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內文：

白血病引起的廣泛性牙齦腫大

#### A) Abstract

##### 1. Background 背景:

Acute myeloblastic leukaemia is a malignant bone marrow neoplasm of myeloid precursors of white blood cells. Due to its high morbidity rate, early diagnosis and appropriate medical therapy is essential.

急性骨髓性白血病 (AML) 是影響白血球的先驅骨髓細胞的惡性骨髓腫瘤。由於它有很高的發病率，早期診斷和適當的藥物治療是非常重要的。

##### 2. Methods 方法:

The article highlights normal blood alterations like anaemia, thrombocytopenia, leukocytosis and advanced diagnostic aids like flow cytometry, special staining as a diagnostic modality as well as for prognostic information in acute leukaemia, particularly as a tool for assigning lineage and facilitating further pathologic classification which may be helpful in influencing treatment strategies.

文章強調了正常血液的變化，如貧血、血小板減少、白血球增多和以流式細胞術，特殊染色作為診斷方式和預後資料，特別是作為促進進一步的病理分類的一種工具，可能有助於影響在急性白血病的治療策略。

##### 3. Results 結果:

On clinical examination the case presented with features of inflammatory gingival enlargement with presence of local deposits and calculus. Routine blood examination anaemia, thrombocytopenia, leukocytosis with haemoglobin 5.6 gm% and total leukocyte count of 1,12,000/cu mm suggestive of leukaemia. Myeloperoxidase and leukocyte nonspecific esterase (NSE) special stain were used which showed presence of myeloblasts in the peripheral smear suggestive of acute myelocytic leukaemia. Flow cytometry were done which further helped in interpretation of these cells which showed to be strongly positive for CD45, CD13, CD14, and anti HLADR and moderately positive for CD4, CD34 and Anti MPO confirming to be case of AML-M4 with 57.73% gating.

經過臨床檢查，病例有牙齦腫大發炎和牙結石的情況。經血液常規檢查，病人有：貧血、血小板減少症、血紅蛋白 5.6 gm %、白血球增多和總白血球總數1,12,000 / cu mm的情況都表示病人患有白血病的可能性。過氧化物酶和白細胞非特異性酯酶 (NSE) 特殊染色所採用的顯示的週邊塗片中檢測存在表示著病人有急性髓細胞性白血病的可能性。流式細胞術進一步分析了這些細胞。大量讀數的 CD45、CD13、CD14，和anti- HLADR 和適度的 CD4、CD13、CD34 和anti- MPO 確認了病人屬於AML-M4種類的白血病。

##### 4. Conclusions 結論:

Fact that gingival alterations are sometimes the first manifestations of the disease implies that dental professionals must be sufficiently familiarized with the clinical manifestations of systemic diseases. The timely referral by the general dentist for

a suspicious lesion provided an early diagnosis and early intervention reducing the patient morbidity.

牙齦型態的改變有時是白血病的比較明顯的表現形式。這表示牙科專業人員必須充分熟悉全身疾病的臨床表現。一般牙醫及時轉診可疑病變令病人可以及早診斷和接受治療可以減少病人的發病率。

## B) INTRODUCTION 簡介

Leukaemia is a hematologic disorder resulting from the proliferation of a clone of abnormal hematopoietic cells with impaired differentiation, regulation, and programmed cell death. Leukaemic cell multiplication at the expense of normal hematopoietic cells lines causes marrow failure, depressed blood cell count, and death as a result of infection, bleeding, or both. The oral manifestations of leukaemia include gingival enlargement, oral ulcerations, gingival bleeding, petechia and mucosal pallor. Oral lesions occur in both acute and chronic form of all types of leukaemias; myeloid, lymphoid and monocytic. However, the oral manifestations are far more common in the acute stages of the disease and are most common in monocytic leukaemia.

白血病是因為一克隆的異常造血細胞的進行受損的分化增殖，管制和程式性細胞死亡的一種血液系統紊亂。白血病細胞增殖損害正常的造血細胞的生產線會導致骨髓衰竭、血細胞數量減少、出血和因感染而死亡、或兩者。白血病的口腔表現形式包括牙齦腫大、口腔潰瘍、牙齦出血、牙齦瘀斑和粘膜蒼白。口腔病變可能發生在急性和慢性白血病；和所有類型的白血病，包括：髓細胞、淋巴細胞和單核細胞。然而，口腔表現在白血病的急性期是比較常見，最常見的是單核細胞白血病。

Gingival enlargement because of infiltration of premature leukocytes in leukaemia is well documented in literature and is one of the most common symptoms leading to the diagnosis of leukaemia that directs the patients to seek dental consultation.

因為不白血病的成熟粒白血球細胞滲透而形成牙齦腫大有記載在文獻中，而且是其中一個常見的診斷白血病的指示，同時也是指示病人尋求牙科諮詢最常見的症狀之一。

## C) CASE DESCRIPTION AND RESULTS 病例說明與結果

- 1) 32 years old male patient.
- 2) Chief complaint: bleeding gum from last five months.  
過去五個月牙齦出血
- 3) Present illness: He was apparently normal 5 months before and gradually developed pain and bleeding on brushing. On eliciting the medical history, patient was hospitalized 6 months before for breathlessness and enterocolitis. Patient also gave a history of mild weight loss and loss of appetite from last few months.

目前疾病：他5個月前是正常，逐漸刷牙痛和流血。醫療史：病人6個月前因的呼吸急促和小腸結腸炎住院。病人過去幾個月也有輕度體重和食欲減輕的歷史。



Figure 1. Generalized gingiva enlargement.



Figure 2. Bluish gingiva and ecchymosis in floor of the mouth.

- 4) General physical examination : moderately built, poorly nourished had signs of anaemia and skin looked pale but did not have signs of cyanosis and jaundice.

一般體檢：身型適中、營養不良，貧血和臉色蒼白，但沒有紫紺和黃疸的跡象。

- 5) On intraoral examination: generalised gingival enlargement was noticed. Gingival was bluish in colour with presence of ecchymosis in the floor of the mouth. His oral hygiene was poor with presence of local factors. On palpation, gingiva was soft and oedematous without stippling and was tender on palpation.

廣泛性牙齦腫大。Gingival 是淡藍色的，口底有瘀斑存在。他口腔衛生較差。

觸診：牙齦無點彩，水腫和軟。

- 6) Based on systemic and intraoral examination patient was advised to undergo routine blood investigations and was also advised to report back with all old blood and hospitalization reports. He was diagnosed with acute myeloid leukaemia (AML- M4) a day later by peripheral smear examination by special staining and flow cytometry. His old reports of hospitalization were checked which revealed that he had hepatomegaly and fluid filled oedematous bowel loops suggestive of enterocolitis. His comparative blood profile and normal blood count is given in Table 1.

基於對系統性和口腔內檢查醫生建議病人接受血液調查和還建議複查所有舊的血液和住院報告。他一天後由週邊塗片特殊染色檢查與流式細胞術被確診患急性骨髓性白血病 (AML M4)。他住院的舊報告檢查結果顯示了他有肝腫大、流體填充水腫和小腸結腸炎。他新舊血液報告的比較在表一。

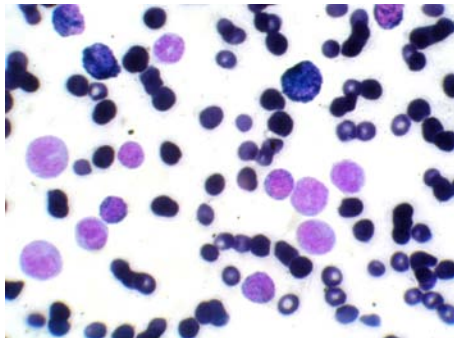


Figure 3. Peripheral smear MPO Positive (Myeloperoxidase) myloid cells.  
週邊塗片 MPO 陽性 (Myeloperoxidase) myloid 細胞。

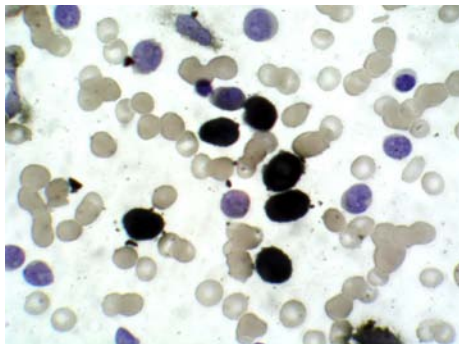


Figure 4. NSE Positive (Leukocyte nonspecific esterase) monocytyoid cells.  
NSE 陽性 (白血球非特異性酯酶) monocytyoid 細胞

	Initial blood picture (old hospitalization report)	Present blood picture (in department)	Normal value
Haemoglobin	6.9 gm%	5.6 gm%	11.5 - 16.5 gm%
RBC	3.17 million / cu mm	1.41 million / cu mm	3.5 - 6.0 million / cu mm
Platelets	75,000 / cu mm	25,000 / cu mm	1,50,000 - 4,50,000 / cu mm
TLC	98,000 / cu mm	1,12,000 / cu mm	4,000 - 11,000 / cu mm
DLC		Neutrophils 0.4%	
		Lymphocytes 10%	Neutrophils 40 -70%
	Neutrophils 15%	Myeloblasts 25%	Eosinophil 1 - 6%
	Eosinophil 4%	Monoblasts 15%	Basophils 0 - 1%
	Basophils 0%	Promonocytes 22%	Lymphocytes 20 - 40%
	Lymphocytes 77%	Monocytes 20%	Monocytes 2 - 10%
	Myelocytes 4%	Promyelocytes 0.1%	
		Myelocytes 0.1%	
	Metamyelo + band forms 0.2%.		

RBC = Red blood corpuscles; TLC = Total leukocyte count; DLC = Differential leukocyte count.

Table 1. Comparison of blood indices 血液指標的比較

- 7) Flow cytometry was done with forward scattering (FSC) versus side scattering (SSC) in which 57.73% cells were gated and the cells included all atypical cells. Further interpretation of these cells revealed strongly positive for CD45, CD13, CD14, and anti HLADR and moderately positive for CD4, CD34 and Anti MPO (Figure 5). These cells were negative for CD10, CD79a, CD7 and CD20 giving an impression of AML-M4.

流式細胞術做前向散射 (FSC) 與側散射 (SSC) 包括了57.73%細胞其中包含非典型的細胞。進一步解釋的這些細胞對CD13, CD45 CD14 和 anti-



HLADR顯示強烈陽性為和對CD4、CD13、CD34 和anti-MPO適度陽性（圖 5）。這些細胞對CD10、CD79a、CD7 和 CD20呈陰性。表示病人有可能患上急性骨髓性白血病(AML M4)。

The patient was referred to haematologist for further management and chemotherapy but the patient expired four days later due to multi organ failure and secondary infection.

病人經轉診到血液腫瘤科接受化療，但四天以後因多器官功能衰竭和繼發性感染死亡。

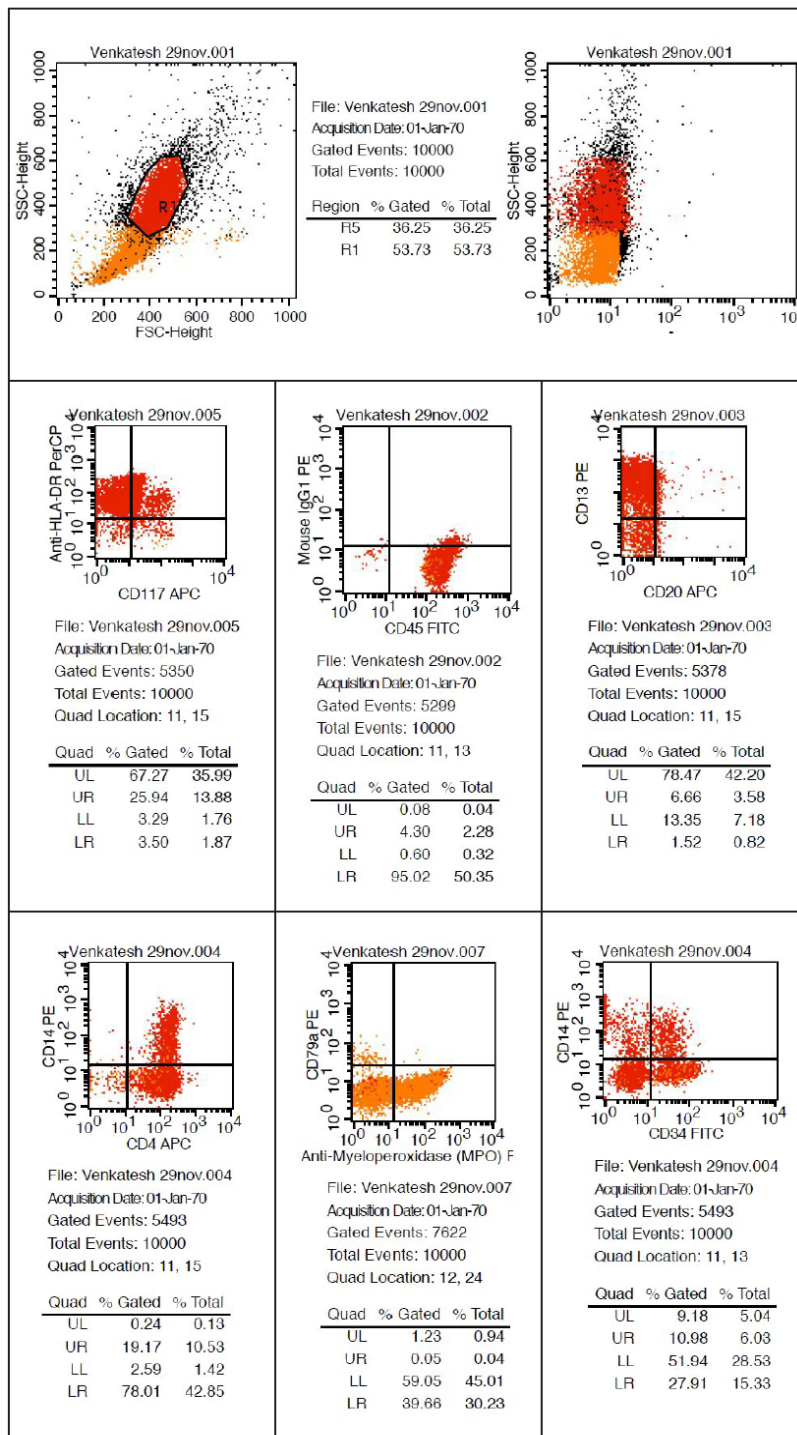


Figure 5. Flow cytometry (Positive for CD34, CD45, CD13, CD33, CD14, CD4, Anti-HLA DR, CD11 and anti MPO).

流式細胞術 (陽性 CD13、CD34、CD45、CD13、CD33、CD14、CD4、anti-HLADR、CD11 和 anti-MPO)。

#### D) DISCUSSION 討論

Leukaemia is classified as lymphocytic or myelocytic according to the lineage of white blood cells (WBC) involved; a subgroup of the myelocytic leukaemias is monocytic leukaemia.

白血病根據白血球 (WBC) 的參與被分類為淋巴細胞或骨髓細胞類；髓細胞性白血病的一個分組是單核細胞白血病。

Leukaemias can be:

Acute which is rapidly fatal, the primitive "blast" cells are released into the peripheral circulation

白血病可以是：

急性 這是迅速致命，原始"爆炸"的細胞被釋放到周圍迴圈

Sub-acute; or chronic, the abnormal cells tend to be more mature with normal morphologic characteristics and function when released into the circulation.

亞急性；或慢性，異常細胞往往會更成熟，具有正常的形態學特徵和功能時釋放到流通。

Classification for AML 急性骨髓性白血病：

World Health Organization (WHO) system classify AML into four subtypes as:

世界衛生組織系統把AML分為四個子類型為：

AML with characteristic genetic abnormalities (有特徵的遺傳異常)

AML with multilineage dysplasia (分化發育異常)

AML and myelodysplastic syndrome (MDS) 骨髓增生異常綜合征

myeloproliferative diseases therapy related AML not otherwise categorized.

骨髓增生異常疾病治療有關的AML不另行分類。

French-American-British (FAB) classification commonly classify AML under 8 subgroups as :

法美英分類通常對AML分類下 8 子群為：

M0 (undifferentiated leukaemia) 無分化的白血病

M1 (acute myeloblastic leukaemia) 急性髓系白血病

M2 (acute myeloblastic leukaemia with maturation) 急性髓系白血病成熟型

M3 (acute promyelocytic leukaemia) 急性前髓細胞白血病

M4 (acute myelo-monocytic leukaemia) 急性骨髓單核細胞白血病

M5 (acute monocytic leukaemia) 急性單核細胞白血病

M6 (acute erythroblastic leukaemia) 急性造血白血病

M7 (acute megakaryoblastic leukaemia) 急性巨細胞爆發型白血病

The morphologic subtype of AML also include a rare type not included in FAB system as ninth subtype, M8, as acute basophilic leukaemia.

AML的形態學子類型還包括不包括在 FAB 系統作為第九亞型的M8，作為急性嗜鹼白血病罕見類型。

Patients with AML generally present with symptoms related to complications of pancytopenia (anaemia, neutropenia, and thrombocytopenia) including weakness, and easy fatigue, infections of variable severity, and/or hemorrhagic findings such as gingival bleeding, ecchymoses, epistaxis or menorrhagia. In some cases atypical features like chin numbness and tooth pain has also been reported. The expression of these signs is more common in acute and sub-acute forms of leukaemia than in chronic forms.

AML急性骨髓性白血病的患者普遍有不同嚴重程度的併發症如全血細胞減少（貧血、中性粒細胞減少和血小板減少症）、牙齦出血、瘀斑或月經過多等出血性症狀，並容易疲勞、感染。在某些情況下非典型的情況像下巴麻木和牙齒疼痛也有報告。這些跡象在急性、亞急性白血病比慢性白血病較為常見。

Oral manifestations in patient with leukaemia have been described in:

在白血病患者中口腔顯示:

all subtypes of AML急性骨髓性白血病

chronic myeloid leukaemia (CML) 慢性骨髓性白血病

acute lymphocytic leukaemia (ALL) 急性淋巴性白血病

chronic lymphocytic leukaemia (CLL) 慢性淋巴性白血病

Gingival infiltration represents a 5% frequency as the initial presenting complication of AML. Gingival infiltration of leukemic cells is most commonly seen in acute monocytic leukaemia (M5) and acute myelomonocytic leukaemia (M4). Dreizen et al. in an observational study have reported gingival involvement in 66.7% of 1076 cases of AML M5 cases and 18.5% in M4.

牙齦滲透作為初期的併發症在AML是 5%。白血病細胞的牙齦滲透在 (M5)急性單核細胞白血病和急性骨髓單核細胞白血病(M4) 中最常見。Dreizen在觀測研究中報告了有影響牙齦的1076 個案66.7% AML M5和18.5% 是M4

Leukaemia cell gingival infiltrate is not observed in edentulous individuals, suggesting that local irritation and trauma associated with the presence of teeth may play a role in the pathogenesis of this abnormality.

白血病患者牙齦滲透是在無牙的病人觀察不到，這表明局部刺激和創傷與牙齒的存在關聯可能在此異常的發病中發揮作用。

Special leukaemia stains help to distinguish one cell type from another to investigate specific type of leukaemia in order to provide the best treatment and most accurate prognosis.

特別白血病染色可準確區分細胞類型，同時協助分辨不同類型的白血病，以提供最適當的治療和預後。

Commonly used special staining methods:

sudan black, periodic acid-schiff, terminal deoxynucleotidyl transferase stain, leukocyte alkaline phosphatase, tartrate-resistant acid phosphatase stain, myeloperoxidase (MPO), leukocyte specific and nonspecific esterase.

常用特殊染色方法：

蘇丹黑色，定期酸城、終端 deoxynucleotidyl 轉移酶染色、白血球鹼性 phosphatase、抗酒石酸酸性磷酸酶染色、髓過氧化酶 (MPO)、白細胞具體和非特異性酯酶。

Special stain used in our case which showed presence of myeloblasts in the peripheral smear suggestive of acute myelocytic leukaemia:

在這例子顯示檢測存在週邊塗片中表示了急性髓細胞性白血病中使用的特殊染色：

myeloperoxidase - The myeloperoxidase stain distinguishes between the immature cells in acute myeloblastic leukemia (cells stain positive) and those in acute lymphoblastic leukemia (cells stain negative).

過氧化物酶 -急性髓性白血病（細胞染色測試為正）的未成熟細胞和那些在急性淋巴細胞性白血病（細胞染色為負）區分的過氧化物酶。

leukocyte nonspecific esterase (NSE) - Nonspecific esterase stain identifies

monocytes and immature platelets (megakaryocytes), which show positive black granules.

白細胞非特異性酯酶 (NSE) -非特異性酯酶染色標識單核細胞和未成熟血小板 (巨核細胞)，其中顯示陽性的黑色顆粒。

Flow cytometry

The report of flow cytometry has confirmed the present case to be a case of AML M4 as the cells were strongly positive for : CD45, CD13, CD14, anti - HLADR

流式細胞術的報告已確認本病例是急性骨髓性白血病- M4型。

流式細胞術呈強陽性的細胞分析結果是: CD45, CD13, CD14, anti – HLADR

Treatment of AML

AML still remains a highly specialised one associated with high mortality and morbidity

- aggressive multidrug chemotherapy
- allogenic bone marrow transplantation

急性骨髓性白血病有著很高的死亡率和發病率，它的治療屬於很專門的一項。

- 積極的混合性藥物化療
- 同種異體骨髓移植

Periodontal and dental treatment for patients with leukaemia:

- should always be planned after medical evaluation and physicians consent.
- If systemic condition allows periodontal debridement (scaling and root planing) should be performed under antibiotic coverage
- Twice daily rinsing with 0.12% chlorhexidine gluconate is recommended after oral hygiene procedures but, periodontal surgeries should be avoided until remission.

白血病患者牙周和牙科治療:

- 在醫學上的評估和醫生的同意之下應擬定好治療計畫。
- 如果系統性條件允許牙周清創，應抗生素覆蓋下進行
- 每天兩次刷牙後用 0.12% CHX漱口，但應避免牙周手術直到情況改善

**E) CONCLUSIONS** 結論

A patient seeking dental treatment for bleeding gums was incidentally diagnosed as leukaemia based on thorough dental and medical history followed by definitive diagnosis by peripheral staining and flow cytometry as presented in this case. Therefore, the dentist may be the first person to diagnose such cases. The timely referral by the general dentist for a suspicious lesion provided an early diagnosis and early intervention reducing the patient morbidity. 尋求牙科治療的牙齦出血病人同時附帶地被診斷為白血病，這是基於徹底的牙科和醫科檢查和病歷記載，還有外周血液染色測試和流式細胞測試在這種情況下提出的確切分析。因此，牙醫可能是有機會接觸及診斷此類病例的第一人。一般牙醫及時轉診可疑病變令病人可以及早診斷和接受治療可以減少病人的發病率。

題號	題目
1	Leukemias are probably the result of a combination of environmental and genetic factors. Certain syndromes are associated with an increased risk. These genetic disorders include the following, except _____: 白血病的，很可能是組合的遺傳和環境因素的結果。有綜合症會增加患病的風險。這些遺傳疾病包括下列，_____除外： (A) Down Syndrome



	(B) Neurofibromatosis type I (C) AIDS (D) Wiskott-Aldrich Syndrome
答案(C)	出處：Oral and Maxillofacial Pathology, 3 <sup>rd</sup> Edi, Neville, Saunders Elsevier, Ch 13
題號	題目
2	Some environmental factors are associated with an increased risk of leukemia include the following, except: 有些環境因素會令患白血病的風險增加,包括以下,除了_____:
	(A) Exposure to pesticides, benzene, and benzene-like chemicals 暴露于殺蟲劑、苯和苯類化學物質 (B) Ionizing radiation (atomic bomb blasts survivors in WWII) 電離子的輻射 (在第二次世界大戰中原子彈爆炸的倖存者) (C) Spontaneous gingival hemorrhage, especially with platelet counts less than 10,000 to 20,000/mm <sup>3</sup> 自發的牙齦出血,尤其是與血小板計數小於 10,000 至 20,000/mm <sup>3</sup> (D) Retrovirus human T-cell leukemia/lymphoma virus type 1 (HTLV-1), transmitted by contaminated blood from infected to uninfected individual. 逆轉錄病毒人類 T 細胞淋巴瘤白血病/病毒類型 1 (第三型白血球-1), 由從感染到未受感染的個人受到污染的血液傳播。
答案(C)	出處：Oral and Maxillofacial Pathology, 3 <sup>rd</sup> Edi, Neville, Saunders Elsevier, Ch 13