

INTRODUCTION

PAMI syndrome is a rare hereditary autoinflammatory condition caused by pathogenic variants in the PSTPIP1 gene. The PSTPIP1 protein plays an important role in immune regulation by influencing T-cell signaling, phagocytic cell activation, cytoskeletal organization, and interleukin-1-mediated inflammatory pathways.

Clinically, PAMI syndrome presents with chronic systemic inflammation and hematologic abnormalities, including anemia, neutropenia, and thrombocytopenia. Additional features include arthritis, cutaneous lesions, growth impairment, hepatosplenomegaly, lymphadenopathy, and elevated zinc and calprotectin levels

ETIOLOGY AND EPIDEMIOLOGY

Prevalence: Estimated at 1/1,000,000 with fewer than 50 cases reported worldwide.¹

Age of Onset: Median age 11 years (range: birth to 46 years).²

Genetics: PAMI syndrome follows an autosomal dominant inheritance pattern and results from mutations in the PSTPIP1 gene (CD2BP1) located on chromosome 15q24–q25.1 Most cases are de novo mutations, though familial cases have been reported.

Pathophysiology: Missense mutations in PSTPIP1—most commonly p.E250K and p.E257K—enhance binding to pyrin, promoting excessive inflammasome activation and increased production of IL-1 β , along with downstream activation of nuclear factor-kappa B and interferon signaling pathways.¹

DIAGNOSIS AND MANAGEMENT

Clinical Triad:

- Recurrent high-grade fevers
- Neutrophilic dermatosis (pustules, abscesses, pyoderma gangrenosum-like lesions)
- Aseptic osteomyelitis/bone pain

Diagnosis: Abnormal lab values, MRI/bone scans, bone biopsy (neutrophilic infiltration), and definitive diagnosis via genetic analysis.

First-Line Therapy (Gold Standard): I L-1 inhibitors are most effective

Second-Line/Alternative Therapies: Corticosteroids, TNF- α inhibitors, colchicine, DMARDs (methotrexate), NSAIDs

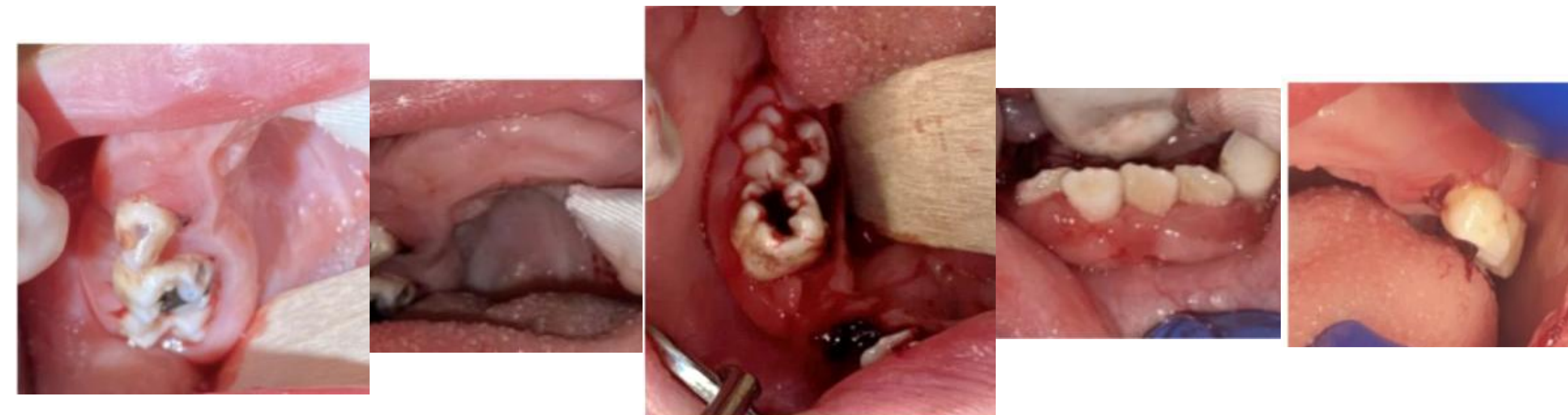
CASE REPORT

A 4-year-old female with PAMI syndrome, iron deficiency, arthralgia, anemia, neutropenia, and Factor XII deficiency presented for dental evaluation with multiple caries, gingivitis, and mobile teeth. Medications included chlorhexidine (Peridex).

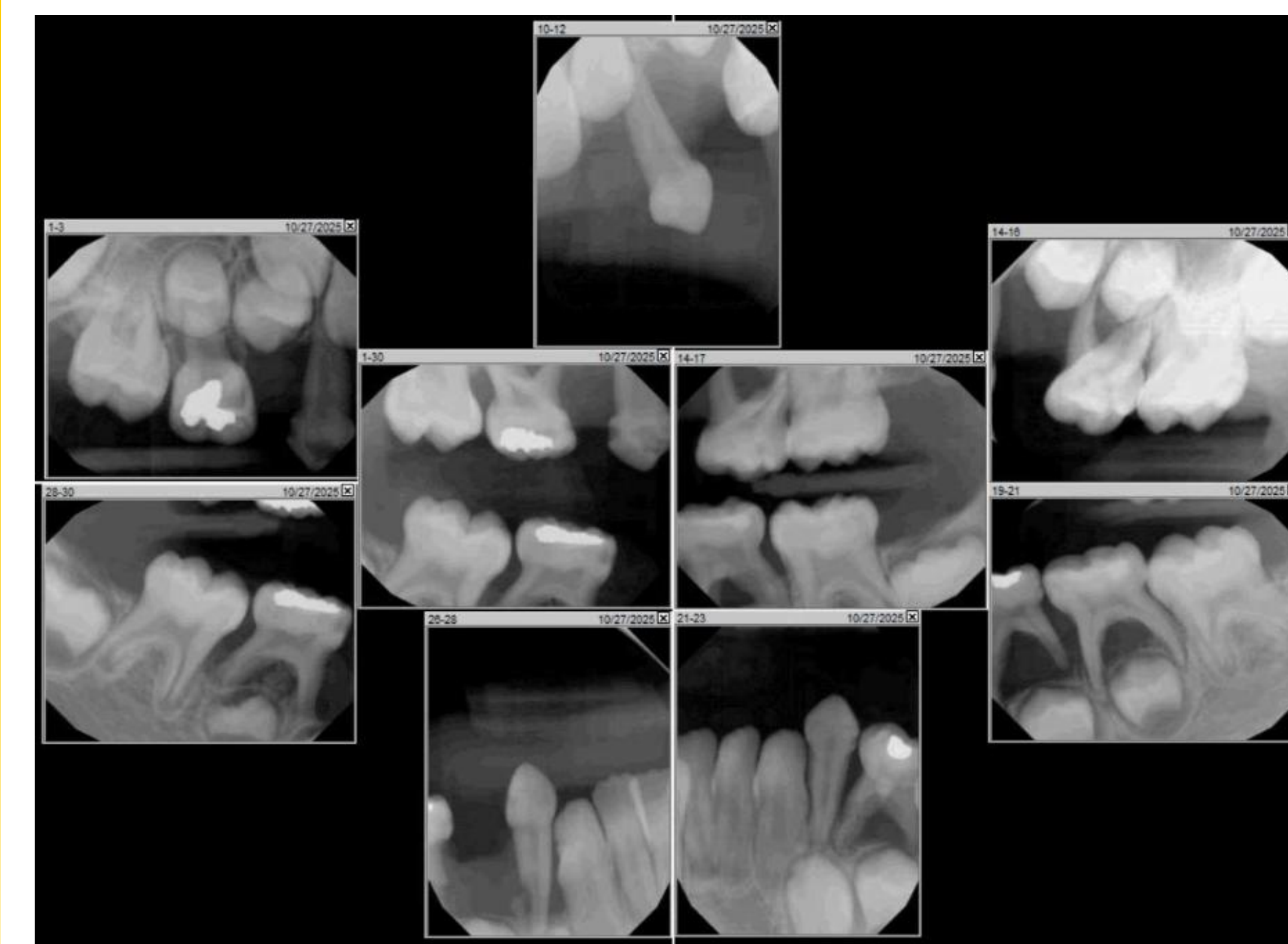
Clinical Findings:

- Multiple dental caries
- Heavy plaque with moderate calculus
- Severe gingival inflammation
- Extensive alveolar bone loss consistent with neutropenia
- Excessive mobility was noted on all primary teeth.

Comprehensive dental care was provided under general anesthesia with the extraction of all remaining primary teeth due to extensive bone loss. Sutures were required for hemostasis secondary to Factor XII deficiency.



Figures 1. Preoperative intraoral images.



Figures 2. Preoperative radiographs.



Figure 3. Two-month postoperative radiographs.

DENTAL IMPLICATIONS or CLINICAL FEATURES

Profound neutropenia and immune dysregulation render patients particularly susceptible to severe oral infections that would typically be manageable in otherwise healthy individuals.

Limited research exists on PAMI and its oral manifestations, with few cases documented in the literature.

Some of the more common oral findings include:

- Ludwig's angina - most notable severe manifestation reported in a few cases.³
- Severe periodontal disease with extensive alveolar bone loss
- Premature tooth loss due to neutropenia and poor oral health
- Gingival bleeding and inflammation
- Recurrent oral infections due to an immunocompromised state
- Increased risk of severe odontogenic infections

CONCLUSION

Individuals with PAMI syndrome require frequent dental follow-up with special attention to periodontal health. The immunocompromised state, particularly severe neutropenia, predisposes patients to periodontal disease, premature tooth loss, and life-threatening oral infections, including Ludwig's angina.

Early intervention, meticulous oral hygiene, periodontal maintenance, antibiotic prophylaxis before dental treatment and close multidisciplinary collaboration are essential for optimal oral health outcomes.

REFERENCES

1. Iseppi, M., Savonitto, G., Tommasini, A., Pin, A., Sinagra, G., & Stolfo, D. (2023). A very rare cause of pre-capillary pulmonary hypertension: The PAMI syndrome. *Pulmonary Circulation*, 13(4), e12300.
2. Mejbri, M., Renella, R., Candotti, F., Jaques, C., Holzinger, D., Hofer, M., & Theodoropoulou, K. (2023). PSTPIP1-associated myeloid-related proteinemia inflammatory (PAMI) syndrome: A systematic review. *Genes*, 14(8), 1655.
3. Zhang, D., Su, G., Liu, Y., & Lai, J. (2021). Clinical and genetic characteristics of PSTPIP1-associated myeloid-related proteinemia inflammatory syndrome. *Pediatric Rheumatology Online Journal*, 19(1), 151.