Clinics in Surgery

Research Article
Published: 05 Feb, 2022

Oral Health in Patients with Osteopetrosis: A Literature Review

Hedvig Hasselby[1], Karin Danielsson[1] and Mats Sjostrom[2]*

[1]*Department of Odontology, Umea University, Sweden*

[2]*Department of Odontology, Oral and Maxillofacial Surgery, Umeå University, Sweden*

Abstract

Background: Osteopetrosis is a rare hereditary bone disease caused by mutated osteoclasts that are either in scarce abundance or have reduced efficiency. This condition leads to less bone resorption, and thus, denser, more fragile bones. Osteopetrosis leads to complications that can be severe and even fatal.

Aim: To summarize the current knowledge of (a) how Osteopetrosis affects the oral health, dentition, and facial skeleton of patients with different disease subtypes, and (b) which treatment options are used worldwide to treat the different orofacial complications and provide symptom relief in the oral cavity.

Methods: This review was based on published studies on oral health among patients with osteopetrosis that focused on diagnosis and treatment. Two searches were performed in PubMed, based on seven search terms: Osteopetrosis, oral, jaw, dental, craniofacial, mandible, and maxilla. After screening based on predefined inclusion and exclusion criteria; 30 articles were selected.

Results: All 30 articles were case studies, which have a low grade of evidence. Thus, the data studied were at high risk of bias. The 30 articles included 40 patients. The most common observed complication was osteomyelitis.

Conclusion: The data highlighted the importance of good oral hygiene and tissue-conservative treatment in preventing complications from infection. Osteomyelitis should be treated with a combination of surgery, antibiotics, and hyperbaric oxygen therapy. Follow up should continue throughout life to ensure successful treatment of this chronic disease.

Keywords: Osteopetrosis; Oral status; Dental treatment complications

OPEN ACCESS

Correspondence:
Hedvig Hasselby, Department of Odontology, Umeå University, SE-90185 Umeå, Sweden, E-mail: hedwig_hasselby@hotmail.com

Received Date: *22 Dec 2021*
Accepted Date: *28 Jan 2022*
Published Date: *05 Feb 2022*

Citation:
Hasselby H, Danielsson K, Sjostrom M. Oral Health in Patients with Osteopetrosis: A Literature Review. Clin Surg. 2022; 7: 3411.

Introduction

Osteopetrosis (from the Greek, osteon and petra, for bone and stone is a rare hereditary bone disease that produces bones that are denser, heavier, and more fragile than normal [1]. In this disease, mutations limit osteoclast function or abundance, which causes an imbalance in the remodeling bone process and leads to impaired bone resorption. Osteopetrosis was first described in 1904, by the German radiologist, Heinrich Albers-Schonberg, who discovered the benign subtype, known as Autosomal Dominant Osteopetrosis (ADO) [2,3]. There are three main types of osteopetrosis, based on increasing disease severity: ADO, Intermediate Autosomal Osteopetrosis (IARO), and Autosomal Recessive Osteopetrosis (ARO).

Autosomal recessive osteopetrosis (ARO)

ARO also called malignant or infantile osteopetrosis, is the most serious type. It is often diagnosed early after birth, and it is lethal without treatment. In ARO, bone remodeling is extremely inhibited, due to non-functional or scarce osteoclasts. This lack of osteoclasts is favorable to osteoblasts, and thus, tips the remodeling balance towards bone synthesis. However, as bone synthesis continues, pressure is exerted on the nervous system. Moreover, newly synthesized bone fills all the available space, which results in dense, compact bone. This condition leads to a lack of red bone marrow, which results in anemia and immunodeficiency, due to reduced production of red and white blood cells. Without a sufficient immune system, the patient is at high risk of severe infections [3-5].

In ARO, osteoclasts might exist in large numbers, but due to mutations in the TCIRG1, CLCN7, OSTM1, SNX10, and PLEKHM genes, their function is limited, and they have difficulty producing

the acid needed to break down bone. Alternatively, when mutations occur in theTNFSF11/RANKL and TNFRSF11A/RANK genes, osteoclasts are few in number, and thus, they cannot compete with the normal number of osteoblasts. Thus, a TNFSF11 deficiency shifts the balance of bone remodeling to favor bone synthesis [6].

Most children with ARO are visually impaired to some degree. This impairment is caused by growing bone pressing on the optic nerve; it mostly occurs in the child's first year after birth. Children that retain vision after two years of age will continue to have sight, because the deterioration plateaus with age. Moreover, approximately one third of children with ARO have hearing loss, but the pathology remains unclear. One theory is that hearing impairments occur due to a combination of sclerosis in the ear bones and compression of the auditory nerve [7]. In addition, compression of cranial nerve VII causes facial paralysis, and compression of cranial nerve VIII leads to deafness, and occasionally, balance disorders [5]. Likewise, balance disorders can be caused by pressure on the peripheral motor nerves, which can also cause problems with swallowing. Furthermore, when ossification of the cranium fontanels begins too early, the brain does not have sufficient room to grow, and cognitive disabilities can occur [7]. Depending on which gene has been mutated, the disease can lead to intellectual disabilities that vary from mild to severe. Mutations in the CLCN7 and OSTM1genes causes' severe disability and mutations in the TCIGR gene cause mild disability [5]. Additionally, because the bones are dense and fragile, bone fractures occur with little force [3].

ARO carries a substantial risk of dental complications, such as caries, due to effects on enamel and dentin. Individuals with ARO often have little or no tooth enamel and misshaped dentin, which leads to deformed primary and permanent teeth. Eruption is delayed in both primary and permanent teeth, most likely due to the difficulty in erupting through the compact bone. In addition, aplasia is common [1-3,8].

ARO is also associated with a high risk of osteomyelitis, which results in osteopetrosis of the jaw. This occurs more frequently in the mandible than in the maxilla, because the maxilla has vascular-rich areas and thin cortical bone, which prevents osteomyelitis and osteonecrosis [1-3,9]. Children with untreated ARO seldom live past ten years of age [7]. The estimated prevalence is 3 to 34 individuals per million [1,3].

Intermediate autosomal recessive osteopetrosis (IARO)

IARO is similar to ARO, except IARO is typically discovered during late infancy or early childhood, and the symptoms develop more slowly [3]. Mutations in the TNFSF11/RANKL gene lead to few, but fully functional osteoclasts. Children with this mutation are prone to multiple fractures and shorter bone lengths. Children with mutations in the carbonic anhydrase II gene develop renal tubular acidosis, short bone lengths, and mental retardation [10]. However, children with IARO seldom display enlargements of the liver and spleen or bone marrow complications. Thus, the prognosis of IARO is more favorable than that of ARO, and some children survive to adulthood without treatment [11].

In Sweden, in the region of Västerbotten, there is a version of IARO caused by a mutation in the SNX10 gene, which has been traced back to the Viking age, around 950 AD. This IARO subtype is more severe than the main IARO, and patients develop symptoms in early infancy. The symptoms are almost the same as those associated with ARO, except this IARO subtype is not fatal at infancy, and patients live past early childhood. Palagano et al. [5] classified the Västerbotten subtype as ARO, due to of severity; however, Stattin et al. [11] argued that, because this subtype is not fatal until later childhood, it should be classified as IARO. Hematopoietic Stem Cell Transplantation (HSCT) treatment is critical for preventing disease progression and early death [5,11]. The estimated prevalence of IARO is three individuals per million [3].

Autosomal dominant oseopetrosis (ADO)

Patients with ADO, also called Albers-Schönbergs disease or benign osteopetrosis, often have mild symptoms, and some individuals do not experience symptoms. ADO does not affect the lifespan of an individual. It is typically discovered in older children or young adults, based on radiographs of bone fractures. Patients typically display the classic sign of 'sandwich vertebrae', where the vertebral endplates exhibit parallel, dense bands of sclerosis [1].

ADO was divided into two subtypes: ADO1 and ADO2. New gene discoveries have led to the need to redefine type 1, from non-functional bone resorption to increased bone formation. ADO1 is believed to be caused by a mutation in the LDL receptor-related protein 5 genes [12]. This discovery also changed the classifications of several other diseases [1,13]. Due to the rarity of ADO, confusion remains regarding its classification, and several recently published studies have continued to categorize ADO into subtypes 1 and 2 [5,10].

ADO2 is caused by a mutation in the CLCN7 gene, which encodes an H^+/Cl^- exchange transporter [10]. This mutation causes frequent bone fractures, and patients carry some risk of cranial nerve compression (5%) and moderate risks of anemia and immune insufficiency [1]. These patients have the same oral complications as those observed in ARO, IARO, and ADO1, but the complications are less severe [1,8]. In one study on 37 patients with ADO2, the most frequent complications were femur and rib fractures. Each patient had, on average, more than four bone fractures. The oral complications were: Dental fractures, multiple and severe dental decay, mandibular osteomyelitis multiple dental abscesses, and mandibular fractures [4]. No cure exists, thus, only the symptoms are treated [3]. The prevalence of ADO varies from two per million, in Brazil [4] to 50 per million, in Denmark [3].

Cure for osteopetrosis

When osteopetrosis is diagnosed in early life (i.e., before three years of age), HSCT can cure ARO and IARO, except when associated with some mutations. However, in future, when gene mutations prevent a cure with HSCT, osteopetrosis might be susceptible to treatments that specifically target RANKL/RANK signaling. Moreover, mouse studies on HSCT performed in utero have shown promising outcomes; thus, together with an early molecular diagnosis, it might be possible to treat osteopetrosis before birth [6].

Treating oral complications of osteopetrosis

Dental disorders, like tooth root deformation, osteomyelitis, and caries, are most often caused by hypomineralization. These disorders can occur, despite a successful HSCT treatment; however, HSCT increases the likelihood of tooth eruption [6,14].

Hyperbaric oxygen therapy increases the partial pressure of oxygen in the blood, which promotes oxygen to penetration into tissues [15]. Chen et al. [16] reported that hyperbaric oxygen treatments for osteomyelitis of the mandible had an 80% success rate.

After a 21-day treatment, patients showed improved healing, less pain, and less swelling. Hyperbaric oxygen also significantly increased angiogenesis, which promoted bone and tissue regeneration [17].

The literature suggests that osteopetrosis is a rare, but severe disease. Nevertheless, it has a significant impact on the patient's general health, life, and oral health. New and improved diagnostics and treatments have increased the likelihood that dental professionals will encounter patients with osteopetrosis. Without knowledge of appropriate treatments, dentists may cause patients harm.

The present literature review aimed to summarize the current knowledge on how osteopetrosis affects dentition and the facial skeleton and to describe the oral treatment options available for symptom relief and for rehabilitation from disease-related complications.

Methods

Search strategy

We searched PubMed (November 19th, 2020) with seven search terms: Osteopetrosis, oral, jaw, dental, craniofacial, mandible and maxilla. We then divided the search into two separate searches by including the MESH terms: Therapeutics and diagnosis. For both searches, we excluded articles without abstracts, non-English articles, articles that focused on animal trials, and articles over 20 years old. After a manual review of the search results, the abstracts were included or excluded, based on the following criteria:

Inclusion criteria

- Osteopetrosis (the primary focus of the study)
- Osteopetrosis types: Infantile, intermediary, or benign
- Dental or oral data: Treatments, complications, or diagnosis
- No limitation on the number of patients
- English language

Exclusion criteria

- Studies with non-human study participants
- Patients diagnosed with ADO1, due to uncertainty regarding the classification

The inclusion and exclusion criteria were met by 26 articles (Figure 1). An additional search was conducted on September 09th, 2021, and we included four articles published after the first search was conducted.

Data extraction and analysis

Data on relevant variables were extracted from the articles into Excel. These variables were: The number of patients, country of origin, patient sex, patient age, osteopetrosis type, how and when the patient received the diagnosis, laboratory findings, the reason for contacting the clinic, and patient dental hygiene before and after treatment. The oral diagnoses included: Caries, periodontics, osteomyelitis, osteonecrosis, cysts, abscesses, delayed eruption, tooth deformation, dental aplasia, oligodontia, and endodontic disease. Treatments included: Oral hygiene treatment, surgery, extractions, antibiotics, other medication, endodontic treatment, fillings, implants, fixed prosthetics, and removable prosthetics. Follow-up data included the follow-up time, mortality, recurrence, and control of oral hygiene.

Ethical considerations

This study was based on published articles with anonymous patient data; thus, no ethical considerations were relevant.

Results

Patients

The literature search provided data from 30 articles describing a total of 40 patients. The sex distribution was nearly 1:1, with 21 women and 18 men, and one patient did not indicate their sex. The median age was 20 years (range 1 to 71). Figure 2 presents the geographic origins of the patients. India had the highest number of patients, with ten cases.

The most common way to diagnose osteopetrosis was a combination of radiography and hematology (n=16, 40%). Most blood analyses included only hemoglobin and white blood cell counts, but in some cases, they included acid phosphatase, serum calcium, and serum phosphorous levels. Six patients (15%) were diagnosed based on their medical history and clinical examination. Four patients were diagnosed after a genetic evaluation (n=3 with TCIRG1mutations, n=1 with a TNFSF 11 mutation). Other diagnoses were based on a combination of clinical history and radiography (n=2); radiography alone (n=1); or a combination of radiography and biopsy (n=1). In one out of every four patients (n=10), the diagnostic methods were not presented.

Patients with ADO were diagnosed in their late teens up to adulthood; the oldest patient was 37 years old. Patients with ARO were diagnosed early; several were diagnosed at birth or a few months later. The oldest patient diagnosed with ARO was eight years old. The two patients with IARO were diagnosed at ages 1 and 13 years.

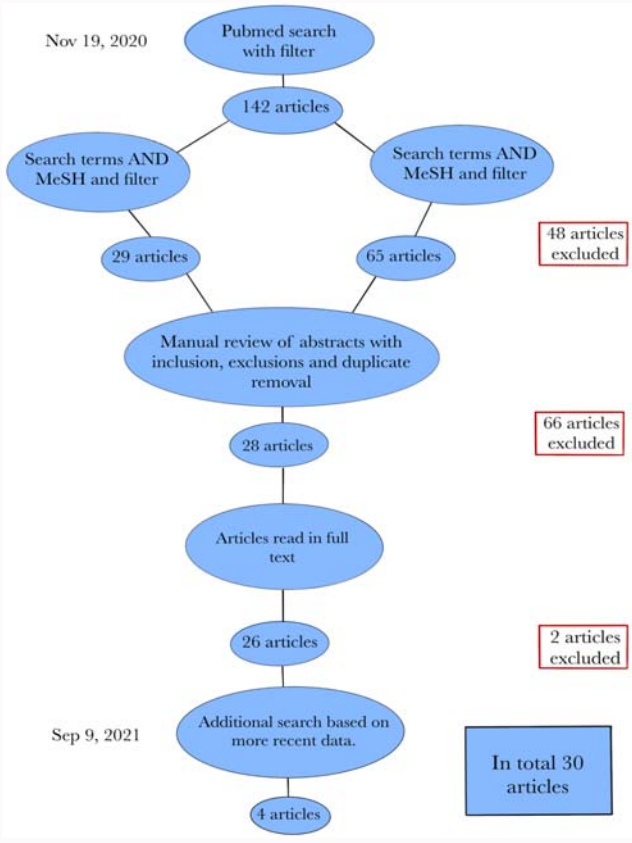

Figure 1: The search strategy applied to identify articles that focused on oral health. One year after the initial search, we repeated the search, and identified four additional articles.

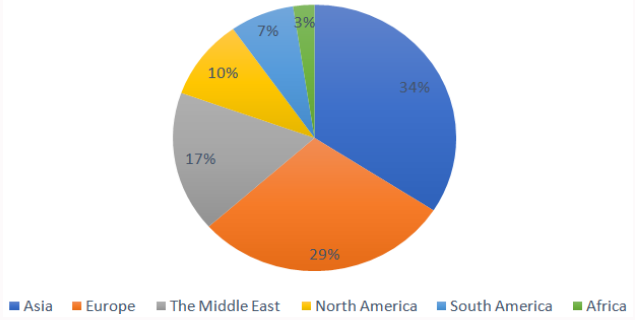

Figure 2: Pie chart shows the geographic origin of the 40 included patients.

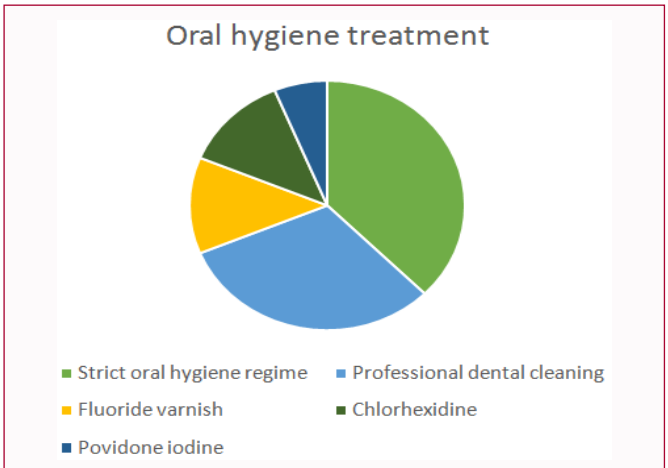

Figure 3: Different types of oral hygiene treatments given to the 12 patients with data available on the oral hygiene regime. The fluoride varnish was combined with professional dental cleaning.

Patients were classified by the type of osteopetrosis in 55% of cases. Seven patients with ARO were treated with HSCT. One patient that underwent HSCT did not respond positively to the treatment, and later, that patient died after complications from the disease. Two of the remaining six patients had good oral hygiene and did not display any problems other than tooth deformations. Four patients had poor oral hygiene and caries. Of these four, one had osteomyelitis and was treated with antibiotics, followed by an unspecified surgical treatment, but the treatment result was not reported. Four patients with ARO were not treated at all, and of these, one patient died.

Among all 40 patients, two thirds (n=28) had no data available on dental hygiene. Among the remaining 12 patients, dental hygiene was poor or less than optimal for a majority. Caries were commonly reported; only four patients did not have caries, but for 15 patients, data on caries were not available.

Orofacial complications

The most common complication was osteomyelitis (78% of patients), and a majority of patients had a combination of several complications. Caries and tooth extraction were the most common etiologies reported for osteomyelitis. Among patients with osteomyelitis, 45% had fistulas. Twenty-nine patients had osteonecrosis, and six patients had abscesses. Every other patient of the total patient cohort had delayed tooth eruptions. Two patients had periapical periodontitis, and one patient had a dentigerous cyst. Oligodontia was present in 38% of patients. Periodontitis was reported in four patients, and one patient that was treated with an implant developed peri-implantitis.

Treatments

One third of the patients received some form of dental hygiene treatment (Figure 3).

Twenty-eight patients were treated with antibiotics, and all of these had osteomyelitis. Two other patients with osteomyelitis did not have data available on the use of antibiotics. Eighteen articles mentioned what types of antibiotics were used, and the most common were amoxicillin-clavulanic and metronidazole. The treatment period was reported in 11 articles. The treatment times ranged from five days to three months.

Among the patients with osteomyelitis, 77% underwent surgery. The surgical treatments included sequestrectomy, debridement, and combinations of sequestrectomy and debridement. Two patients were treated with mandibular segmental resections, one received a corticotomy, one received a hemimandibulectomy, two received curettage, and one received an unspecified surgical clean up. Teeth were extractedin48% of patients. Among these, two patients had all their primary teeth extracted, and one patient had all teeth, both primary and permanent, extracted. All extractions were combined with antibiotics, except in two cases, where the use of antibiotics was not reported. Several extractions were performed concurrent with a bone treatment. One patient underwent hyperbaric oxygen therapy combined with surgical debridement of necrotic tissue, and antibiotics were administered.

Three patients with osteomyelitis were treated with antibiotics alone. Of these, two had osteomyelitis recurrences, and of these, one died of the disease. The third patient was followed up monthly, but the success or failure of the treatment was not reported. One patient underwent endodontic tooth treatments, but the use of antibiotics, follow up, and the success of the treatment were not reported.

Restorations

One patient was treated with dental fillings. Some defective teeth were protected with fissure sealing and deformed teeth were rebuilt with resin-based composite. One patient with ADO had previously been treated with amalgam and composite fillings, and after two molar extractions in the lower jaw, she developed osteomyelitis. Three patients were treated with implants; of these, one was later diagnosed with peri-implantitis. The etiology could not be determined, because no data were available on common risk factors, like smoking, dental hygiene, or diabetes. One patient had three fixtures in the lower jaw and a removable prosthetic for the maxilla. Two patients were treated with fixed dental prostheses. Six patients were treated with removable prosthetics in both jaws. One patient was treated with obturator prosthesis in the maxilla and a removable prosthesis in the lower jaw.

Follow up

Most patients had at least one follow up within a three-year period, and of those, the majority had a follow up during the first year. Osteomyelitis recurred in 30% of patients, and of these, three patients had chronic osteomyelitis. Two patients did not achieve complete healing. Most osteomyelitis recurrences occurred within 6 months, but in one patient, it recurred after five years. One patient was free from osteomyelitis after receiving a mandibular segmental resection and a titanium plate treatment.

Oral hygiene was followed in eight patients. Follow-ups were

performed annually (n=4), every month for 6 to 12 months for up to a year (n=2), and every third month (n=2). None of the patients reported a recurrence of any kind. Two patients died at 5 and 10 years old, after recurring pneumonia, which was most likely a complication of the disease. Another patient died at age 57 years, from a fever unrelated to the disease.

Discussion

Osteopetrosis is a rare disease, and criteria for its diagnosis have shifted with the availability of genome mapping [1,5,11]. This review covered the oral health of patients with osteopetrosis, based entirely on case studies. These studies had low-grade evidence, which carries a high risk of bias. Most studies were published within the past 20 years; thus, only a few diagnoses were based on genetic evidence. Currently, 75% of patients with ARO are diagnosed based on genetic tests [3]. The age at determination of the diagnosis was similar to those observed in earlier studies. This finding highlighted the limitation of using case studies as the basis for a review, because only 55% of the articles defined the different types of osteopetrosis. In future studies, when genetic testing is a routine procedure, underreporting may occur less commonly.

A patient diagnosed with osteopetrosis has fragile bones and is prone to infections. Oral hygiene is important for these patients to minimize the risk of infections. In this review, most included studies focused on osteomyelitis as a complication of osteopetrosis. There did not seem to be a uniform model for treating osteomyelitis or osteonecrosis in patients with osteopetrosis [15]. All patients that underwent a mandibular segmental resection, corticotomy, oral hemi-mandibulectomy had an uneventful healing process, which most likely did not require are-surgery. However, the included studies did not comment on loss of teeth or impairments in alveolar bone that resulted in impaired function, effects on eating, or the need for a dental prosthesis. It has been suggested that, when osteomyelitis is a complication of osteopetrosis, treatment should be similar to the treatment for osteoradionecrosis. That is, a more aggressive surgical approach is required, with a combination of antibiotics and prolonged hyperbaric oxygen therapy [15]. In the present review, we included one case where hyperbaric oxygen therapy was applied, but the surgeon chose a less invasive approach of surgical debridement; in that case, complete healing was not achieved [18].

In patients with ADO2, it is not feasible to treat maxillary osteomyelitis with antibiotics alone, such as amoxicillin and clavulanic acid, because the high density of bone does not allow the penetration of antibiotics. This limitation is similar in osteonecrotic jaw bones, which cannot be penetrated with antibiotics, due to the complete lack of blood flow [17]. This effect could explain the two studies that described unsuccessful treatments with antibiotics alone. Carvalho et al. [15] also advocated that antibiotic treatment alone would not be sufficient for positive results. Remission would more likely be achieved by surgically removing necrotic and infected bone, combined with antibiotics for treating soft tissue infections.

The literature stresses the importance of oral hygiene in preventing complications for patients with osteopetrosis. Nevertheless, oral hygiene treatments continue to be underreported, or they are not performed at all. Among the studies we reviewed, three patients with good oral hygiene at diagnosis displayed no problems with caries or osteomyelitis. The only study that described a prophylactic treatment [14], reported a change from bad hygiene with caries to good hygiene and no re-surgery. Moreover, treatments for caries were often not reported. Jalevik et al. [14] described tissue-conservative treatments, like fillings and fluoride varnishes, but the other studies chose to perform only extractions, or they did not report fillings as a treatment. One other patient that received fillings only developed complications after the extraction of her molars, which resulted in the loss of all her teeth, except the first and second molars in the mandible [19].

In most studies, the follow-up time was less than one year, or it was not reported. Thus, we could not perform a long-term evaluation of different oral treatments. One explanation for the short or lack of follow-ups was that most patients were treated by oral and maxillofacial surgeons for current complications, and therefore, the data were not available. In future, when a patient continues treatment with a general practitioner, communication between professionals should be the rule.

The main strength of this study was that it highlighted an area that lacks knowledge. On the other hand, the main limitation of this literature review was that it included a small number of patients, and it was largely limited to case-based articles. Thus, we could not fully investigate all the different types of oral-facial complications.

Conclusion

Good oral hygiene is highly important in preventing complications from infection in patients with osteopetrosis. The most common treatment for osteomyelitis was a combination of surgery, antibiotics, and hyperbaric oxygen therapy, similar to the treatment for osteoradionecrosis. Dental extractions should be the last treatment option; they should only be performed when no other treatment option can stop the infection and relieve the pain. Dentists should be observant of patients with frequent bone fractures and a combination of oral complications, like hypomineralization, delayed eruption, or aplasia. Follow-ups should be conducted over longer time periods to confirm successful treatment of this chronic disease.

Authors' Contribution

Conceptualization: M.S. and H.H.; methodology: M.S. and H.H.; investigation: H.H.; resources: M.S.; data curation: H.H.; writing–original draft preparation: M.S., H.H., and K.D.; project administration: M.S., H.H., and K.D. All authors have read and agreed to the published version of the manuscript.

References

1. Stark Z, Savarirayan R. Osteopetrosis. Orphanet J Rare Dis. 2009;(4):5.
2. Medlineplus. Osteopetrosis. Bethesda: U.S. Department of Health and Human Services; 2010.
3. Socialstyrelsen. Osteopetros. Stockholm: Socialstyrelsen. 2019.
4. Bénichou OD, Laredo JD, de Vernejoul MC. Type II autosomal dominant osteopetrosis (Albers-Schönberg disease): Clinical and radiological manifestations in 42 patients. Bone. 2000;26(1):87-93.
5. Palagano E, Menale C, Sobacchi C, Villa A. Genetics of osteopetrosis. Curr Osteoporos Rep. 2018;16(1):13-25.
6. Sobacchi C, Schulz A, Coxon F. Osteopetrosis: Genetics, treatment and new insights into osteoclast function. Nat Rev Endocrinol. 2013;9(9):522-36.
7. Wilson CJ, Vellodi A. Autosomal recessive osteopetrosis: Diagnosis, management, and outcome. Arch Dis Child. 2000;83(5):449-52.
8. Lam DK, Sándor GK, Holmes HI, Carmichael RP, Clokie CM. Marble

bone disease: A review of osteopetrosis and its oral health implications for dentists. J Can Dent Assoc. 2007;73(9):839-43.

9. Barry CP, Ryan CD. Osteomyelitis of the maxilla secondary to osteopetrosis: Report of a case. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2003;95(1):12-5.
10. Michou L, Brown JP. Genetics of bone diseases: Paget's disease, fibrous dysplasia, osteopetrosis, and osteogenesis imperfecta. Joint Bone Spine. 2011;78(3):252-8.
11. Stattin EL, Henning P, Klar J, McDermott E, Stecksen-Blicks C, Sandström PE, et al. SNX10 gene mutation leading to osteopetrosis with dysfunctional osteoclasts. Sci Rep. 2017;7(1):3012.
12. Bollerslev J, Henriksen K, Nielsen MF, Brixen K, Van Hul W. Autosomal dominant osteopetrosis revisited: Lessons from recent studies. Eur J Endocrinol. 2013;169(2):R39-57.
13. Van Wesenbeeck L, Cleiren E, Gram J, Beals RK, Bénichou O, Scopelliti D, et al. Six novel missense mutations in the LDL receptor-related protein 5 (LRP5) gene in different conditions with an increased bone density. Am J Hum Genet. 2003;72(3):763-71.
14. Jälevik B, Fasth A, Dahllöf G. Dental development after successful treatment of infantile osteopetrosis with bone marrow transplantation. Bone Marrow Transplant. 2002;29(6):537-40.
15. Carvalho P, Moura LB, Real Gabrielli MF, Cabrini Gabrielli MA, Antonio Pereira Filho V. Maxillary osteomyelitis associated with osteopetrosis: Systematic review. J Craniomaxillofac Surg. 2018;46(11):1905-10.
16. Chen CY, Lin KP, Lu SH, Chen YJ, Lin CF. Adjuvant hyperbaric oxygen therapy in the treatment of hemodialysis patients with chronic osteomyelitis. Ren Fail. 2008;30(2):233-7.
17. Re K, Patel S, Gandhi J, Suh Y, Reid I, Joshi G, et al. Clinical utility of hyperbaric oxygen therapy in dentistry. Med Gas Res. 2019;9(2):93-100.
18. Sharma A, Ingole SN, Deshpande MD, Kazi N, Meshram D, Ranadive P. A Rare Case of Osteoclast-poor Osteopetrosis (RANKL Mutation) with recurrent osteomyelitis of mandible: A case report. Int J Clin Pediatr Dent. 2020;13(6):717-21.
19. Allal S, Rabuel V, Gengler C, Douchet C, Allal F, Zwetyenga N. Case report of osteomyelitis of the mandible in osteopetrosis and management considerations. Int J Surg Case Rep. 2021;81:105813.

Articles Included in the Literature Review of Oral Health

1. Allal S, RabuelV, Gengler C, Douchet C, Allal F, Zwetyenga N. Case report of osteomyelitis of the mandible in osteopetrosis and management considerations. Int J Surg Case Rep. 2021;81:105813.
2. Athanasiadou E, Vlachou C, Theocharidou A, Tilaveridis I, Vargiami E, Antoniadis K, Arapostathis K. When a pedodontic examination leads to the diagnosis of osteopetrosis: A case report. Spec Care Dentist. 2020;40(1):113-20.
3. Bansal V, Kumar S, Arunkumar KV, Mowar A, Khare G. Dental management in autosomal recessive (intermediate) osteopetrosis: a case report. Pediatr Dent. 2010;32(7):542-5.
4. Barry CP, Ryan CD. Osteomyelitis of the maxilla secondary to osteopetrosis: report of a case. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2003;95(1):12-5.
5. CelakilT, DoganM, RohligBG, EvliogluG, Keskin H. Oral Rehabilitation of an Osteopetrosis Patient with Osteomyelitis. Case Rep Dent. 2016;2016:6930567.
6. Chattopadhyay P, Kundu AK, Saha AK, Karthak RO. Mandibular osteomyelitis and multiple skeletal complications in Albers-Schönberg disease. Singapore Med J. 2008;49(9):229-33.
7. da Silva Santos PS, Esperidião AP, de Freitas RR. Maxillofacial aspects in malignant osteopetrosis. Cleft Palate Craniofac J. 2009;46(4):388-90.
8. de Oliveira Hdo C, Pereira Filho VA, Gabrielli MF, Gabrielli MA, Vieira EH. Marginal resection for treatment of mandibular osteomyelitis associated with osteopetrosis: case report. J Craniomaxillofac Surg. 2011;39(7):525-9.
9. Detailleur V, Vansteenkiste G, Renard M, Verdonck A. Dental care approach in patients with osteopetrosis. Eur Arch Paediatr Dent. 2016;17(6):435-43.
10. Eppley BL, Coleman JJ. Free fibular flap reconstruction in mandibular osteopetrosis. J Craniofac Surg. 2001;12(4):369-72.
11. Infante-Cossio P, Gonzalez-Perez LM, Martinez-de-Fuentes R, Infante-Cossio M, Castaño-Seiquer A, Jimenez-Castellanos E. Maxillomandibular osteomyelitis associated with osteopetrosis. J Craniofac Surg. 2014;25(1):e79–e82.
12. Junquera L, Rodríguez-Recio C, Villarreal P, García-Consuegra L. Autosomal dominant osteopetrosis and maxillomandibular osteomyelitis. Am J Otolaryngol. 2005;26(4):275-8.
13. Jälevik B, Fasth A, Dahllöf G. Dental development after successful treatment of infantile osteopetrosis with bone marrow transplantation. Bone Marr Transplant. 2002;29(6):537-40.
14. Kant P, ShardaN, Bhowate RR. Clinical and Radiological Findings of Autosomal Dominant Osteopetrosis Type II: A Case Report. Case Rep Dent. 2013;2013:707343.
15. Krithika C, Neelakandan RS, Sivapathasundaram B, Koteeswaran D, Rajaram PC, Shetkar GS. Osteopetrosis-associated osteomyelitis of the jaws: a report of 4 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009;108(3):e56-65.
16. Kulyapina A, Verdaguer MartinJ, Navarro Cuellar C& Navarro Vila C. Long-Term Follow-Up of Bimaxillary Osteomyelitis Associated with Autosomal Dominant Osteopetrosis: A Case Report. J Maxillofac Oral Surg. 2016;15(1):121-6.
17. LiuYP, Lin XH, Yan MY, Lin BQ, Zhuo MY. Debridement in chronic osteomyelitis with benign osteopetrosis: A case report. Exp Ther Med. 2016;12(5):2811-14.
18. Luzzi V, Consoli G, Daryanani V, Santoro G, Sfasciotti GL, Polimeni A. Malignant infantile osteopetrosis: dental effects in paediatric patients. Case reports. Euro J Paediatr Dent. 2006;7(1):39-44.
19. Machado Cde V, da Rocha MC, Telles PD. Infantile osteopetrosis associated with osteomyelitis. BMJ Case Rep. 2015;bcr2014208085.
20. Mills CB, Steinberg J, Rubenstein JE, Lee PP. A successfulimplant-supported fixed prosthesis in a patient with osteopetrosis: A clinical report. J Prosthet Dent. 2021:S0022-3913(21)341-3.
21. Naval L, Molini MS, Herrera G, Naval B. Dental implants and osteomyelitis in a patient with osteopetrosis. Quintessence Int. 2014;45(9):765-8.
22. Raiteb M, Elmrini S, & Slimani F. Surgical management of chronic osteomyelitis with benign osteopetrosis: A case report. Annalsmedi Surg. 2021;65:102-296.
23. Satomura K, Kon M, Tokuyama R, Tomonari M, Takechi M, Yuasa T, et al. Osteopetrosis complicated by osteomyelitis of the mandible: a case report including characterization of the osteopetrotic bone. Int J Oral Maxillofac Surg. 2007;36(1):86-93.
24. Sekerci A E, Sisman Y, Ertas E T, Sahman H, Aydinbelge M. Infantile Malignant Osteopetrosis: Report of 2 Cases With Osteomyelitis of the Jaws. J Dent Child (Chic). 2012;79(2):93-9.
25. Sharma A, Ingole S N, Deshpande M D, Kazi N, Meshram D, Ranadive P. A Rare Case of Osteoclast-poor Osteopetrosis (RANKL Mutation) with Recurrent Osteomyelitis of Mandible: A Case Report. Int J Clin Pediatr Dent. 2020;13(6):717-21.

26. Sun H J, Xue L, Wu CB, Zhou Q. Clinical Characteristics and Treatment of Osteopetrosis Complicated by Osteomyelitis of the Mandible. J Craniofac Surg. 2016;27(8):e728–e730.

27. Tabrizi R, Arabi AM, Arabion HR, Gholami M. Jaw osteomyelitis as a complication in osteopetrosis. J Craniofac Surg. 2010;21(1):136-41.

28. Tohidi E, Bagherpour A. Clinicoradiological findings of benign osteopetrosis: report of two new cases. J Dent Res Dent Clin Dent Prospects. 2012;6(4):152-7.

29. Yamada T, Mishima K, Imura H, Ueno T, Matsumura T, Moritani N, et al. Osteomyelitis of the mandible secondary to infantile osteopetrosis: A case report. Oral Surg, Oral Med Oral Path Oral Radio Endo. 2009;107(6):e25-e29.

30. Vinay C, Uloopi KS, Rao RC, Kumar RS, Madhuri V. Oligodontia associated with osteopetrosis: a rare case report. J Dent Child (Chic). 2011;78(1):53-6.