# Oral Manifestations of Autoimmune Neutropenia: A Case Report

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*Autoimmune neutropenia is a self-limiting condition characterized by the presence of granulocyte-specific autoantibodies. This case report describes a 2-year-old female who presented to the Department of Pediatric Dentistry with a history of oral ulceration, complicated by high temperature, gingival hypertrophy and gingival hemorrhage. These symptoms had precipitated an admission to a district general hospital and diagnosis of viral tonsillitis. The severity of the presentation to the Pediatric Dental Department prompted a review of recent discharge blood investigations, which revealed a neutrophil count of $0.07x10^9/L(1.0\text{-}8.5\ x10^9/L)$ indicating severe neutropenia. Urgent referral to Pediatric Hematology resulted in same-day admission and a diagnosis of autoimmune neutropenia was established. The patient was managed with chlorhexidine mouthwash, prophylactic antimicrobial and antifungal medication and granulocyte colony stimulating factor (G-CSF). Neutropenia may present with features exclusive to the oral cavity. Recognition of atypical presentations such as oral ulceration with associated systemic illness may assist in early diagnosis.*

***Keywords**: Autoimmune Neutropenia, Oral Manifestations, children*

## INTRODUCTION

Autoimmune neutropenia (AIN) is a benign condition characterized by the production of anti-granulocyte antibodies to the patient's own neutrophils resulting in a reduction in the absolute neutrophil count (ANC). It is a self-limiting condition most frequently recorded in children under the age of 3 years with the mean average onset of 8-20 months.[1,2] The reported incidence of autoimmune neutropenia is 1/100,000 children.[33] Children with AIN can present with minor infections such as otitis media, upper respiratory tract infection and gastroenteritis, however, in some cases serious infection may result in pneumonia and septicemia.[4] Oral manifestations of AIN also occur due to the presence of impaired neutrophil function in the oral cavity resulting in an increased degree of susceptibility to infection.[5] Clinical presentations in the oral cavity include ulceration, hyperplastic edematous desquamative gingivae, gingival inflammation, gingival recession, periodontitis, horizontal bone loss and increased tooth mobility. [6,7,8]

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Children presenting with recurrent infection secondary to AIN require supportive care, which may include prophylactic antibiotic and antifungal therapy.[93] In the presence of severe infections, Granulocyte Colony Stimulating Factors (G-CSF), has been demonstrated to reliably increase the neutrophil count.[10]

### Case Report

A 2-year-old female presented to the Pediatric Department at the University Dental Hospital Manchester on an urgent basis. Her mother reported a three-month history of temperature, swollen gingivae and pain whilst eating. Additionally, she described multiple episodes of spontaneous gingival hemorrhage, which was self-limiting and of small volume. Within the previous three months the patient had attended a district general hospital with these symptoms. She had been admitted with a working diagnosis of tonsillitis made by the Paediatric team. However, neutropenia was not suspected and subsequently the patient was discharged with a diagnosis of a viral infection. Following several days of distress, the patient was taken to an out of hours' dentist and an urgent referral to the Paediatric Dental department was sought the next day. Her presenting complaint was identical to that which precipitated her attendance at the district general hospital and was consistent with intra-oral signs of neutropenia.

On clinical examination, severely hyperplastic, erythematous gingivitis affecting the upper and lower anterior gingiva was noted with areas of desquamation as demonstrated in Fig 1 and 2. Radiographs in Fig.3 demonstrated horizontal bone loss interproximal to the deciduous incisors.

The severity of the presentation prompted a review of her recent hospital investigations. A discharge summary obtained from her

GP showed a neutrophil count of *0.07x10$^9$/L* (*1.0-8.5 x10$^9$/L)* indicating significant neutropenia. Differential diagnoses included acute leukaemia, congenital neutropenia, drug induced neutropenia and autoimmune neutropenia.

An urgent referral to the Pediatric Hematology team at the Royal Manchester Children's Hospital resulted in immediate hospital admission. Hematological investigations included full blood count, renal and liver function tests, CRP, immunoglobulin serum level, serum electrolyte, indirect anti-neutrophil antibodies detection, antibody screening and genetic testing. A bone marrow aspirate showed normal cellularity, marked reduction in regulating neutrophils with the presence of anti-granulocyte antibodies in her serum, confirming a diagnosis of primary autoimmune neutropenia. Prophylactic antimicrobial and antifungal medications were prescribed. The gingival lesions were treated with topical chlorhexidine 0.02% mouthwash. The importance of excellent oral hygiene was explained to her mother. G-CSF resulted in increased circulating neutrophils, upon commencement in October 2015 as shown in Fig.4 . The patient is currently under regular hematological review and continues to receive G-CSF three times weekly to maintain neutrophil levels above *0.5x10$^9$/L*. In episodes of febrile illness with fever over 38° a febrile neutropenia protocol is initiated. One-year bone marrow cytogenetics was normal. At dental examination at six months and one year, resolution of gingival inflammation was noted in Fig 5 and radiographs did not show any further progression of alveolar bone loss shown in Fig.6.

**Figure 1. Clinical photographs of 2 year old female on initial presentation of maxillary primary dentition noting hyperplastic, erythematous gingivitis and an area of desquamative gingivitis is denoted by the arrow.**

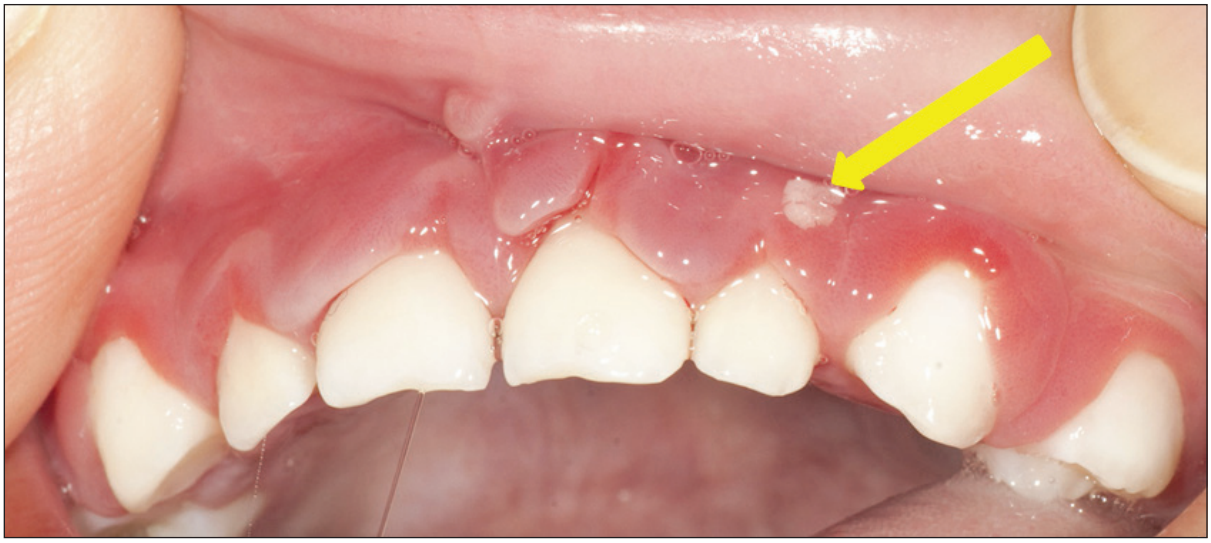


**Figure 2. Initial clinical presentation of mandibular primary dentition, the arrow demonstrates the severe hyperplastic erythematous gingivitis.**

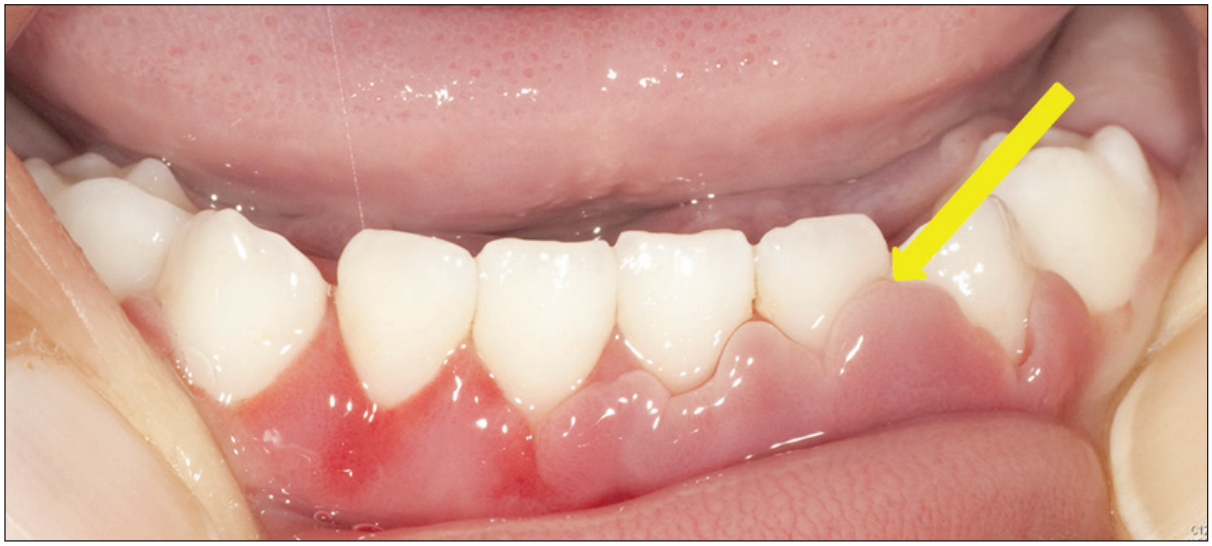


**Figure 3. Upper standard occlusal radiograph on initial assessment, the arrow demonstrates an area of horizontal bone loss interproximal to the primary incisors.**

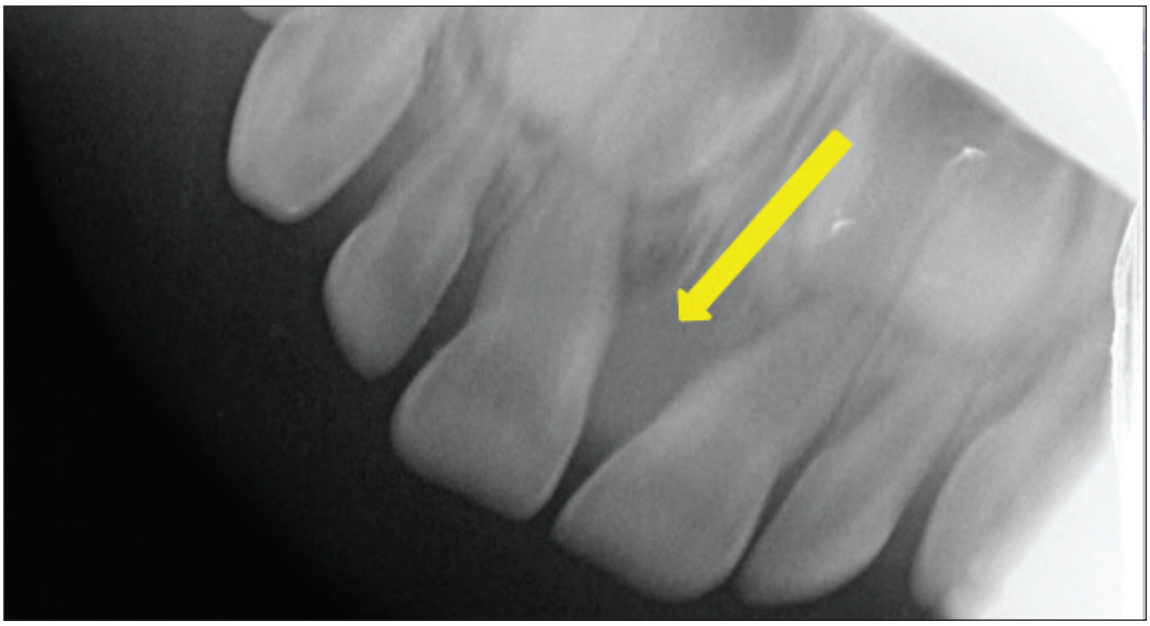


**Figure 4. Neutrophil blood count of 2 year old patient undergoing treatment with GSF. The 1st administration of GSF October 2015 showing a gradual improvement in neutrophil levels, from 1st admission in August 2015.**

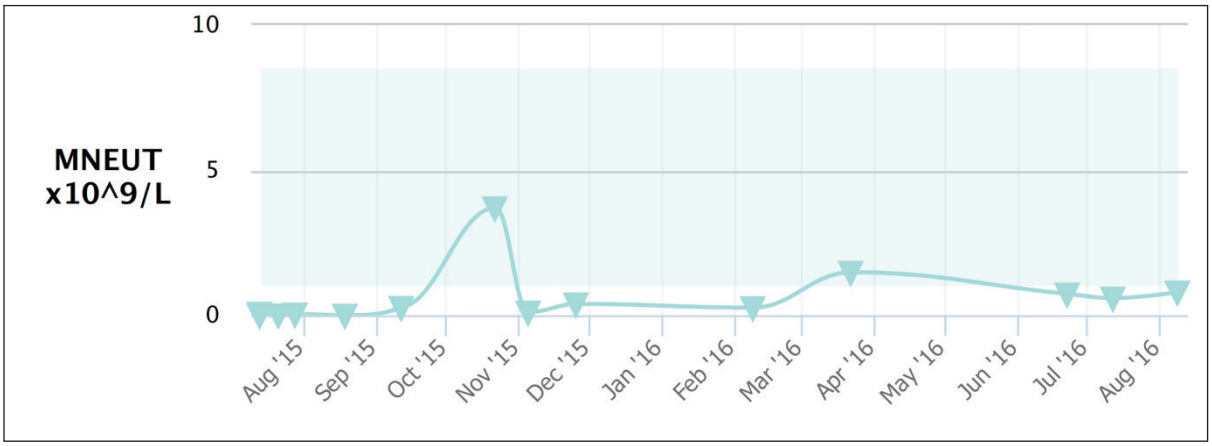



**Figure 5. Post clinical treatment photograph demonstrating resolution in clinical symptoms**

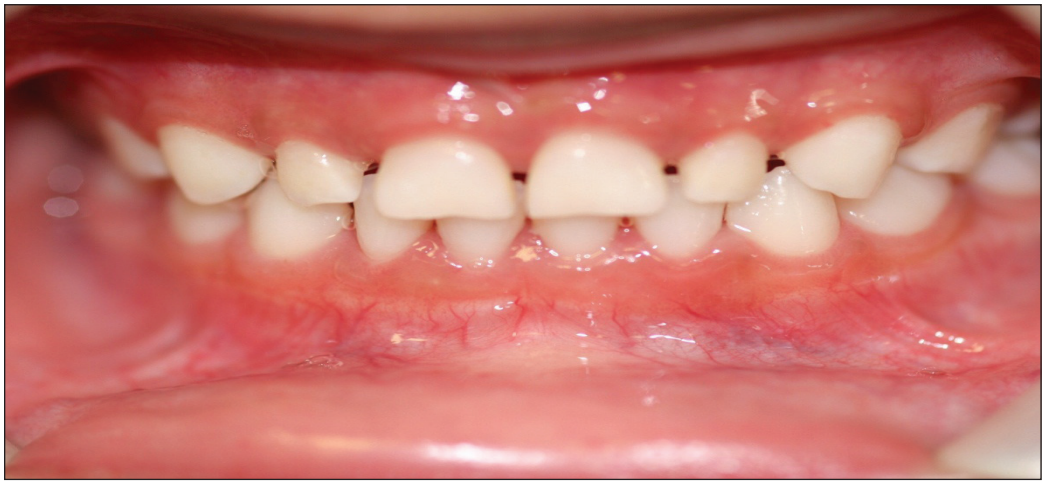
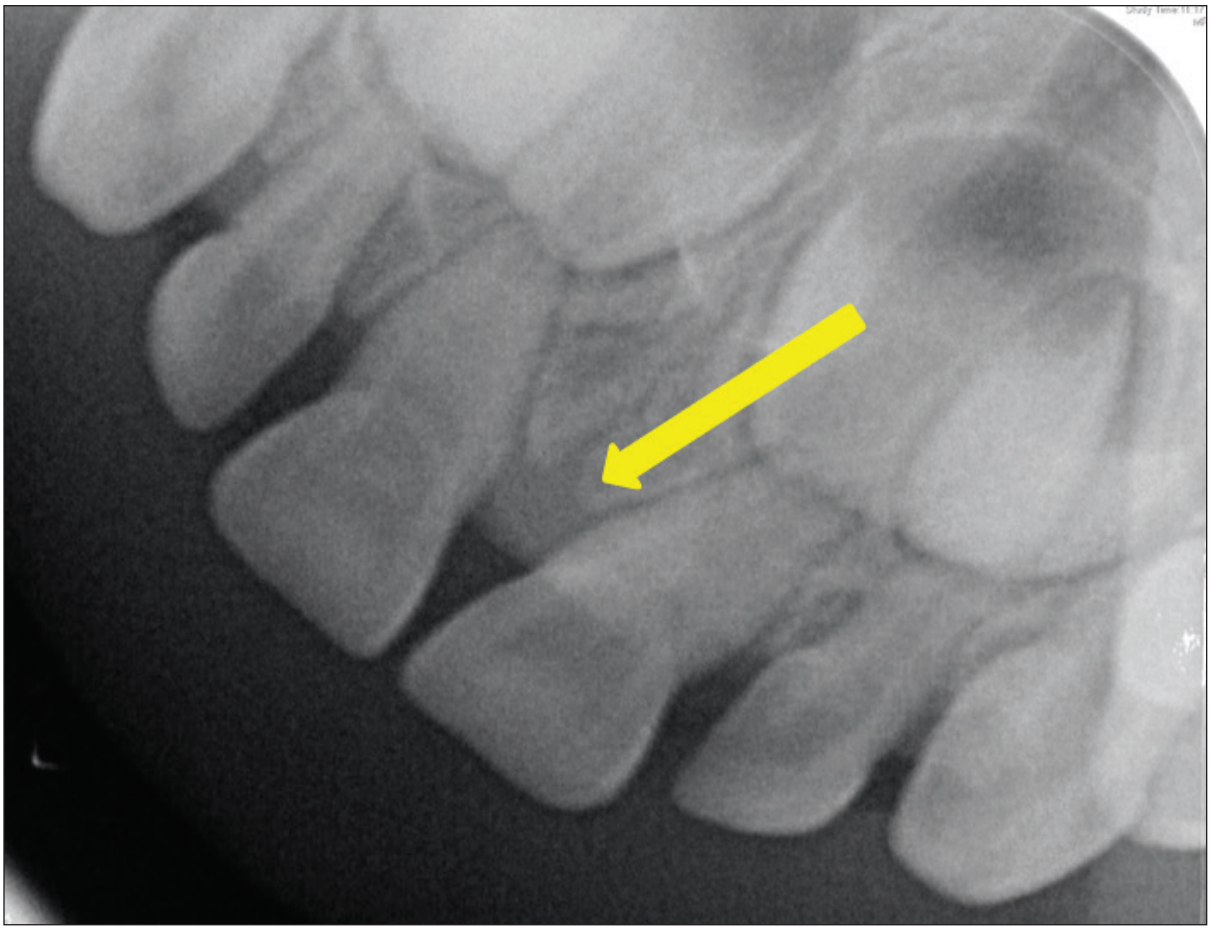


**Figure 6. Upper standard occlusal radiograph post clinical treatment demonstrating no further bone loss as shown by the arrow.**



## DISCUSSION

Neutropenia can be divided into many classifications including autoimmune and congenital.[11] Autoimmune neutropenia occurs when autoantibodies become targeted towards PMN antigens. Neutrophils are then bound together in clusters and eliminated from the body via phagocytic mechanisms leading to a subsequent decrease in the number of circulating active neutrophils. Severe infectious sequels are less common in cases of autoimmune neutropenia in comparison to the genetic neutropenia.[12] Nevertheless, patients with AIN may present with multiple infective episodes and troublesome oral symptoms.

This case highlights the intraoral signs and symptoms of a possible neutropenia, which should alert the clinician to the potential of a more severe illness. A similar case has been noted in the literature and showed a 20-month old girl who presented with severe recurrent stomatitis as an early sign of chronic benign neutropenia.[13] This highlights the importance of oral symptoms in the diagnosis of neutropenic conditions.

The link between periodontal disease and neutropenia is well documented due to the resultant reduced immune response in periodontal tissues. Previous literature[14] describes the management of gingival hyperplasia in established cases of AIN, however there is a paucity of published cases documenting oral signs and symptoms as precipitating factors to a medical diagnosis. It is commonly accepted that oral manifestations are common in these conditions. Despite this it is prudent to remember that gingival inflammation is a common presentation to the paediatric dentist and most commonly relates to poor dental hygiene. However, as this case highlights it may be the oral manifestation of systemic disease including blood and immune disorders, infection or genetic conditions.[154] The underlying causes can cause a complex diagnostic challenge and this case highlights a missed clinical diagnosis.

## CONCLUSIONS

Although neutropenia is a relatively rare condition, it should be considered in the differential diagnosis when characteristic oral symptoms present in association with systemic disturbance. This case emphasizes the importance of vigilance by both the dental and medical communities in cases of gingival hypertrophy with hemorrhagic oral ulceration. Timely referral for appropriate management was paramount to the successful outcome in this case.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ETHICS STATEMENT

Written consent documented in clinical records has been obtained for publication of clinical images.

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