Oral Thrombus: Report of 122 cases with clinically descriptive data

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Received: 06/09/2016
Accepted: 09/12/2016

Abstract
Background: The aim of the present study was to assess the frequency and characterize clinic-pathologic aspects of thrombus occurring as a single lesion or in association with other oral pathologies.
Material and Methods: 122 cases of thrombus from the oral cavity were retrieved. Information regarding site of the lesion, age, sex and clinical diagnosis or hypothesis and associated lesions were collected from the patients’ records.
Results: The lesions occurred in a wide age range but the 5th decade was the most prevalent and female patients were more affected. The most frequent site for the lesion was the lip, followed by tongue, buccal mucosa, alveolar ridge, gingiva, floor of the mouth and vestibule. Thirty-five cases were associated with other vascular anomalies or actinic cheilitis. Microscopically, typical thrombus morphology was present. Organized thrombus presented neovascularization and fibroblasts, associated with hemorrhagic areas.
Conclusions: Only 4 cases of oral thrombus have been described in the oral cavity. Given the limited number of cases reported, the importance of a thrombus in the oral cavity is not well established. This study contributes to establishing the profile of patients presenting oral thrombus, a lesion not rare but not well documented.

Key words: Oral cavity, phlebothrombosis, thrombosis.

Introduction
Thrombosis is a multifactorial disease and multiple risk factors are prerequisite for thrombus progress. Major risk factors other than age include exogenous factors such as surgery, hospitalization, immobility, trauma, pregnancy, puerperium and hormone use. The endogenous factors comprise diseases such as overweight, malignant neoplasm, and disorders of hypercoagulation (1-3). Venous thrombus, also called phlebothrombosis, usually presents as deep-vein thrombosis of the lower limbs and are less common in other veins (2,4). The
involvement of the oral and maxillofacial region is probably not uncommon, but only four cases have been reported (5-8).

In this study, we aimed to evaluate a series of thrombus affecting the oral cavity and discussed their epidemiological and histopathological aspects.

Material and Methods
This study was approved by the Human Research Ethics Committee of the Dental School- University of São Paulo, approval number: 754-618/2014.

All cases histologically diagnosed as thrombus at the Oral Pathology Service at the School of Dentistry, University of São Paulo, between the years 1997 and 2014, were retrieved and one hundred and twenty two (122) were included in the present study. Information regarding site of the lesion, age, sex and clinical diagnosis or hypothesis and associated lesions were collected from the patients’ records.

The slides from each case, included in this study, were reviewed by two pathologists according to the histological features described.

Results
Within the 18-year period, 122 cases of oral thrombus were retrieved. The lesions occurred at any age, but the 5th decade was the most prevalent, for both men and women (Fig. 1A), with a mean age of 52 years old. Moreover, the incidence rates were slightly higher in women during childbearing years (16-44 years), compared to men of similar age (30% of the women at that age were affected and 28% of the men were affected). The higher incidence rates were after age 45 years, comprehending ~70%. Women were more affected, at a ratio of 1.56:1 (Fig. 1B).

The prevalent site of the lesion in the oral cavity was the lip (65 cases), followed by tongue (22 cases), buccal mucosa (13 cases), alveolar ridge (6 cases), gingiva (3 cases), floor of the mouth (4 cases), vestibule (3 cases) and not specified (6 cases) (Table 1).

![Fig. 1. Oral thrombus clinical characteristics: (A) Age incidence in decades. Note the prevalence of the 50th decade. (B) Sex incidence: Females are more affected in a ratio of 1.56:1.](image)

<table>
<thead>
<tr>
<th>Distribution of the thrombus</th>
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<tbody>
<tr>
<td>Lip</td>
<td>53%</td>
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<tr>
<td>Tongue</td>
<td>18%</td>
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<tr>
<td>Buccal mucosa</td>
<td>11%</td>
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<tr>
<td>Alveolar ridge</td>
<td>5%</td>
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<tr>
<td>Gingiva</td>
<td>3%</td>
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<tr>
<td>Floor</td>
<td>3%</td>
</tr>
<tr>
<td>Vestibule</td>
<td>2%</td>
</tr>
<tr>
<td>Not specified</td>
<td>5%</td>
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<table>
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<tr>
<th>Thrombus-associated lesions</th>
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<tbody>
<tr>
<td>Vascular malformation</td>
<td>37%</td>
</tr>
<tr>
<td>Actinic cheilitis</td>
<td>17%</td>
</tr>
<tr>
<td>Papillary endothelial hyperplasia</td>
<td>17%</td>
</tr>
<tr>
<td>Varix</td>
<td>14%</td>
</tr>
<tr>
<td>Phleboliths</td>
<td>9%</td>
</tr>
<tr>
<td>Pyogenic granuloma</td>
<td>6%</td>
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</table>

Only 5% of surgeons made a diagnosis of thrombus as the first clinical impression. Forty-seven percent of the clinical hypotheses were vascular anomalies and the most common was hemangioma (30%). Other clinical hypotheses were fibroma (14%), mucocele (14%), followed by others less mentioned such as soft tissue tumor and salivary gland lesions. Only 1% of surgeons diagnosed as malignant tumor or an infectious disease. Thirty-five cases (29%) were associated with another lesion (Table 1), as follows: 13 with vascular malformations (37%) (Fig. 2A), six with papillary endothelial hyperplasia (PEH) (17%) (Fig. 2B), six with actinic cheilitis (17%) (Fig. 2C), five with varix (14%), three with phleboliths (9%) and two with pyogenic granuloma (6%) (Fig. 2D).

Microscopic aspects were typical of thrombus (Fig. 3A) located in any other site of the body. These aspects
mainly occurred in veins of which the lumen was partially or completely fulfilled by laminations formed by the presence of deposits of platelet and fibrin, as in the Zahn’s lines (Fig. 3B). In most cases, a focal area was attached to the vessel wall (Fig. 3C). Depending on the maturation, thrombus organization showing neovascularization (Fig. 3D) and fibroblasts could be observed. Calcifications were present in 9% of the cases.

**Fig. 2.** Thrombus in association with other pathologies. (A) Vascular malformation; (B) Pyogenic granuloma; (C) Actinic cheilitis, (black arrow shows solar elastosis); (D) Papillary endothelial hyperplasia.

**Fig. 3.** Histopathological aspects of thrombus: (A) An entire thrombus; (B) A detail of the lumen fulfilled by laminations (Zahn’s lines) and deposits of platelet and fibrin; (C) Thrombus partially attached to the vessel wall (black arrow); (D) Organized thrombus showing neovascularization.
The main cause of development for a thrombus could be one or more of the components that Virchow described in 1856. The Virchow’s triad, as it is called, is composed of 1. endothelial injury; 2. abnormal blood flow and 3. Hypercoagulation (15). Arterial or cardiac thrombi usually begin after a rupture of an atherosclerotic plaque and at sites of turbulence or endothelial injury, whereas venous thrombi characteristically occur at sites of stasis and hypercoagulability (16). Thrombus could develop because of a pre-existing lesion or syndrome such as varicose (varix) (17) and antiphospholipid (6), respectively. In the present cases an association with vascular anomalies and actinic cheilitis was found in some cases.

When associated with vascular anomalies, thrombus formation in the oral cavity is likely to be caused by the presence of tortuous vessels, which can disturb the normal blood circulation leading to the adherence and aggregation of the platelets, even without vessel injury, hypercoagulability or trauma (16,18). For instance, in the cases studied, association with varicose veins was observed in five cases. A varicose vein is the main cause of superficial vein thrombosis (17,19). There are both reflux and dysfunction of the valves, as well as dilatation, caused by an increase of the venous pressure, which causes functional changes in the vein wall. This tension increases the metalloproteinase activity, which can affect the structural integrity of the vein wall (20).

In the cases associated with actinic cheilitis, the chronic physical exposure to the sun leads to a degeneration of collagen and elastic fibers (21,22). This aggression could eventually cause an alteration of the walls of the vein. But, it is difficult to affirm that the thrombus was secondary to the actinic cheilitis because actinic cheilitis occurred in only 6 of the 122 cases, with no other cases reported in the literature. On the other hand, the other lesions associated with thrombus in the present study are more likely to be secondary to the thrombus, such as PEH, a non-neoplastic lesion of unclear pathogenesis (23-25) and phleboliths (26).

Oral thrombus is not a rare lesion, but it is not well reported, probably due to the low risk of embolization and mortality. To our knowledge, there is no report showing embolization of an oral thrombus. However, even superficial vein thrombosis can undergo a venous thromboembolism (11,17).

In conclusion, this study contributes to the establishment of the profile of patients affected by oral thrombus and its association with other entities. Moreover, our results open new avenues for future studies in the causes and possible consequences of an oral thrombus.

References