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Oral Health and Dental Management Strategies in Noonan Syndrome: A Case Report

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Noonan syndrome is a genetic condition characterized by various systemic issues, including cardiac defects, short stature, bleeding problems, and intellectual disabilities. This disorder also shows several manifestations in the oral and maxillofacial region, highlighting the dentist's role in diagnosing and addressing related complications. This report represents the effective dental management of a 15-year-old boy with Noonan syndrome who suffered from several oral and dental problems and was clinically and radiographically asymptomatic in a nine-month follow-up session. Awareness of the medical conditions and orofacial manifestations of patients with Noonan syndrome can be effective in determining a better treatment plan, providing more effective and safer treatment, and subsequently enhancing the long-term prognosis.

Keywords: Case Report; Dental Care; Endodontics; Giant Cell Granuloma; Noonan Syndrome

Introduction

Identified in 1963, Noonan syndrome (NS) is a relatively common multisystem disorder (occurring in 1 per 1000-2500 live births affecting individuals of both genders) [1]. This syndrome is classified as a subset of RASopathies due to its association with mutations in genes involved in RAS/Mitogen Activated Protein Kinase (MAPK) signaling pathway [2]. As a disorder with autosomal dominant inheritance, NS occurs with a wide range of phenotypes, even among members of the same family [3]. Key characteristics of this syndrome include congenital heart defects (making NS the second most common cause of congenital heart disease after Down syndrome), as well as chest and facial deformities, mental retardation, and bleeding disorders [1, 4]. Additionally, NS is linked to various orodental manifestations documented in several studies. High-arched narrow palate, hypodontia, micrognathia, and macrodontia, which can result in malocclusion and misalignment of teeth, as well as abnormal root shape and periodontal disease, are among these manifestations [1, 3-6].

Moreover, multiple giant cell lesions have been reported in these patients [2, 7-9], a typical complication of RAS/MAPK pathway dysregulation [9]. Central giant cell granulomas (CGCGs) are benign lesions more commonly found in the mandible and mainly in young adults [10].

To our knowledge, the literature provides limited information on the management and necessary modifications in dental treatment planning for NS patients. This report details the comprehensive orodental management of a 15-year-old Persian male patient diagnosed with NS.

Case Presentation

Medical history

A 15-year-and-6-month-old Persian boy was referred to the endodontics department at Mashhad dental school, Mashhad, Iran, with a chief complaint of pain on the left side of his jaw. Diagnosed with NS, he has been under the care of a cardiologist, pulmonologist, and endocrinologist since the age of five. An echocardiography showed mild stenosis at the origin of the pulmonary artery branch, floppy mitral and tricuspid valves, peripheral pulmonary stenosis, an increased left ventricle mass index, and slight dilation of both the right atrium and ventricle. The cardiologist indicated that antibiotic prophylaxis was

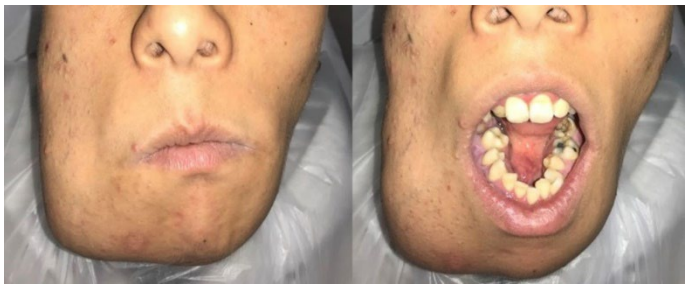

Figure 1. Patient's lower half facial appearance with an evident swelling in the lower right side of his jaw

unnecessary. The patient was taking a long-acting beta-agonist (LABAs) inhaler as prescribed by his pulmonologist. Giving his history of prolonged bleeding following tooth extraction, his coagulation status was assessed which was within the normal ranges (blood test results: partial thromboplastin time (PTT)=33 sec, prothrombin time (PT)=13 sec, international normalized ratio (INR)=1, bleeding time (BT)=2 min). Our physical examination revealed a boy with normal stature and normal intelligence. Notably, there was a swelling on the lower right side of his face with a bony, hard consistency, which, according to the patient, had been noticed about three years ago, with minimal growth since then (Figure 1).

Intra-oral examination

Both the upper and lower arches were extremely narrow, featuring a high-arched palate, deep bite, and severe crowding (Figures 2A-C). There was significant plaque accumulation and severe dental caries attributed to poor oral hygiene. An asymptomatic expansion was observed in the right mandibular buccal and lingual cortex extending from the distal of the canine to the ramus, characterized by bony hard consistency on palpation and purplish-red covering gingiva and mucosa. A smaller asymptomatic bony hard expansion was also noticed in the left mandibular buccal and lingual cortex from the canine to the distal of the second molar (Figure 2C). No mobility or abnormal probing depths were recorded. Teeth numbers #16, 25, 27, 36, and 37 were hyper-responsive to thermal tests and tender upon percussion, while other teeth responded normally to the pulpal and periapical tests.

Radiographic examination

Figure 3 represents a panoramic view of both jaws on admission. The orthopantomograph (OPG) showed palatal impaction of the left maxillary canine, multiple missing teeth without a history of extraction, and severe caries in teeth #25, 26, 27, 35, 36, and 47. There was a central lesion located in the body of the mandible characterized by an expansile swelling in the lower border of the jaw. It displayed a very fine internal pattern with vague, wispy granular septa and an ill-defined outline. The lamina dura of the teeth within the lesion and the inferior alveolar canal borders were not evident. The lesion had displaced the inferior alveolar canal in an inferior direction.

Histopathologic examination

An incisional biopsy was collected from the buccal vestibule of the right mandibular premolar region and sent for histopathological analysis. The hematoxylin and eosin-stained images showed bone tissue within marrow spaces, accompanied by extensive fibrovascular tissue and vascular aneurysmal spaces (Figure 4). This was diagnosed as a giant cell lesion compatible with an aneurysmal bone cyst.

Treatment

The multidisciplinary treatment plan and alternatives were discussed with the patient and his parents, who signed the informed consent form. After an oral hygiene instruction, teeth #26 and 47 were considered unrestorable and were extracted. Teeth #16 and 36 were restored with composite resin, while teeth #25, 27, and 37 were diagnosed with chronic irreversible pulpitis and symptomatic apical periodontitis [11] and were scheduled for endodontic treatment. After receiving periodontal and restorative consultations, the patient's overall prognosis was assessed as poor to fair. However, with proper oral hygiene education, management of jaw lesions and dental caries, the prognosis can be improved to fair to good.

Figure 5A illustrates the radiographic appearance of tooth #27 at the beginning of the treatment. After local anesthesia with lidocaine 2% and epinephrine 1:100,000 (DarouPakhsh, Tehran, Iran) infiltration, complete caries removal, and rubber dam isolation, it was discovered that the mesiopalatal portion of the crown was a supernumerary tooth (Figure 5B) [12] which was decided to be kept and treated after consulting with the periodontics department and considering the possibility of irreparable periodontal defect in case of its extraction. The root canals were negotiated using K-files #10 and 15 (Mani, Utsunomiya, Japan) (Figure 5C). Cleaning and shaping were performed with rotary instrumentation (T-pro; Dental Perfect, Shenzhen, China) up to size 25/0.04 and alternating irrigation with 5.25% sodium hypochlorite and normal saline [13, 14]. The palatal canal of tooth #27 and the supernumerary tooth root canal were filled with MTA (L Root, Tehran, Iran) due to their open apices [15-17]. The mesiobuccal and distobuccal root canals were obturated with gutta-percha (Meta, Chugbuk, South Korea) and AH-26 sealer (Dentsply DeTrey, Konstanz, Germany) using a warm vertical obturation technique [18] after master cone fit and radiographic confirmation (Figures 5D and 5E). The tooth was temporized with resin-modified glass ionomer

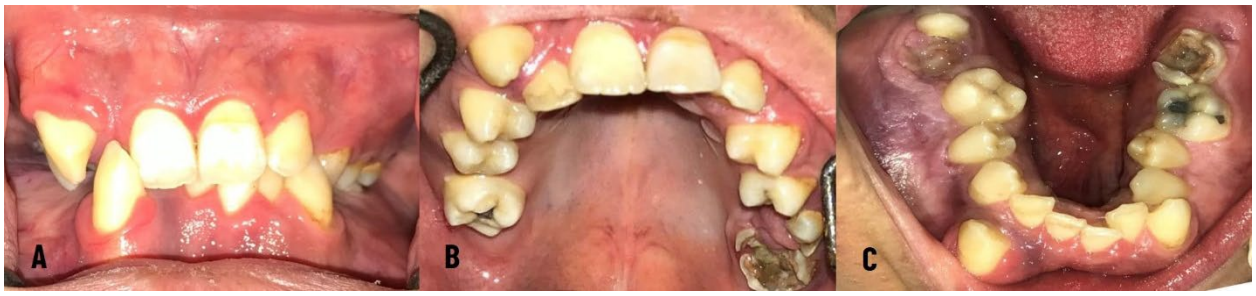

Figure 2. A-C) Patient intra-oral views at presentation

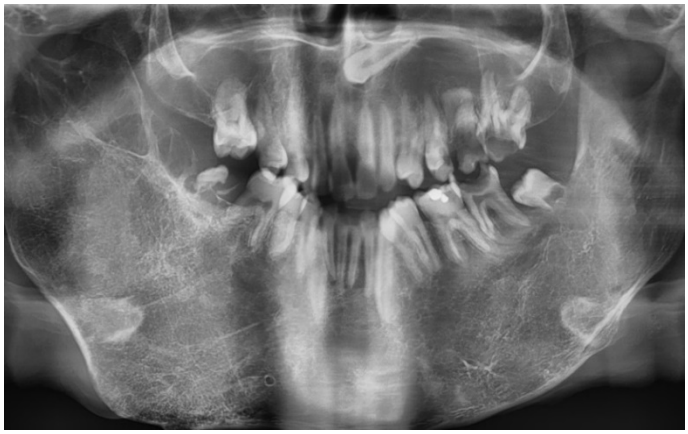

Figure 3. Patient panoramic view on admission

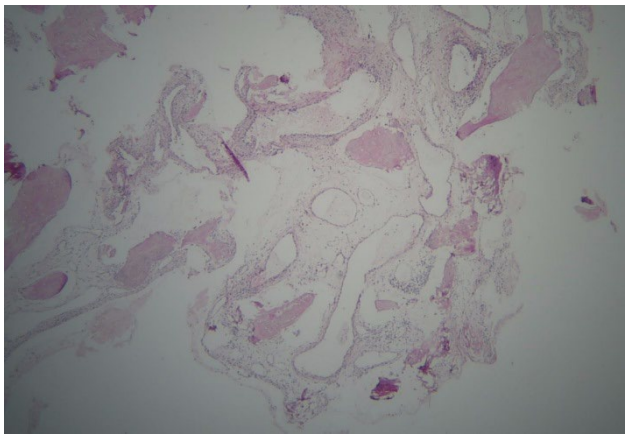

Figure 4. Histopathologic photomicrograph (hematoxylin and eosin-stained) of the tissue collected from an incisional biopsy from the buccal vestibule of the right mandibular premolar region depicting bone marrow spaces accompanied by fibrovascular tissue

and referred for permanent restoration (Figure 5F). Tooth #25 was a minimolar with two buccal and one palatal root canals. The negotiation, cleaning and shaping, and obturation process were similar to those of tooth #27 (Figures 6A-6F). The root canal treatment for tooth #37, which had three mesial canals and two distal ones, followed a similar approach as tooth #25 (Figures 7A-7F). A follow-up evaluation conducted nine months later showed that all treated teeth were asymptomatic both clinically and radiographically (Figures 8A-8F).

The patient was scheduled for corrective surgery in the jaw enlargement area. An orthodontic treatment was recommended, but declined by the patient declined due to financial constraints.

Discussion

The present study detailed the successful orodental management of a teenage patient diagnosed with NS. This syndrome is relatively common and has an almost uniform global distribution [19]. NS is associated with major medical issues such as heart defects, cryptorchidism, mental retardation, and bleeding disorders and has been studied more in the literature from this point of view [1, 4]. However, the diagnosis of NS primarily relies on clinical features according to the Van Der Burgt scoring system [20]. Given the numerous oral and maxillofacial manifestations, dentists can play a crucial role in NS diagnosis. Uloopi *et al.* [21] reported multiple permanent tooth impactions and submerged deciduous teeth, which were not observed in our patient. Malocclusion (jaw size discrepancies, crossbite, open bite), high-arched palate, crowding, dental and periodontal anomalies (hypodontia, delayed eruption, gum disease), and multiple jaw lesions have been reported repeatedly in case reports and retrospective studies [4, 22-26]. However, comprehensive studies on the orodental management of NS patients are still lacking. Due to the interplay of medical conditions and oral manifestations, managing these patients can be complex and requires special considerations and modifications. Considering the possibility of needing antibiotic prophylaxis due to heart-related problems, conducting a full hematologic workup before any treatment, keeping procedures as non-invasive as possible during rubber dam isolation and clamp placement or tooth extraction, along with avoiding medications that interfere with coagulation, such as aspirin, are vital. Takagi *et al.* [27] reported methemoglobinemia induced by prilocaine during dental management of a child with NS. It is also important to note that obtaining appropriate intraoral radiographs is difficult due to the deep, highly arched palate. The use of film holders or extraoral

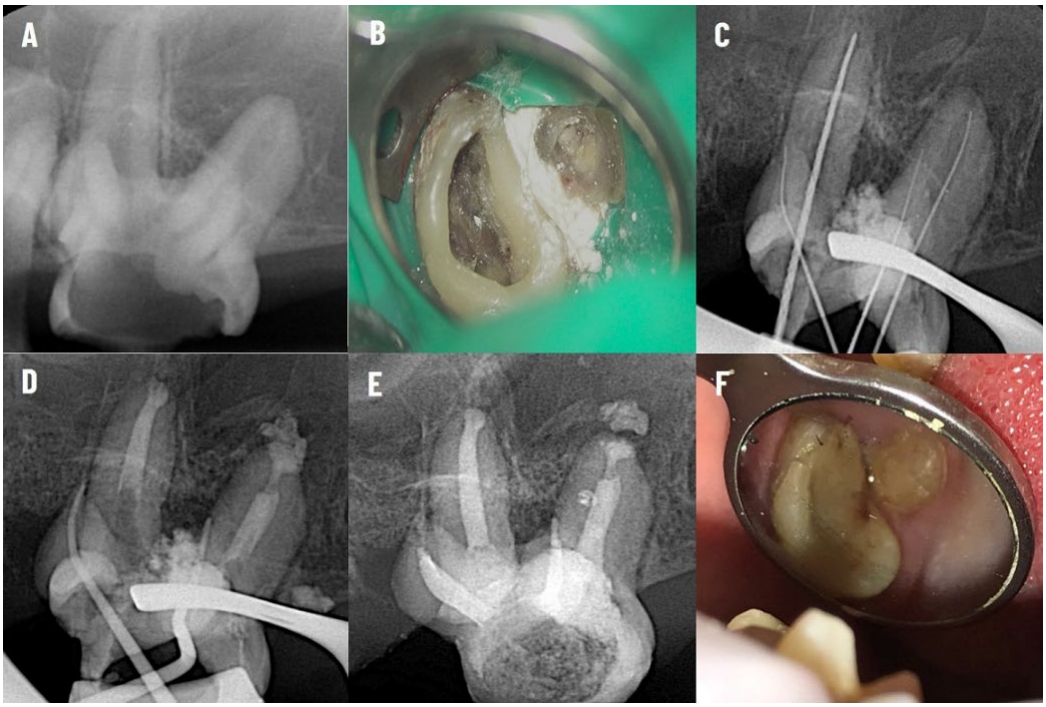

Figure 5. Clinical and radiographic evaluation of the instrumentation and obturation of tooth #27 showing: *A)* Initial radiograph; *B)* Clinical view after isolation; *C)* Radiograph with K-file confirming the root canals working length; *D)* Master-cone confirming radiograph; *E)* Post-op radiograph; *F)* Clinical view after temporization

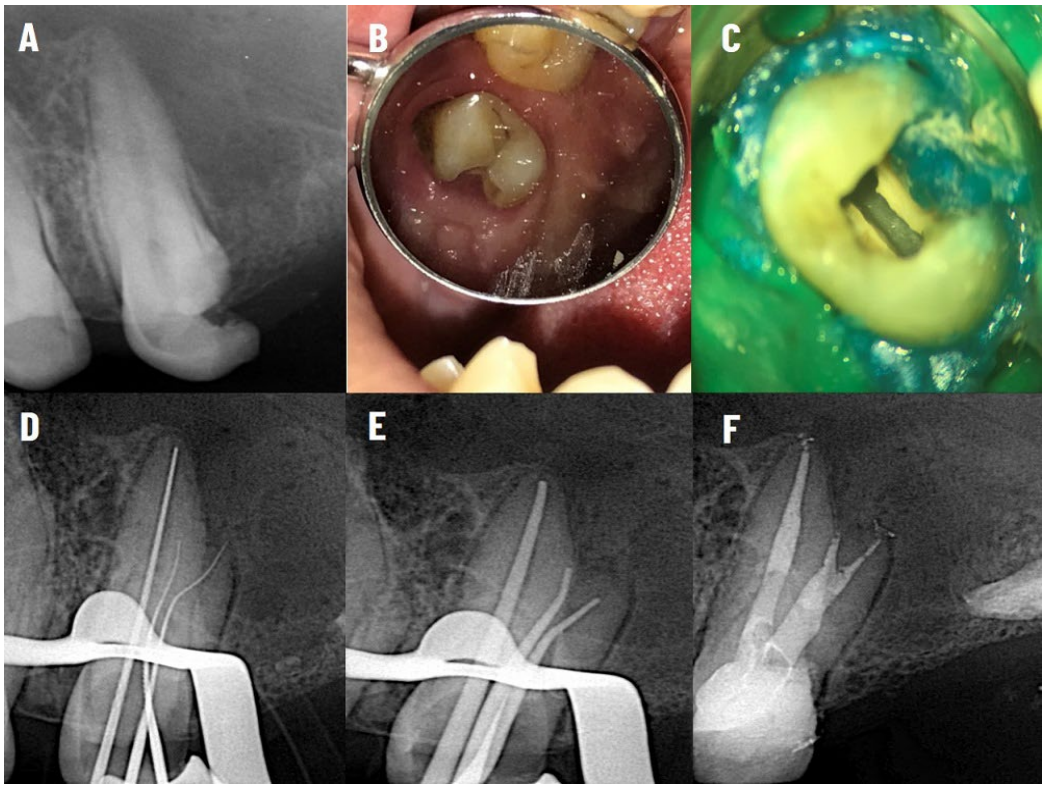

Figure 6. Clinical and radiographic evaluation of the instrumentation and obturation of tooth #25 showing: *A)* Initial radiograph; *B)* Clinical view at admission; *C)* Clinical view after isolation; *D)* Radiograph with K-file confirming the root canals working length; *E)* Master-cone confirming radiograph; *F)* Post-op radiograph

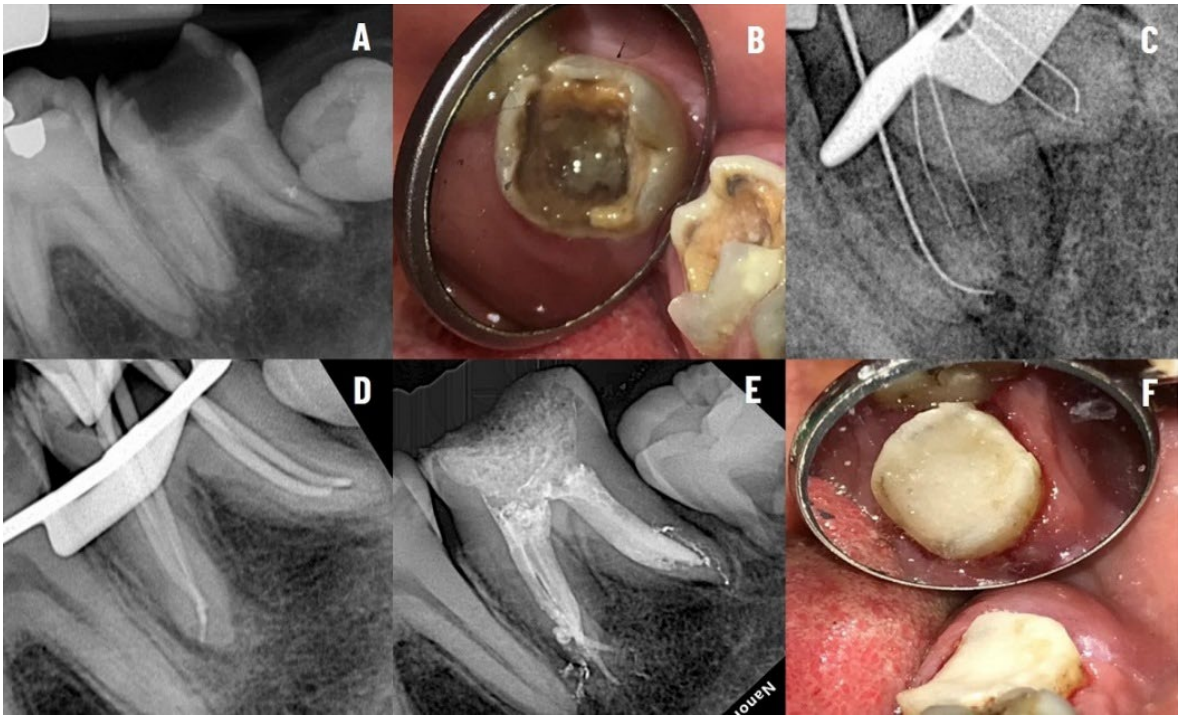

Figure 7. Clinical and radiographic evaluation of the instrumentation and obturation of #37 showing: *A)* Initial radiograph; *B)* Clinical view at admission; *C)* Radiograph with K-file confirming the root canals working length; *D)* Master-cone confirming radiograph; *E)* Post-op radiograph; and *F)* Clinical view after temporization

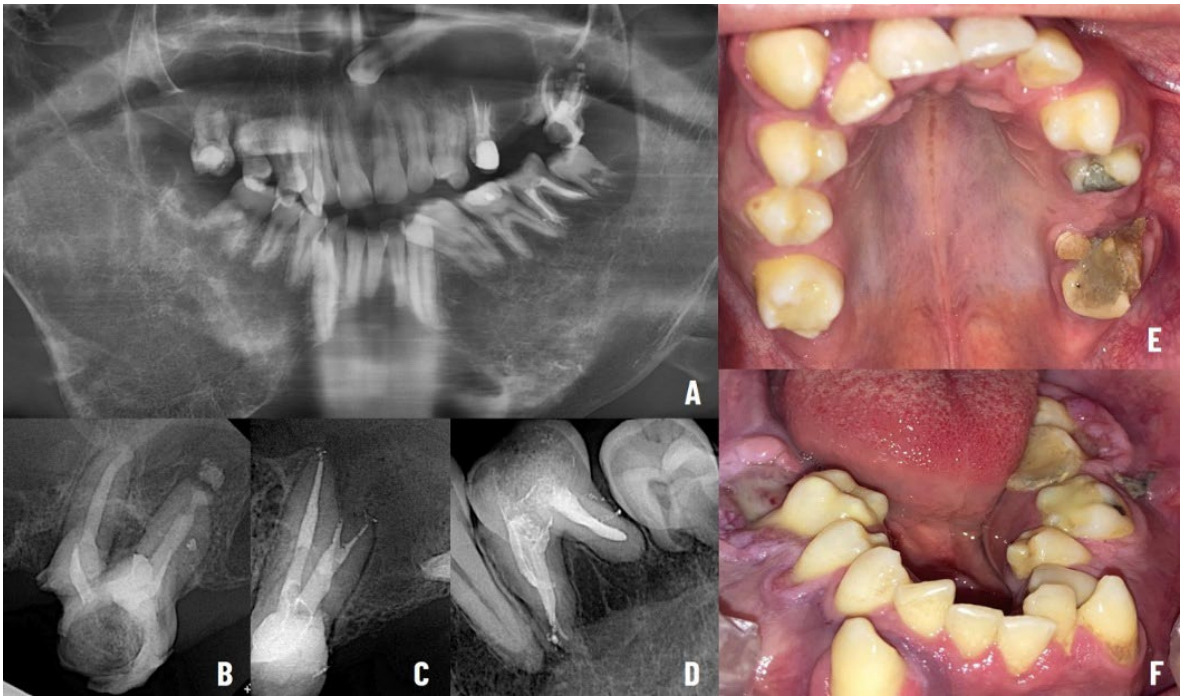

Figure 8. 9-month follow-up radiographs: *A)* Panoramic view; *B)* Tooth #27 periapical view; *C)* Tooth #25 periapical view; *D)* Tooth #37 periapical view; *E)* Clinical view of maxillary arch; *F)* Clinical view of mandibular arch

placement of the radiographic sensor can be helpful. Additionally, the placement of clamps and isolation in narrow arches with severe crowding requires special considerations and sometimes clamp modification. Regarding the management of jaw lesions in NS, there is currently no established treatment protocol. Surgery is often considered, although the main problem is the recurrence [28]. Recently, denosumab, a monoclonal antibody against "receptor activator of nuclear factor kappa beta ligand" (RANKL), has been used to treat these lesions [7, 9, 29]. But according to the reports of bone anomalies in preclinical studies, its use in children and adolescents is not generally accepted [29]. Therefore, corrective surgery continues to be regarded as a viable treatment option. Finally, the dental treatment of medically compromised patients with syndromes should receive special attention in both post- and undergraduate training [30].

Conclusions

This report highlights the effective dental management of a patient with NS. Our patient is currently under follow-up, experiences no dental symptoms or pain, and has surgery scheduled for his jaw lesion. A more precise understanding of characteristics related to NS, enables the clinician to offer better counseling regarding the prognosis to the family and provide a specific treatment plan according to the patient's condition, in order to improve the outcomes. Regular dental checkups, oral hygiene instruction, and preventive treatments like fluoride therapy and fissure sealants can minimize the necessity for more complex interventions in the future. It is also important to be aware of the patient's medical conditions and adjust the treatment plan as necessary in consultation with their physician

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Conflict of interest

None.

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Authors' contributions

Conceptualization: PS/MF; Methodology: PS/SK; Formal Analysis and Investigation: PS/MF; Writing-Original draft preparation: PS/MF/SK; Writing-review and editing: PS/MF/SK; Supervision: PS/MF/SK. All authors read and approved the final manuscript.

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