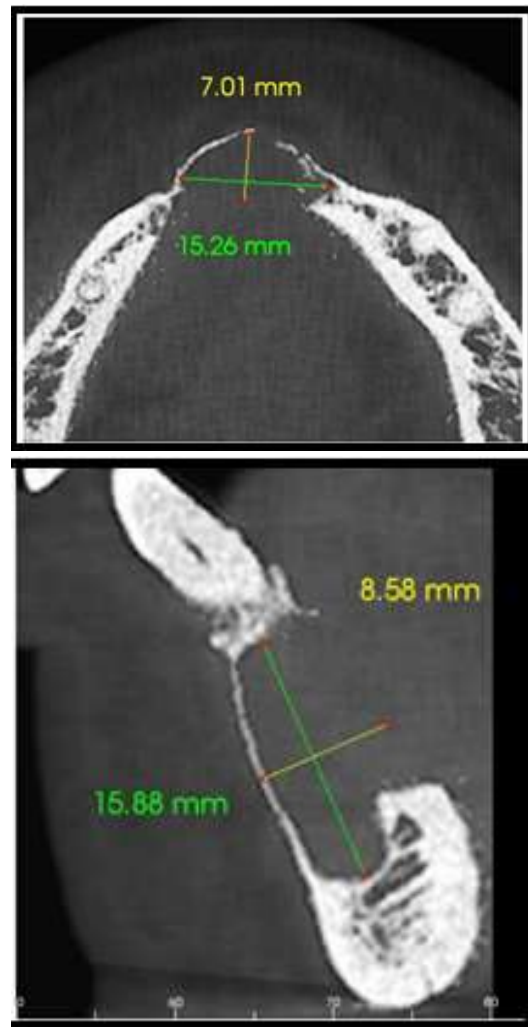


Figure 3 : Three dimensional CBCT reconstruction of the osteolytic lesion.

Incisional biopsy was performed under local anesthesia and histopathology showed hyperkeratosis and hyperplasia of surface squamous epithelium. Subepithelium with patchy chronic inflammation and deeper areas showed myxoid stroma containing haphazardly arranged cells with round to slightly oval deep stained nuclei and tapering cytoplasm. No nuclear atypia/mitotic activity was present. Based on these findings the diagnosis of Benign myxoid lesion consistent with nerve sheath myxoma was established.

The immunohistochemical (IHC) examination with S-100 protein revealed intense positivity in the cells of the lesion. With a score of 4+ in spindle shaped cells (immunoreactive in 76-100% cells). The immunohistochemical diagnosis was benign nerve sheath tumour with extensive myxoid change favouring neurofibroma.



Figures 4 a, b : Axial & cross sectional view of the lesion

The patient was posted for surgery and wide excision under general anaesthesia was carried out. Extraction of 35,34,33,32,31,41,42,43,44 was done.

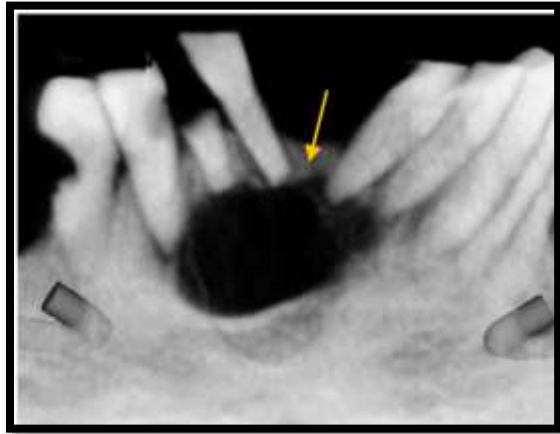


Figure 5 : Scalloped margins



Figure 6 : Honey comb pattern of the lesion

The excised mass measured 3.5 cm x 2.5 cm x 2.5 cm with soft tissue attached to hard tissue specimen and was creamy brown in color. Histopathology reports of the excised

surgical specimen revealed multinodular mass of lesional tissue surrounded by a fibrous capsule, Alternating Antoni A & B areas with xanthomatous degeneration and hyalinization in numerous areas. Antoni A areas shows ill-defined fascicles without characteristic nuclear palisading. Cystic degeneration, perivascular hyalinization, partially thrombosed blood vessels and epithelioid islands were also found. This findings presented to a final diagnosis of Schwannoma with degenerative changes.



Figure 7: Surgical excision using intraoral approach

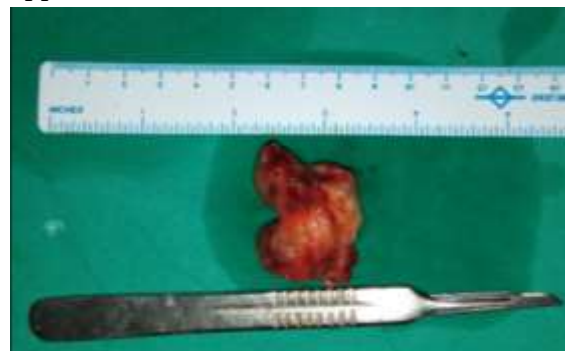


Figure 8 : The excised specimen

Postoperative period was uneventful and the patient was stable and afebrile. She was

recalled after one month for routine checkup and was found to be stable.



Figure 9: Post-operative photograph after one month

Discussion

Benign nerve sheath tumours, including schwannoma (neurilemmoma) and neurofibroma, are encountered in oral and perioral locations.⁶ Neurilemmomas are well-encapsulated, benign, slow-growing tumors that are usually solitary. Masses may be attached to the originating nerve or surrounded by the nerve. Although the etiology of neurilemmomas remains unknown, it is postulated that the lesions arise through the proliferation of Schwann cells, compressing and displacing the surrounding nerve.⁷ Masses are typically between 0.5 to 3 cm in size, rarely exceeding 5 cm.⁶ Multiple nerve schwannomas require evaluation for Von-Recklinghausen disease, while bilateral vestibular schwannomas raise suspicion for neurofibromatosis-II.⁷ Based on its location, schwannomas have been classified either as central (bone) or

peripheral (soft tissue) type. The tumor may arise centrally in the bone, may arise within the nutrient canal, or a soft tissue tumor may secondarily erode into the bony tissue.⁸ Central neurilemmoma is rare, comprising less than 1% of all bone tumors, but when it does occur the mandible is the most common intraoral site.⁹ Intraosseous schwannoma is a slow-growing tumor that frequently produces expansion of the affected bone and causes swelling. Pain and paresthesia may be found in 50% of the patients.¹⁰ There are two clinical forms of oral schwannomas: the encapsulated form, surrounded by dense fibrous connective tissue, and the pediculate/nonencapsulated form, in which the tumor is located just below the mucous membrane.¹¹

Most of the cases are asymptomatic, while most of the lesions are slow-growing. A sudden increase in size may be due to internal hemorrhage.¹² The clinical presentation depends upon the site of the tumor, the size of the tumor, and upon the anatomy of the affected nerve.³

Radiographically, intraosseous schwannomas appear as unilocular radiolucencies with very thin sclerotic border. Sometimes the neighboring teeth may show external root resorption and cortical expansion.¹³

There are four major histological types of schwannoma: conventional, plexiform, cellular, and ancient variant. According to Erlandson, schwannomas are classified into

seven subtypes: conventional, cellular, plexiform, cranial nerve, melanotic, ancient, and granular cell schwannomas.¹⁴ However, they have mainly two distinct histological patterns: Antoni types A and B. Antoni patterns were first described by Prof. Nils Ragnar Eugene Antoni. Antoni A areas consist of a hypercellular proliferation of fusiform cells, often arranged in a palisading pattern around a central acellular eosinophilic area known as Verocay bodies, while Antoni B areas are hypocellular and less organized. The conventional variant consists mostly of Antoni A areas and Verocay bodies, with the occasional presence of Antoni B areas. The additional presence of acute/chronic inflammatory infiltrate, areas of hyalinization, and thin vessels containing thrombin are noted in the conventional variant.¹⁵

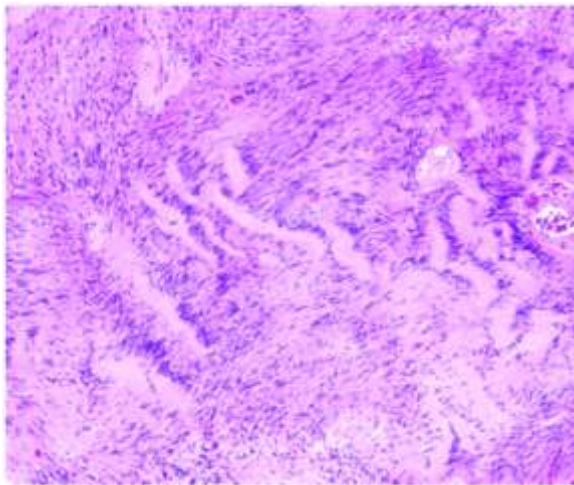


Figure 10: Antoni A areas

The cellular variant is characterized by a marked increase in cellularity, with a

compact arrangement of spindle cells in fascicles, variable nuclear hyperchromasia and pleomorphism, lack of Verocay bodies, and a predominance of Antoni A areas.¹⁶ The ancient variant is characterized by degenerative changes, such as calcification, mild pleomorphism and bizarre nuclei, microcyst formation, dilated vessels, and hemorrhagic phenomena.³ The plexiform type consists of both Antoni A and B regions with prominent Verocay bodies, like the conventional variant; however, the Schwann cells show a nodular arrangement with capsular delineation.¹⁷

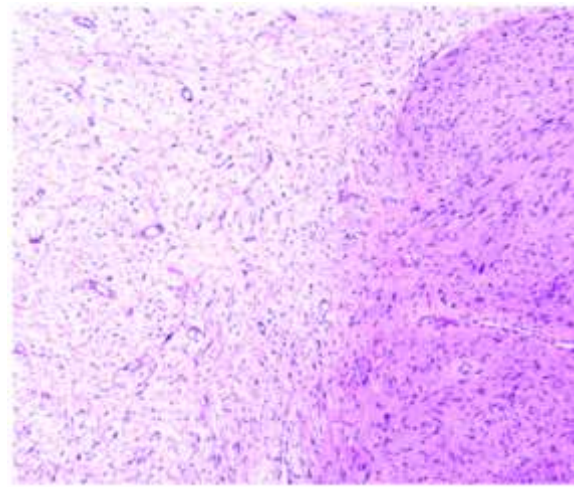


Figure 11: Antoni B areas

Immunohistochemistry is important to distinguish schwannoma from other close differentials, and can aid in its diagnosis; however, it is not mandatory to confirm the diagnosis. S-100 is undoubtedly the first immunostaining that comes into mind when dealing with suspected peripheral nerve tumors. Both schwannomas and

neurofibromas show moderate to strong reactivity to S-100. However, S-100 has low specificity for diagnosing peripheral nerve cell tumors.¹⁸

The major differentials are benign salivary gland tumors, benign peripheral nerve tumors (neurofibroma, traumatic neuroma, and PEN), other benign mesenchymal tumors (lipoma and hemangiomas), and odontogenic tumors.¹⁹

Conclusion

Schwannoma represents a lesion not often encountered in clinical practice. The lesion is usually indistinguishable from other neoplasms. The final diagnosis should be done after histopathological examination and in some cases after immunohistochemical analysis. Schwannomas rarely undergo malignant transformation and are managed by surgical excision with recurrence being rare.

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Case Report

ORAL MELANOTIC MACULE

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Abstract

Melanotic macule is one of the most common pigmented lesions involving the oral cavity. The most common intraoral locations include gingiva, palate and buccal mucosa. The lesion is completely benign and shows very little tendency to recur or become malignant. Most often, it is difficult to distinguish it clinically from other pigmented lesions such as nevus, malignant melanoma in situ or incipient malignant melanoma. Presented here is a case report of a 53-year-old male with a pigmentation on his palate involving the interdental papilla and extending to the buccal aspect. Patient was reviewed for 6 months on a regular basis with no remarkable changes.

Key Words: oral melanotic macule, pigmentation, melanoma

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Introduction

Melanotic macule is one of the most common pigmented lesions involving the oral cavity. It is a benign lesion resulting from increased melanin production with occasional increase in melanocyte number.¹ Lesions have been reported in patients aged 1–98 years, with a mean of approximately 42 years.^{2,3} The majority of melanotic macules are found in females. Most investigators report an average 2:1 female to male ratio, however Gupta et al. reported a 5:1 female to male ratio in a series of 79 cases.^{2,4-6}

Clinically, melanotic macule presents as a solitary, well-defined, homogenously pigmented, flat lesion varying from tan to

dark brown in color. Rarely multiple lesions have also been reported.^{5,8,9}

Lesions can vary in size from 0.1 to 2.0 cm, with the majority appearing less than 1 cm.^{1,10} The most common intra-oral locations include gingiva, palate and buccal mucosa. Both labial and intraoral lesions are typically asymptomatic. Some patients are unaware of the presence of the pigmented macules, while others report noting their appearance since weeks to years.^{5,10,11}

Treatment usually consists of surgical excision and biopsy to rule out the possibility of an early malignant melanoma. Although the lesion is completely benign and shows very little tendency to recur or

become malignant, most often it is difficult to distinguish it clinically from other pigmented lesions such as nevus, malignant melanoma in situ and incipient malignant melanoma.⁷

Case Report

A 53 year old male reported to the dental OPD with a chief complaint of broken tooth on the upper front region since 7 years. On intra-oral inspection, it was noticed that besides the offending tooth, there was a well-circumscribed, flat, irregular macule with varying shades of black on the palatal gingiva, extending from the distal aspect of 23 to mesial aspect of 26, measuring 2 cm × 0.5 cm. Lesion appeared to involve the palatal interdental papillae between teeth 23, 24, 25 and 26, and extending to involve the buccal interdental papilla between teeth 23 and 24. The surrounding tissues appeared normal. On palpation, it was non-tender and not raised. There were no restorations or dental caries of the adjacent teeth. Moderate recession of gingival margin was observed in relation to palatal aspect of tooth 26 and buccal aspect of tooth 24. Cervical abrasion was also noted in relation to buccal aspect of teeth 23, 24, 25 and 26.

Based on the clinical examination, the lesion was provisionally diagnosed as oral melanotic macule. The patient was reviewed after one week and again after 6 months. There were no signs of increase in size of lesion in both visits.



Fig 1a&b: Palatal gingival ; (b) Buccal gingival extension (first visit)



Fig 2: Palatal gingival pigmentation (after 6 months)



Fig 3: Buccal gingival extension (after 6 months)

Discussion

The term melanotic macule has been used to describe a benign pigmented lesion of the oral cavity, characterised by an increase in melanin pigmentation along the basal cell layer of the epithelium and the lamina propria.⁷

These lesions tend to occur in the fifth decade of life and are most frequently seen on the gingiva, followed by the buccal mucosa and palate. The lesions are usually solitary, smaller than 1 cm, but they may also occur as multiple lesions. There is no sex predilection, and a number of etiologic factors have been reported in literature. In a few cases, long term follow-up was possible. There is no indication of a tendency toward recurrence or development of malignant lesions.¹²

Microscopically, melanotic macules exhibit increased melanin pigmentation within melanocytes and keratinocytes located at the

basal layer of otherwise normal stratified squamous epithelium. Melanin pigmentation has been reported to be the most intense at the tips of the rete ridges. Mild hyperkeratosis and/or mild acanthosis of the spinous layer may be observed, however elongation of the rete ridges is absent. Typically, no increase in numbers of melanocytes is reported although Page et al. reported melanocytic hyperplasia in 24% of cases. Additionally, Sexton and Maize found a statistically significant increase in the number of melanocytes present within the basilar epithelial layers of labial melanotic macules when compared to control tissue of clinically normal adult lip. The superficial lamina propria may exhibit incontinent melanin, melanophages, and varying amounts of chronic inflammation. Lesions should not exhibit atypia or nesting of melanocytes. In the series by Ho et al. of 36 labial melanotic macules, all were negative with immunohistochemical marker HMB-45.

A biopsy is usually required for a definitive diagnosis of melanotic macule. If presenting with classic features on the lower lip, a clinical diagnosis may be established with recommendation of periodic monitoring by a dental or medical provider. Lambertini et al. suggested sequential photography for melanotic macules of size 0.5 cm. Uribe et al. reported in vivo reflectance confocal microscopy to be useful in differentiating between labial melanotic macules and melanoma, however, biopsy was still

necessary for definitive diagnosis. If labial lesions have border irregularity, uneven pigmentation, color change, ulceration or other suspicious features, regardless of size, biopsy is recommended to rule out melanoma.¹³

Conclusion

Melanotic macule is a benign entity which needs follow up because it closely resembles and has a potential to transform into malignant melanoma. Periodic follow up and patient reassurance are important aspects in the management of such cases.

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