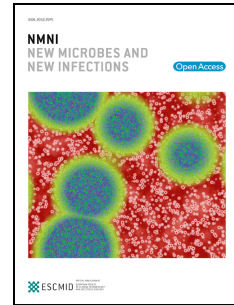


# Journal Pre-proof

*Alloprevotella rava* isolated from a mixed infection of an elderly patient with chronic mandibular osteomyelitis mimicking oral squamous cell carcinoma

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## First clinical case report

### ***Alloprevotella rava* isolated from a mixed infection of an elderly patient with chronic mandibular osteomyelitis mimicking oral squamous cell carcinoma**

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Running title: ***Alloprevotella rava* in chronic mandibular osteomyelitis**

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1 ***Alloprevotella rava* isolated from a mixed infection of an elderly patient with**  
2 **chronic mandibular osteomyelitis mimicking oral squamous cell carcinoma**

3  
4 **Abstract**

5 The anaerobic, Gram-negative bacillus, *Alloprevotella rava* has recently been  
6 described in human oral cavity. To our knowledge, this species has not been isolated  
7 from chronic osteomyelitis samples. We presented the first case of *A. rava* infection  
8 in a 92-year-old patient with polymicrobial chronic mandibular osteomyelitis,  
9 mimicking oral squamous cell carcinoma.

10

11

12 **Keywords:** *Alloprevotella rava*, anaerobic bacillus, actinomycosis, chronic  
13 mandibular osteomyelitis, oral squamous cell carcinoma

14

15

16 **Introduction**

17 Chronic mandibular osteomyelitis (CMO) is a serious condition requiring early and  
18 accurate diagnosis, antibiotics, and surgical management. The cases are usually  
19 mixed anaerobic infections, reinforcing the concept that osteomyelitis of the jaws are  
20 mainly related to microorganisms from the oral environment [1]. *Alloprevotella rava* is  
21 an obligatory anaerobic Gram-negative bacilli isolated from the human oral cavity,  
22 associated with oral dysbiotic infections such as dental caries and periodontitis  
23 [2,3,4]. We presented the first case of *A. rava* infection in a patient with polymicrobial  
24 CMO initially thought to be oral squamous cell carcinoma (SCC) upon the presence  
25 of clinical and computed tomography findings.

## 26 **Case report**

27 A 92-year-old woman, presented to our hospital with chronic, bloody discharge in the  
28 left mandibular body for 18 months, since the teeth extraction in the same region.  
29 According to her medical history, the patient's cervical lymph node was removed and  
30 received radiotherapy with a diagnosis of lymphoma, 5 years ago. The patient also  
31 received medication for osteoporosis. Tissue specimens, obtained from defective  
32 bone and surrounding soft tissue, were examined histopathologically and  
33 microbiologically. Histopathology made a diagnosis of actinomycosis without any  
34 malignancy. However microbiological examination revealed polymicrobial infection  
35 involving five bacteria. Four organisms were identified by MALDI-TOF MS (VITEK  
36 MS; bioMérieux) as *Veilonella parvula*, *Prevotella nigrescens*, *Klebsiella oxytoca* and  
37 *Corynebacterium durum*. The fifth bacterium, for which MALDI-TOF MS was  
38 insufficient for identification, was identified by 16S rRNA gene sequencing as  
39 *Alloprevotella rava* with 99% nucleotide identity to the strain isolated from the human  
40 oral cavity (GenBank accession no. JQ039190) [2]. The *actinomyces* strain was not  
41 isolated despite of the 14-day incubation period for anaerobic culture [5]. All isolated  
42 organisms were susceptible to amoxicillin-clavulanic acid (AMC). The patient was  
43 given empirical AMC, she was discharged on the fifth day of hospitalization with oral  
44 AMC therapy (2X1g daily) for two months. The clinical condition improved  
45 considerably, mandibular discharge and swelling disappeared.

46

## 47 **Discussion**

48 In our case, three different anaerobic bacteria were isolated, consistent with the  
49 mixed anaerobic etiology of CMO. Several fastidious strictly anaerobic bacteria  
50 commonly present in the dental biofilm suggests the source of infecting pathogens in

51 osteomyelitis of the jaws is likely to be gingivitis, chronic periodontitis, previous dental  
52 extractions or endodontic treatments [1]. *Alloprevotella rava* was firstly isolated from  
53 dental plaque [2]. In our case *A. rava* was isolated from a patient with CMO with a  
54 history of tooth extraction on the same area. This is the first case of CMO, which  
55 consisted of *A. rava* in the world literature. However, it may not reflect the actual  
56 result because phenotypic identification systems have insufficient databases for this  
57 microorganism. *Alloprevotella rava* has been detected from oral microbiota of certain  
58 patients with oral dysbiosis by molecular techniques since 2013, when it was defined  
59 [2-4]. An epidemiological study, conducted among Chinese preschool children,  
60 revealed that the relative proportions of *A. rava* was significantly higher in the  
61 halitosis group compared with the control group [6]. A prospective cohort study  
62 showed a relationship between an increase in dental caries and genera  
63 *Alloprevotella* increment in oral microbiome among Japanese university students  
64 [3]. Another report indicated that the proportion of *A. rava* was significantly increased  
65 in saliva samples of periodontitis patients [4]. On the other hand, Coit et al. [7]  
66 reported that the abundance of *A. rava* in the salivary microbial community was  
67 significantly decreased in Behçet's disease compared to healthy controls. Recent  
68 research, focused on the role of bacteria in oral carcinogenesis, indicated that genus  
69 *Alloprevotella* was among the bacteria that showed significantly higher abundances  
70 [[8], [9]]. However, its features related to pathogenesis have not been clarified yet.

## 71 **Conclusion**

72 Signs and symptoms of oral SCC, which has a poor overall 5-year survival rate, and  
73 CMO can often be similar. The diagnosis of CMO is particularly important as  
74 appropriate treatment, culture-guided antibiotic therapy for the infection and surgical

75 management, provides successful cure. Defining of bacterial community composition  
76 associated with CMO can help understanding the mechanisms of disease and impact  
77 of the bacteria.

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80

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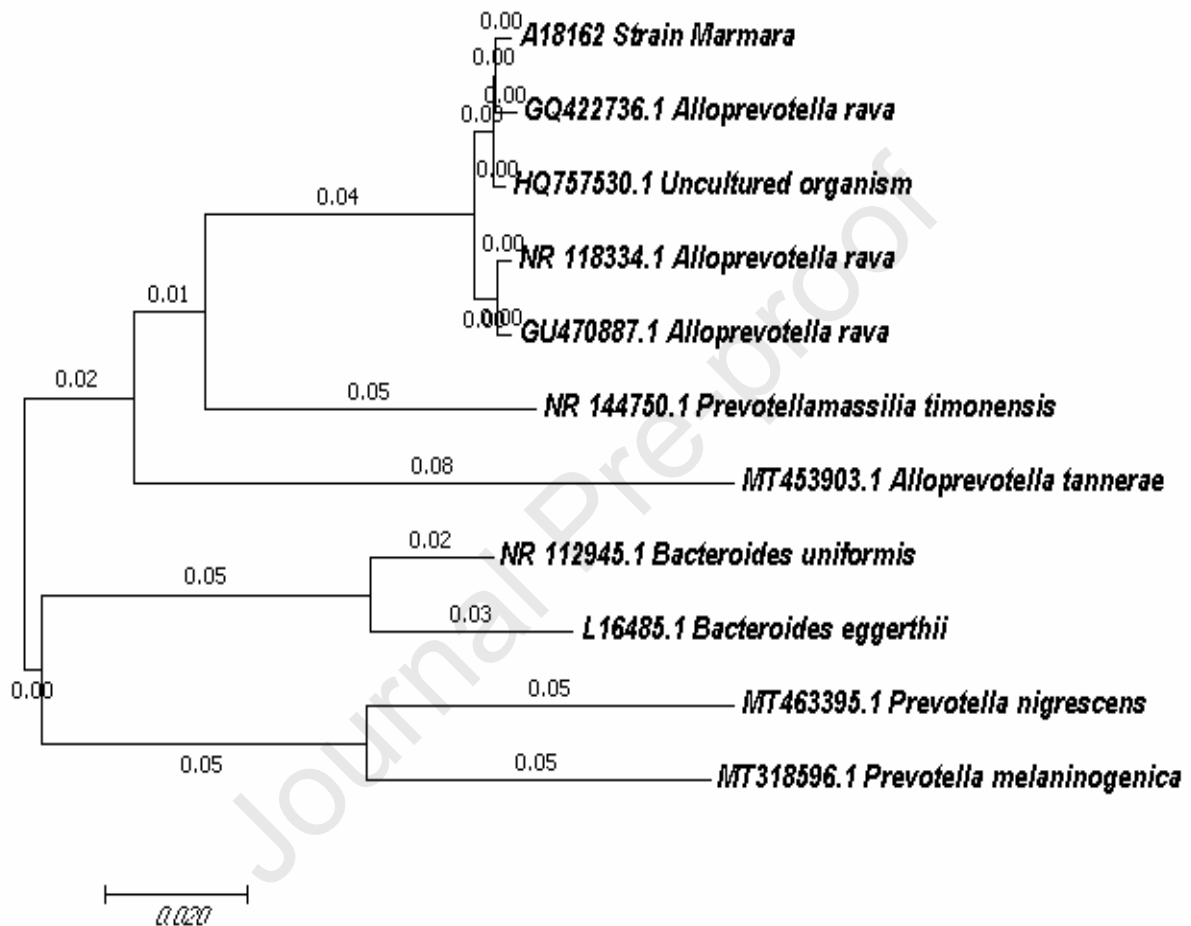


Figure 1.

Neighbour-joining phylogenetic tree based on 16S rRNA gene sequences, showing the relationships between STRAIN MARMARA and some related taxa. GenBank accession numbers are shown in parentheses. Numbers at nodes indicate bootstrap percentages (based on 1000 replicates). Bar represents 0.02 substitutions per nucleotide position.