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CASE REPORT

Gingival overgrowth caused by vitamin C deficiency associated with metabolic syndrome and severe periodontal infection: a case report

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Abstract

It has been suggested that vitamin C deficiency/scurvy is associated with gingival inflammatory changes; however, the disorder is very infrequently encountered in the modern era. Here, we report a case of extensive gingival overgrowth caused by vitamin C deficiency associated with metabolic syndrome and severe periodontal infection.

Keywords

Gingival overgrowth, metabolic syndrome, periodontal infection, supplementation of ascorbic acid, vitamin C deficiency.

Introduction

Gingival overgrowth is defined as an excessive growth of periodontal tissues. The pathogenesis of gingival overgrowth is associated with multiple factors including inflammation, specific drug usage (e.g., cyclosporin A, phenytoin, nifedipine) [1], and systemic disorders (e.g., leukemia, vitamin C deficiency/scurvy) [2–4]. Vitamin C deficiency/scurvy was initially associated with sailors who undertook lengthy sea voyages; their inadequate intake of ascorbic acid during these journeys led to spontaneous bleeding from periodontal tissues and abnormal gingival enlargement. However, vitamin C deficiency/scurvy is infrequently encountered in modern industrialized nations [3, 5, 6].

In the present case report, we note that mild vitamin C deficiency associated with metabolic syndrome and severe periodontal infection is a pathogenic factor associated with extensive gingival overgrowth, and that oral supplementation with ascorbic acid (also known as vitamin C) and periodontal treatment are effective at suppressing recurrent gingival enlargement. We believe that this case report will remind readers of the effect of vitamin C deficiency on periodontal conditions.

Case Presentation

In July 2008, a 37-year-old man with severe gingival overgrowth was referred by his general dental practitioner to the Department of Periodontics and Endodontics at the Okayama University Hospital because of aesthetic and functional difficulties. His medical history was as follows: the patient reported a history of smoking over

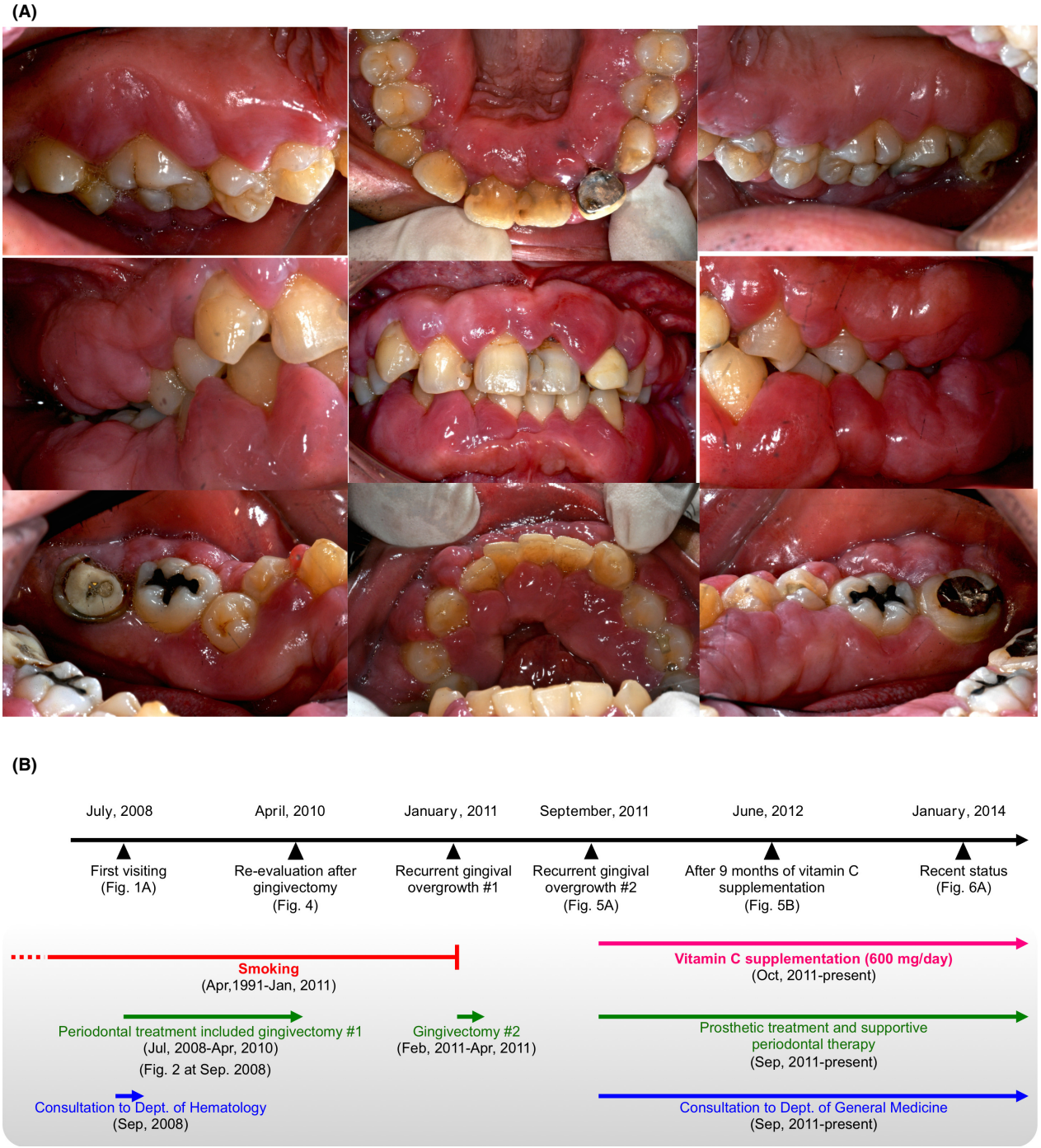


Figure 1. Periodontal images of the patient taken before periodontal treatment. (A) Extensive gingival overgrowth with severe periodontal inflammation was observed in the maxillary and mandibular arches at the first visit (July, 2008), (B) treatment protocol.

20 years but he was not taking any medication that could induce gingival overgrowth, and he had no familial history of similar symptoms. Gingival enlargement began suddenly at the age of 36 years. Intraoral examination revealed severe gingival overgrowth of a firm, thick, and fibrotic consistency with inflammatory signs (redness, swelling, and bleeding from periodontal pockets) in the maxillary and mandibular arches (Fig. 1A). Periodontal examination also revealed severe periodontal inflammation including deep periodontal pockets and high percentage of bleeding on probing (BOP)-positive sites (Fig. 2A). Radiographic findings revealed severe generalized alveolar bone loss associated with periodontal infection and traumatic occlusion (Fig. 2B). Subgingival plaque samples were obtained from the deep periodontal pockets using paper points and periodontal pathogens (*Porphyromonas gingivalis*, Pg; *Aggregatibacter actinomycetemcomitans*, Aa; *Prevotella intermedia*, Pi) were detected in these samples by quantitative real-time polymerase chain reaction (PCR), as described previously [7]. Severe infection by these periodontal pathogens was observed in the subgingival enlarged gingival pockets upon further examination (Table 1). The patient was aware of a clenching habit. The Department of Hematology at Okayama University Hospital was also contacted to screen for hematopoietic problems including leukemia.

(A)

Mobility		0			2			2			2			1			1			1	
BOP	•	•	•	•	•	•			•	•	•	•	•	•	•	•	•	•	•	•	•
Bu-PD (mm)	7	9	10	9	12	11	9	9	7	8	7	8	7	4	7	6	4	7	8	6	7
Tooth #		2			3			4			5			6			7			8	
Pa-PD (mm)	6	6	7	8	8	9	9	11	10	9	8	9	8	7	7	6	6	8	7	8	7
BOP	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•

Mobility		1			1			2			2			2			2			2			2	
BOP	•	•	•	•	•	•	•	•	•			•	•	•	•	•	•	•	•	•	•	•	•	•
Bu-PD (mm)	8	7	10	7	6	7	6	5	7	6	5	6	7	9	8	8	9	9	9	11	10	7	9	8
Tooth #		9			10			11			12			13			14			15			16	
Pa-PD (mm)	8	9	9	8	7	8	10	9	9	9	11	9	9	9	8	9	7	8	8	7	8	8	9	8
BOP	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•

BOP	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
Li-PD (mm)	4	4	5	6	6	6	6	6	8	10	10	10	10	6	8	10	7	8	10	8	7
Tooth #		31			30			29			28			27			26			25	
Bu-PD (mm)	7	6	8	7	8	8	8	8	8	8	6	12	10	8	10	10	6	8	6	6	6
BOP	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
Mobility		0			0			0			0			0			0			0	

BOP	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
Li-PD (mm)	10	8	9	8	8	8	10	10	8	8	8	8	9	8	8	8	8	8	8	7	6
Tooth #		24			23			22			21			20			19			18	
Bu-PD (mm)	6	6	8	8	6	8	10	8	10	10	10	8	8	6	6	8	8	10	8	10	10
BOP	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
Mobility		0			0			0			0			0			1			1	

(B)

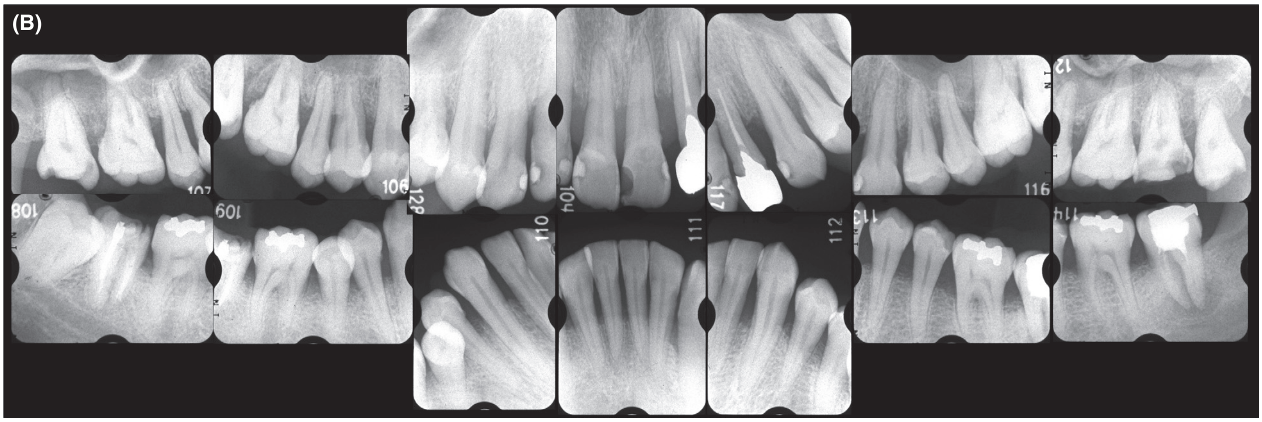


Figure 2. Periodontal examination and full mouth X-ray images taken of the patient before periodontal treatment. (A) The periodontal chart at the first visit revealed pocket probing depths that were significantly higher than normal with a rate of bleeding on probing (BOP)-positive sites of 98%, (B) radiographic evaluation revealed severe bone loss around the incisors and maxillary molars due to severe periodontal infection and traumatic occlusion (July, 2008).

Table 1. Periodontal bacteria identified by quantitative real-time PCR at the first visit.

Sampling site	Probing depth	Total bacteria	Aa	Pg	Pi
#9, BM	8 mm	1.13×10^5	6.75×10^2	3.72×10^2	2.60×10^3
#19, BM	8 mm	1.61×10^6	4.08	1.70×10^3	5.21×10^5
#4, BM	7 mm	3.33×10^5	1.69×10^4	1.28×10^2	3.57×10^4

A periodontal microbiological examination was performed using quantitative real-time PCR, as described previously [7]. The following pathogens were detected and the associated data are shown as DNA copies/sample. Aa, *Aggregatibactor actinomycetemcomitans*; Pg, *Porphyromonas gingivalis*; Pi, *Prevotella intermedia*; BM, buccal mesial.

Table 2. Changes in laboratory parameters.

Parameter	Unit	First visit (September, 2008)	Whole-body screening (September, 2011)	After vitamin C supplementation (April, 2012)	Present (January, 2014)	Standard level
WBC	$10^3/\mu L$	7.62	7.98	6.47	6.54	3.50–8.50
RBC	$10^6/\mu L$	5.33	5.50	5.30	5.33	4.30–5.70
Hb	g/dL	16.2	16.1	16.0	15.9	13.5–17.0
Ht	%	47.5	49.0	48.2	47.5	40.0–50.0
PLT	$10^3/\mu L$	317	301	314	307	150–350
Alb	g/dL	4.4	4.5	4.5	4.1	3.9–4.9
TTT	U	1.5	2.2			0.2–5.3
ZTT	U	10.8	11.9			3.8–14.9
Total bilirubin	mg/dL	1.10	1.56 *			0.33–1.28
Direct bilirubin	mg/dL	0.22	0.30 *			0.08–0.28
AST	IU/L	26	40 *	43 *	19	10–35
ALT	IU/L	20	40	51 *	20	7–42
ALP	IU/L		249			110–360
LAP	IU/L	101 *	118 *	102 *	81 *	28–75
γ-GTP	IU/L	129 *	207 *	140 *	95 *	5–60
CHE	IU/L	501 *	558 *	548 *	484 *	168–470
LD	IU/L	164	211	182	171	120–240
Na	mmol/L	140	140	138	138	136–144
K	mmol/L	4.6	4.1	4.0	4.2	3.7–4.9
Cl	mmol/L	106	103	105	103	102–110
Ca	mg/dL	9.7	9.6	9.2	9.2	8.6–10.1
Mg	mg/dL		2.1			2.0–2.5
Fe	μg/dL		129			80–140
Ferritin	ng/dL		262.2			39.9–465.0
Cu	μg/dL		133			78–141
Zn	μg/dL		100			80–130
UN	mg/dL	12.7	11.1	13.9	13.5	8.1–22.0
Cr	mg/dL	0.88	0.85	0.84	0.86	0.6–1.1
UA	mg/dL	7.0	7.1 *	4.1	4.2	3.5–7.0
UN/Cr		14.8	13.1	16.5	15.7	10.2–27.6
CK	IU/L		124			41–258
Amylase	IU/L		66			38–125
TG	mg/dL		171 *	271 *	343 *	40–150
T-CHO	mg/dL	259 *	273 *			130–220
HDL-C	mg/dL		92 *	74	83	41–85
LDL-C	mg/dL		157 *	144 *	141 *	70–139
LDL/HDL			1.7	1.9	1.7	
HbA1c (NGSP)	%		6.3 *	6.4 *	6.3 *	4.7–6.2
Albumin	%		63.2			60.9–71.3
α1-globulin	%		2.5			1.8–2.7
α2-globulin	%		7.5			5.9–8.5
β-globulin	%		11.0 *			6.9–10.5
γ-globulin	%		15.8			11.0–21.2
Albumin/globulin			1.7			1.50–2.43
hs-CRP	mg/dL	0.04	0.31 *	0.08	0.10	0.00–0.30
IgG	mg/dL		1379.3			870–1818
IgA	mg/dL		353.8			110–424
IgM	mg/dL		81.6			31–252
CH50	U/ml		39			30–50
C3	mg/dL		133.1			65–135
C4	mg/dL		28.7			13–35
Vitamin C	μg/dL		3.8 †	8.1		5.6–15.6
Rheumatoid factor	IU/mL		1.5			0.0–16.0

(*Continued*)

Table 2. Continued.

Parameter	Unit	First visit (September, 2008)	Whole-body screening (September, 2011)	After vitamin C supplementation (April, 2012)	Present (January, 2014)	Standard level
IgG4	mg/dL		17.5			4.8–105.0
HTLV-I Ab			Negative			Negative
HBV Ag			Negative			Negative
HBV Ab			Negative			Negative
HCV Ab			Negative			Negative
HIV Ab			Negative			Negative

Blank data are not measured. WBC, white blood cells; RBC, red blood cells; Hb, hemoglobin; Ht, hematocrit; PLT, platelets; Alb, albumin; TTT, thymol turbidity test; ZTT, zinc sulfate turbidity test; ALT, alanine aminotransferase; ALP, alkaline phosphatase; LD, lactate dehydrogenase; UN, urea nitrogen; Cr, creatinine; UA, uric acid; CK, creatinine kinase; hs-CRP, high-sensitivity C-reactive protein; IgG, immunoglobulin G; IgM, immunoglobulin M; IgA immunoglobulin A; IgG4, immunoglobulin G4; HTLV-1 Ab: anti-human T-cell leukemia virus type 1 antibody; HBV Ag, hepatitis B virus surface antigen; HBV Ab, anti-hepatitis B virus antibody; HCV Ab, anti-hepatitis C virus antibody; HIV Ab, anti-human immunodeficiency virus type 1 and 2 antibody; BMI, body mass index.
*Above upper limit.
†Below lower limit.

General laboratory blood analysis revealed high levels of several metabolic markers (leucine aminopeptidase [LAP]: 101 IU/L, normal level: 28–75 IU/L; γ-glutamyl transpeptidase [γ-GTP]: 129 IU/L, normal level: 5–60 IU/L; cholinesterase [CHE]: 501 IU/L, normal level: 168–470 IU/L; and total cholesterol [T-CHO]: 259 mg/dL, normal level: 130–220 mg/dL); however, no hematological factors were found to be responsible for the gingival overgrowth (Table 2). The case was initially diagnosed as idiopathic gingival overgrowth with severe periodontitis based on the features outlined above. Instructions regarding oral hygiene procedures were provided and the patient was also informed of suitable surgical treatments including extraction of periodontally compromised teeth and periodontal surgery to reduce the overgrown gingivae. The patient initially underwent regular periodontal scaling and root planning; subsequently, a gingivectomy combined with open-flap debridement was performed. The pathological diagnosis of gingival hyperplasia with infiltrated inflammatory cells (primarily plasma cells in connective tissue [Fig. 3]) was determined using extirpated overgrown gingivae. The patient's gingival condition showed good clinical course and improvements following periodontal surgery compared to his first visit; however, residual deep periodontal pockets without BOP remained (April, 2010; Fig. 4).

Unfortunately, in January 2011, recurrence of overgrowth was detected at the lower molar gingivae after the first gingivectomy despite the removal of infectious factors such as dental calculus. The patient stopped

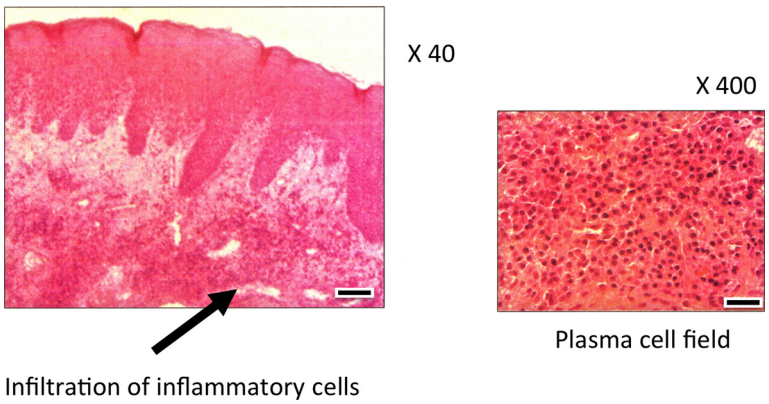
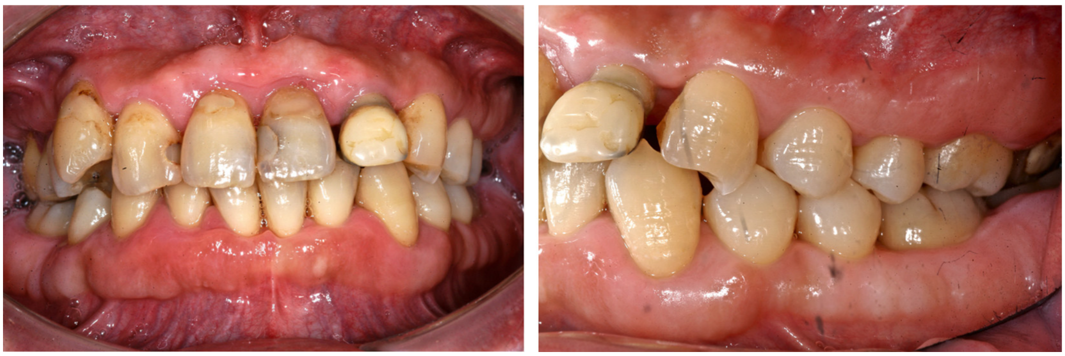


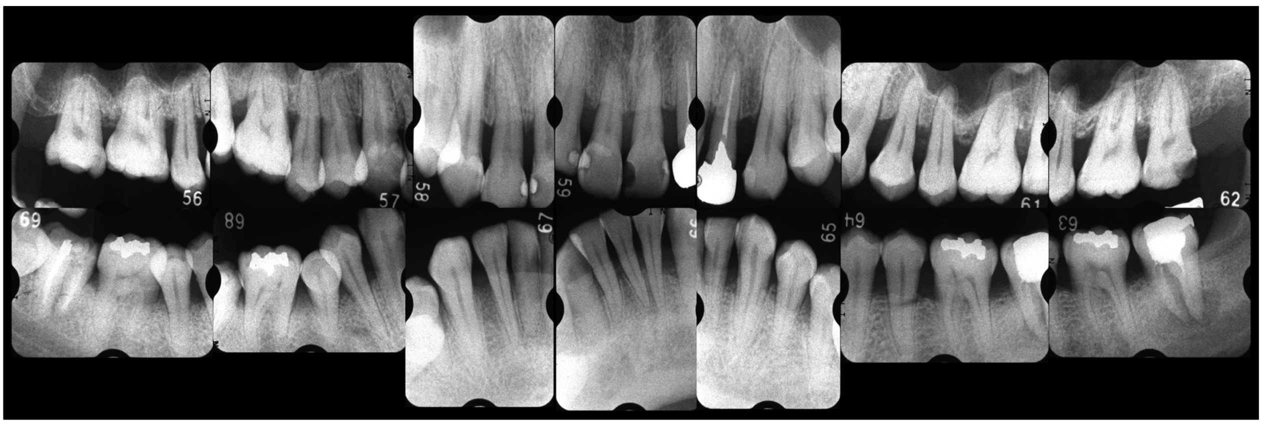
Figure 3. Microscopic evaluation of the specimen taken from the patient showed hyperplasia of the epithelial region and extended epithelial rete ridges in addition to the infiltration of severe inflammatory cells (primarily plasma cells) in the connective tissue. No dense, mature, parallel collagen bundles were observed nor was there any evidence of tumor proliferation or viral or fungal infection. Original magnification = 40 × ; bar = 500 μm, =400 × ; bar = 50 μm, respectively.

smoking at this time, and a second gingivectomy was performed (February, 2011). However, in September 2011 (8 months after the second gingivectomy), further recurrence of gingival enlargement was observed (Fig. 5A). We therefore consulted the Department of General Medicine, Okayama University Hospital, and the patient underwent whole-body screening, including blood tests (general, protein fractionation, plasma vitamin C level, and autoimmune/infectious diseases markers), urinalysis, metal allergy patch test for dental alloys (cobalt, mercury, chromium, nickel, copper, aluminum, gold, tin, iron, platinum, palladium, iridium, zinc, manganese, and silver), chest X-ray, and electrocardiogram. The screening results were as follows: (1) weakly positive allergy to cobalt and mercury; (2) large waist circumference (87.0 cm; normal range: <85.0 cm) according to the Japanese definition and the diagnostic standard for metabolic syndrome [8] and high levels of metabolic markers related to hepatic dysfunction (aspartate aminotransferase [AST]: 40 IU/L, normal level: 10–35 IU/L; LAP: 118 IU/L; γ-GTP: 207 IU/L; CHE: 558 IU/L), hyperlipidemia (triglyceride [TG]: 171 mg/dL, normal level: 40–150 mg/dL; T-CHO: 273 mg/dL; high-density lipoprotein cholesterol [HDL-C]: 92 mg/dL, normal level: 41–85 mg/dL; low-density lipoprotein cholesterol [LDL-C]: 157 mg/dL, normal level: 70–139 mg/dL), and hyperglycemia (HbA1c

(A)



(B)



(C)

Mobility		0			0			0			0			0			1			1			1			2			0			1			1			1			0	
BOP							•	•	•																																	
Bu-PD (mm)	5	5	5	4	4	4	6	3	4	4	2	3	4	3	4	3	2	4	5	3	3	3	4	3	3	2	3	3	3	3	6	4	5	5	5	5	6	6	5	6	3	4
Tooth #		2			3			4			5			6			7			8			9			10			11			12			13			14			15	
Pa-PD (mm)	5	5	6	6	5	8	6	6	6	8	6	3	3	3	3	4	5	5	4	4	4	4	4	4	4	3	4	4	4	6	8	6	6	6	4	4	6	5	4	5	6	6
BOP	•	•	•				•			•																																
BOP																	•																									
Li-PD (mm)	4	4	4	5	5	5	5	5	6	6	6	6	6	4	4	4	3	3	3	3	3	4	4	4	4	4	4	4	4	4	4	4	4	4	5	5	4	5	5	5	5	5
Tooth #		31			30			29			28			27			26			25			24			23			22			21			20			19			18	
Bu-PD (mm)	6	4	6	2	4	5	6	6	6	6	6	4	4	3	3	3	3	3	3	3	3	3	3	3	4	3	5	5	3	3	3	3	3	3	3	3	3	4	6	6	8	8
BOP																																									•	
Mobility		0			0			0			0			0			0			0			0			0			0			0			0			0			0	

Figure 4. Reevaluation after the first gingivectomy. (A) Periodontal images, (B) full mouth X-ray images, (C) periodontal chart (April, 2010).

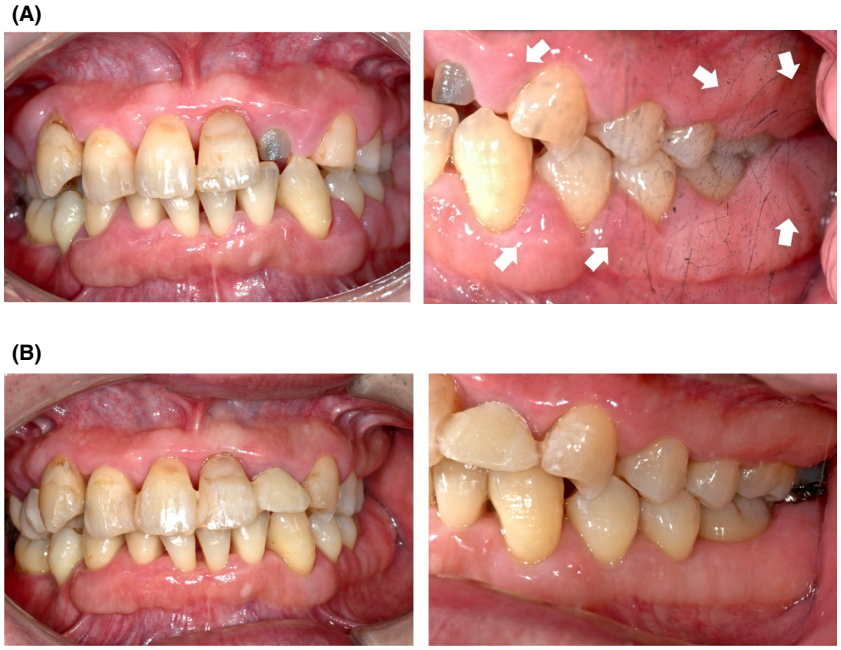


Figure 5. Periodontal images taken before and after ascorbic acid supplementation. (A) Recurrent gingival overgrowth observed after the second gingivectomy and before ascorbic acid supplementation (September, 2011), (B) images taken after 9 months of ascorbic acid supplementation (June, 2012). The white arrows indicate typical sites of recurrent gingival overgrowth.

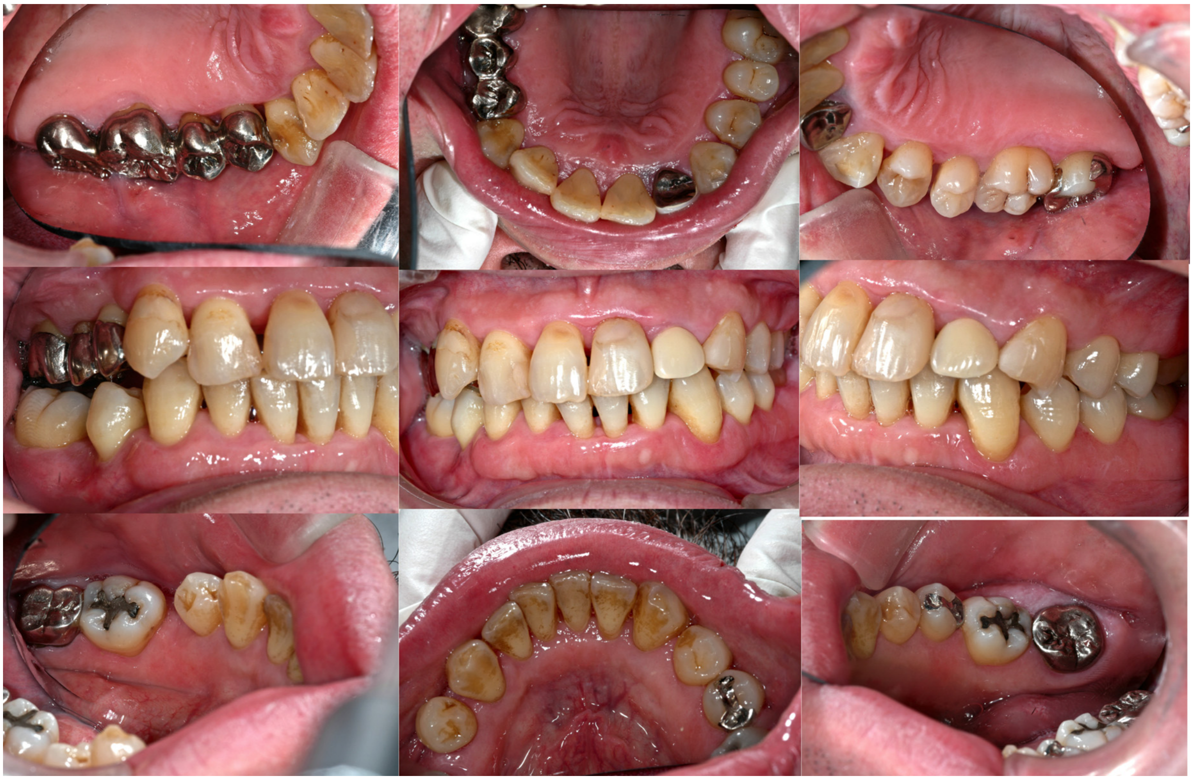
[NGSP] 6.3%, normal level: 4.7–6.2%); and (3) low level of plasma vitamin C (3.8 μg/mL, normal level: 5.5–16.8 μg/mL) (Table 2). A few metal restorations comprising gold–silver–palladium dental alloys were present in the patient's mouth, and a review of his daily diet did not reveal any poor habits that could be responsible for the mild vitamin C deficiency. Based on these test results, we diagnosed gingival enlargement caused by vitamin C deficiency with metabolic syndrome. The patient was instructed to change his lifestyle, and prescribed oral ascorbic acid (600 mg/day). Oral hygiene was maintained without any surgical periodontal treatment with only sonic scaling of the supra- and subgingival tooth surfaces. After 4 months of ascorbic acid supplementation, the gingival overgrowth was markedly reduced, and has remained so for 9 months without recurrence (Fig. 5B). At this time, the patient's plasma vitamin C level was 8.1 μg/mL, but no improvements in metabolic marker levels have been noted (Table 2). Open-flap surgery with osteoplasty was performed before the insertion of metal crown prostheses to ensure ready access to the upper right molar with an internal tooth brush (December, 2012). Supportive periodontal therapy was continued after the prosthetic treatment to control the occlusal force and the patient's radiographic and periodontal status at this time are shown in Figures 6B and C (October, 2013). The most recent assessment of the patient has revealed no recurrence of gingival enlargement after 28 months of ascorbic acid supplementation (Fig. 6A).

Discussion

Gingival overgrowth causes aesthetic and functional difficulties. The pathogenesis of gingival overgrowth is usually associated with factors such as the use of certain drugs or systemic disorders such as vitamin deficiency/scurvy [1–4]. In the present case, we consider the main pathological entity to be related to a deficiency of vitamin C. However, vitamin C deficiency/scurvy is infrequently encountered in the modern era and the vitamin C deficiency was missed when the patient first presented for treatment. Similar cases of vitamin C deficiency leading to gingival hypertrophy have been reported recently [3, 4]. However, extensive gingival enlargement related to a mixed pathology with vitamin C deficiency and severe periodontal inflammation with bone loss is unusual. We found that treatment of both pathologic factors was required with ascorbic acid supplementation and gingivectomy combined with open-flap debridement. We believe this case report will be a useful reminder of the pathological effects of vitamin C deficiency on gingival inflammatory changes.

According to the World Health Organization (WHO), a serum ascorbic acid level <2 μg/mL is defined as defi-

(A)



(B)

Mobility	0	0	0	0	0	0	0	0	1	0	0	0	0	0
BOP									*					
Bu-PD (mm)	1 1 1	1 1 1	1 1 2	1 1 1	2 2 2	1 1 1	3 3 3	2 2 2	3 3 4	3 3 3	3 3 3	3 2 3	3 3 3	1 1 2
Tooth #	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Pa-PD (mm)	3 2 3	2 3 3	3 3 3	2 2 1	2 2 2	2 1 2	2 2 1	2 1 1	1 2 3	1 2 2	2 2 2	2 3 2	2 1 2	2 1 1
BOP														
BOP														
Li-PD (mm)	2 2 2	2 2 2		2 1 2	2 2 2	2 1 2	1 1 1	1 1 1	1 1 2	2 2 2	3 3 3	3 3 2	3 3 4	3 3 3
Tooth #	31	30		28	27	26	25	24	23	22	21	20	19	18
Bu-PD (mm)	2 2 2	2 2 2		2 2 2	2 3 3	3 3 3	3 3 1	2 3 3	3 2 3	3 2 3	2 1 2	3 3 3	4 3 3	4 3 3
BOP														
Mobility	0	0		0	0	0	0	0	0	0	0	0	0	1

(C)

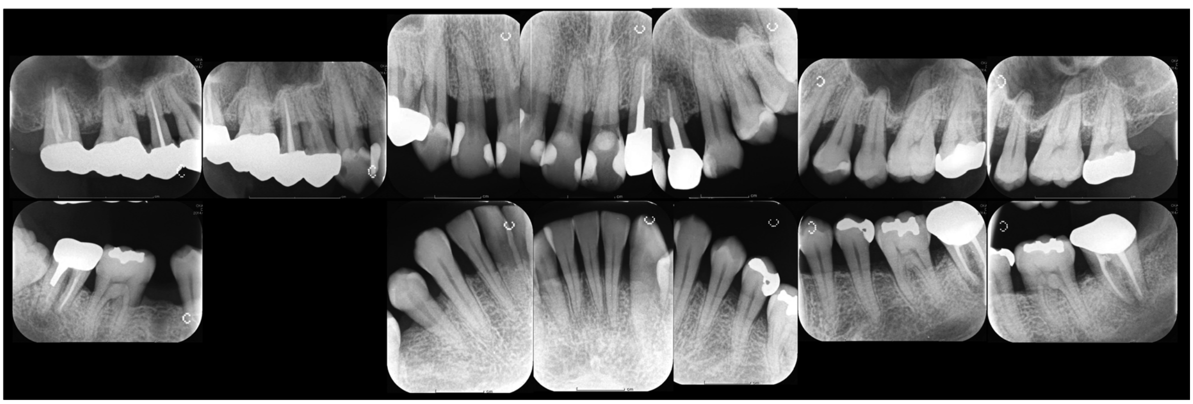


Figure 6. Periodontal status of the patient after periodontal treatment and ascorbic acid supplementation. (A) recent periodontal images revealed no recurrence of gingival overgrowth (January, 2014), (B) periodontal chart revealed a significant reduction in pocket probing depths and in the number of BOP-positive sites compared to the first visit, (C) radiographic evaluation revealed that a stable alveolar bone level was maintained during supportive periodontal therapy (October, 2013).

cient and is associated with a high risk of scurvy [5]. In the present case, the patient's plasma vitamin C level was defined as mildly deficient, and thus was not defined as scurvy. Mild vitamin C deficiency can be the result of several factors, including diabetes, stress, and smoking [5]. Clinical and laboratory data in this case also indicated that the patient had metabolic syndrome (Table 2). The precise direct interaction between metabolic syndrome and vitamin C deficiency remains unclear. However, Kubota et al. reported that serum vitamin C concentration was inversely associated with high-sensitivity C-reactive protein (hs-CRP) levels, which are a marker of oxidative stress, which induces atherosclerosis [9]. In addition, Helmersson et al. reported that low dietary intake of ascorbic acid is associated with increased inflammatory and oxidative stress [10]. In the present case, laboratory data showed that the patient's hs-CRP level was slightly elevated (0.31 mg/dL, normal level: 0.00–0.30 mg/dL). The patient did not have poor dietary habits that would cause a vitamin C deficiency, which suggests that metabolic syndrome-induced microinflammation (oxidative stress) may be associated with mild vitamin C deficiency.

Vitamin C is an essential vitamin for maintaining a healthy body. Recent reports have suggested various roles for vitamin C is divergent (i.e., various hydroxylation reactions; redox homeostasis of subcellular compartments including the mitochondria and endoplasmic reticulum; nucleic acid and histone dealkylation; and proteoglycan deglycation) [6]. In addition, vitamin C plays a major role in collagen biosynthesis and maturation, and it is essential for the maintenance of the basal membrane [6]. In the present case, the mild vitamin C deficiency may have been linked to a decreased ability to cross-link to collagen and therefore to an impaired ability to synthesize stable collagen fibers.

On the other hand, there have not been any previous reports of vitamin C deficiency linked to metabolic syndrome occurring in combination with severe periodontal infection causing extensive periodontal enlargement. The coexistence of these two entities may represent a new manifestation like hereditary gingival fibromatosis associated with generalized aggressive periodontitis, as reported previously [11]. Based on the limited evidence and paucity of clinical cases, further investigation is required to clarify the interaction of these two clinical pathologies.

In the present case, vitamin C deficiency associated with metabolic syndrome and periodontal pathogenic factors (severe periodontal infection and an excessive occlusal force due to a clenching habit) were the likely causes of severe gingival overgrowth. We are convinced that measurement of the plasma vitamin C level with ascorbic acid supplementation and periodontal treatment (if needed) will reduce the need for invasive surgical procedures and improve the quality of life of patients with nondrug-induced gingival overgrowth.

Conclusions

The present case report suggests that mild vitamin C deficiency associated with metabolic syndrome and severe periodontal infection may be associated with the pathogenesis of severe gingival overgrowth. Further, it indicates that measurement of plasma vitamin C level with ascorbic acid supplementation and periodontal treatment if needed may be useful for patients with gingival overgrowth caused by vitamin C deficiency and severe periodontal infection.

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Conflict of Interest

None declared.

References

1. Dongari-Bagtzoglou, A., Research, Science and Therapy Committee, American Academy of Periodontology. 2004. Drug-associated gingival enlargement. J. Periodontol. 75:1424–1431.
2. Tjwa, E., and V. Mattijssen. 2008. Images in clinical medicine. Gingival hypertrophy and leukemia. N. Engl. J. Med. 359:e21.
3. Li, R., K. Byers, and R. R. Walvekar. 2008. Gingival hypertrophy: a solitary manifestation of scurvy. Am. J. Otolaryngol. 29:426–428.
4. Bendick, C., and S. Mey. 2012. Haematomas and gingival bleeding. Lancet 379:2400.
5. World Health Organization. 1999. Scurvy and its prevention and control in major emergencies. WHO, Switzerland. http://apps.who.int/iris/bitstream/10665/66962/1/WHO_NHD_99.11.pdf?ua=1
6. Mandl, J., A. Szarka, and G. Banhegyi. 2009. Vitamin C: update on physiology and pharmacology. Br. J. Pharmacol. 157:1097–1110.
7. Maeda, H., C. Fujimoto, Y. Haruki, T. Maeda, S. Kokeguchi, M. Petellin, et al. 2003. Quantitative real-time PCR using TaqMan and SYBR Green for *Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis, Prevotella*

intermedia, tetQ gene and total bacteria. FEMS Immunol. Med. Microbiol. 39:81–86.
8. Committee to Evaluate Diagnostic Standards for Metabolic Syndrome. 2005. Definition and the diagnostic standard for metabolic syndrome [in Japanese]. Nippon Naika Gakkai Zasshi 94:794–809.
9. Kubota, Y., Y. Moriyama, K. Yamagishi, T. Tanigawa, H. Noda, K. Yokota, et al. 2010. Serum vitamin C concentration and hs-CRP level in middle-aged Japanese men and women. Atherosclerosis 208: 496–500.
10. Helmersson, J., J. Arnlöv, A. Larsson, and S. Basu. 2009. Low dietary intake of beta-carotene, alpha-tocopherol and ascorbic acid is associated with increased inflammatory and oxidative stress status in a Swedish cohort. Br. J. Nutr. 101:1775–1782.
11. Casavecchia, P., M. I. Uzel, A. Kantarci, H. Hasturk, S. Dibart, T. C. Hart, et al. 2004. Hereditary gingival fibromatosis associated with generalized aggressive periodontitis: a case report. J. Periodontol. 75:770–778.

