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**Turkish Running Head:** İki Niemann Pick Olgusunda Diş Tedavileri

**Title:** Dental Treatment of Two Children with Niemann Pick Disease Type B Under General Anaesthesia

**Running Head:** Dental treatment in two Niemann Pick Cases

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## Abstract

Niemann Pick is an autosomal recessive lysosomal lipid storage disorder with symptoms including hepatosplenomegaly and thrombocytopenia. Delayed or extensive dental treatment may need to be delivered under general anesthesia and the management of such treatments in these children may require advanced medical support including intensive care (IC). Two children with Niemann Pick Disease type B who underwent dental treatment with general anesthesia and their post-operative follow-ups requiring IC are presented. Patients with NPD may present with fragile blood clots in extracted tooth socket and should be subjected to strict bleeding control standards. Especially the ones that may require further respiratory assistance since oral intubation is an invasive application to the oral surgical site.

**Keywords:** Niemann Pick Disease, general anesthesia, hemostasis

## Öz

Niemann Pick otozomal resesif geçişli; hepatosplenomegali ve trombositopeni semptomları bulunan bir lizozomal lipit depo hastalığıdır. Gecikmiş ya da kapsamlı diş tedavi gereksinimi olan olgularda genel anestezi altında müdahale ve yoğun bakım desteğine ihtiyaç olabilmektedir. Bu raporda Niemann Pick tip B tanılı iki olgunun genel anestezi altında gerçekleştirilen diş tedavileri ve yoğun bakım ünitesindeki operasyon sonrası takipleri sunulmaktadır. Niemann Pick hastalarında diş çekimi sonrası zayıf pıhtı odakları olabilmektedir, özellikle operasyon sonrasında solunum desteğine ihtiyaç duyabilecek hastalarda oral entübasyon sırasında bu pıhtı odaklarına dikkat edilmelidir. Bu hastalar sıkı kanama kontrol standartlarına tabi tutulmalıdır.

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**Anahtar Kelimeler:** Niemann Pick Hastalığı, genel anestezi, hemostaz

## **Introduction**

Niemann Pick Disease (NPD) is an autosomal recessive disorder caused by pathogenic mutations in SMPD1 gene. It is characterized by lysosomal acid sphingomyelinase deficiency causing accumulation of cholesterol and sphingomyelin in various organs, intercellular space, central nervous system and especially in reticuloendothelial system cells (1). Type A and B exhibit deficient acid sphingomyelinase (ASM) activity 0- 1% and 1- 10% of the healthy individuals respectively. Type C patients cannot metabolize cholesterol and other lipids properly which cause accumulation in tissues (2). Patients with NPD may present with cerebellar ataxia, dysphagia, dysarthria, progressive neurodegeneration, dementia, mental retardation, seizures, impaired motor development hepatosplenomegaly, thrombocytopenia, interstitial pulmonary disease, cardiac symptoms which are of significance to anesthesia procedures (1). Diagnosis is made by tissue biopsy showing characteristic foamy histiocytes or ASM enzyme analysis in leucocytes (2). Thrombocytopenia secondary to hypersplenism is a significant factor that leads to dental management difficulties in these patients (3). We hereby present two children with Niemann Pick Disease type B who underwent dental treatment with general anesthesia (GA) and their post-operative follow-ups in pediatric intensive care unit (PICU).

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## Case Report

### Case 1

Four year old boy was referred for dental treatment due to numerous caries by the ear nose throat specialist who was planning adenoidectomy for oral sleep apnea and adenoid hypertrophy. Offspring of a consanguineous marriage, the child was diagnosed with NPD type B and had undergone a bone marrow transplant at the age of two. Intraoral exam that was performed with the assistance of father due to child's limited ability to hold the head erect and keep the mouth open revealed chronic odontogenic abscesses and deep dentinal caries. Dental radiographs could not be taken because diagnostically valid images could not be obtained. Restorations and extractions were planned under GA in the same session with and before adenoidectomy (Table 1). Preoperative blood panel was shown in Table 2; consulting hematologist recommended regular hemostatic precautions and observation in PICU. Written parental informed consent was taken before the operation.

In GA procedure, a midazolam premedication (0.5 mg/kg) was administered intravenously (i.v) 15 minutes before taken to operating room. Noninvasive blood pressure, echocardiogram and peripheral pulse oximetry were used for standard anesthesia monitorization. Intravenous line using 24 gauge catheter was placed and saline infusion was administered. After 5 minutes of stabilization patient's heart rate, systolic/ diastolic arterial pressure and average arterial pressure were recorded as basal vitals. Before the induction 6 lt/min 100% oxygen insufflation was achieved. Following preoxygenation 1mcg/kg of fentanyl, 3.5 mg/kg of propofol doses administered i.v. Following the disappearance of eyelash reflex patient was ventilated with AMBU and 0.5 mg/kg rocuronium bromide was administered. Patient

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was intubated orally using (spiral) endotracheal tube. 50% Nitrous oxide/oxygen and sevoflurane (2%) were used for the maintenance of anesthesia.

Antisepsis of the oral cavity was performed with 0.12% chlorhexidine swabbing. Ferric sulfate pulpotomy and composite restorations were performed in all second primary molars, maxillary and mandibular canines were also restored with composite. All primary first molars and maxillary incisors were extracted with local anesthesia (articaine and epinephrine) injection (Table 1). Hemostasis was achieved with gauze pressure and suturing was not necessary in these minor wound sites with closed extractions of roots.

Following dental treatment adenoidectomy was performed using curette and nasopharynx was packed with gauze for three minutes until bleeding was controlled. Excised tissue was sent for biopsy and foamy histiocyte appearance was detected. Operation site was irrigated with sterile saline nasally and orally and hemostasis was observed. At the end of the operation patient was extubated and transferred to PICU as planned pre-operatively.

Patient's oxygen saturation declined four hours after the operation and was decided to be reintubated. Oral intubation preparations dislodged the blood clots leading to hemorrhage from anterior extraction site which had to be sutured after hemostatic agent (Gelfoam, Pfizer, USA) was packed into the sockets before the intubation. Patient received IV tranexaminic acid (10 mg /kg /day) for four days and postoperative bleeding from extraction sites stopped in 72 hours. Patient was kept intubated for two days, monitored in PICU for further respiratory distress and discharged on day 11 following surgery.

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## Case 2

A nine year old boy admitted for dental treatments before bone marrow transplant to eliminate any possible oral infection foci. Offspring of a consanguineous marriage, child was diagnosed with NPD type B. Intraoral exam revealed multiple carious and infected deciduous and permanent teeth (Figure 1). Restorations and extractions were planned under general anesthesia due to child's poor rapport (Table 1). Before the dental operation, an anesthesiologist examined the child with pre-operative blood panel that was shown in Table 2. Consulting hematologist suggested regular hemostatic precautions. Written parental informed consent was taken before the operation and the same GA procedure was followed as in case 1 described above. Indirect pulp capping with mineral trioxide aggregate (MTA) in two maxillary first permanent molars were performed and restored with composite. Two mandibular first permanent molars and both primary canines were restored with composite. Ten primary teeth were extracted after local anesthesia. Hemostasis was achieved with gauze pressure and suturing was not necessary in these minor wound sites with closed extractions of roots. Patient was extubated and referred to PICU for overnight observation and discharged the next day uneventfully.

## Discussion

Children with special health care needs often present a high risk of caries activity and oral cavity has frequently been documented as the leading source of sepsis in medically compromised patients (4,5). According to American Academy of Pediatric Dentistry (AAPD) GA is indicated in patients with cooperation problems due to physical/ medical disability and children in need of immediate, comprehensive oral/dental care among others (6). In NPD cases without severe physical disability and mental retardation, treatment on an outpatient basis may be less costly and encourage the family to be

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involved in their child's oral health and motivate for follow-ups (2). Although that is not an ideal scenario, unachievable volume of work has been reported as a reason for dental treatment indication under GA (7). Both cases presented were in need of comprehensive dental treatment due to delayed oral care. Since elimination of both the present and possible odontogenic infections was intended in a single-session GA procedure, mostly extractions were preferred. But extractions in these patients may cause unstable blood clots over the course of healing and may cause post-op hemorrhage. Thrombocytopenia may present secondary to hypersplenism in NPD patients as in case 1, although this level has been reported as clinically insignificant in the literature (8,9). According to American Academy of Pediatric Dentistry guideline platelet count below 75000 cells/ ml levels are recommended to be considered 24 hours before and after the surgery and hemorrhage control can be provided with application of local hemostatic agents, pressure packs (10). Our patient was above this level and local bleeding control with pressure provided hemostasis as suggested by consulting hematologist. But respiratory distress requiring intervention to the oral wound site disorganized blood clots and necessitated impromptu hemostatic control need.

Comprehensive dental treatment under GA in NPD patients may carry risks due to unforeseeable complications. Dental caries may be prevented or treated earlier by referral to the dental team by their primary physicians as part of their medical management plan. This approach may avoid unnecessary advanced procedures or prevent delay to critical treatments.

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## Conclusion

Patients with NPD may present with unstable blood clots and should be subjected to strict bleeding control standards. Especially the ones that may require further respiratory assistance since oral intubation is an invasive application to the oral surgical site.

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**Table 1.** Dental treatments of the cases

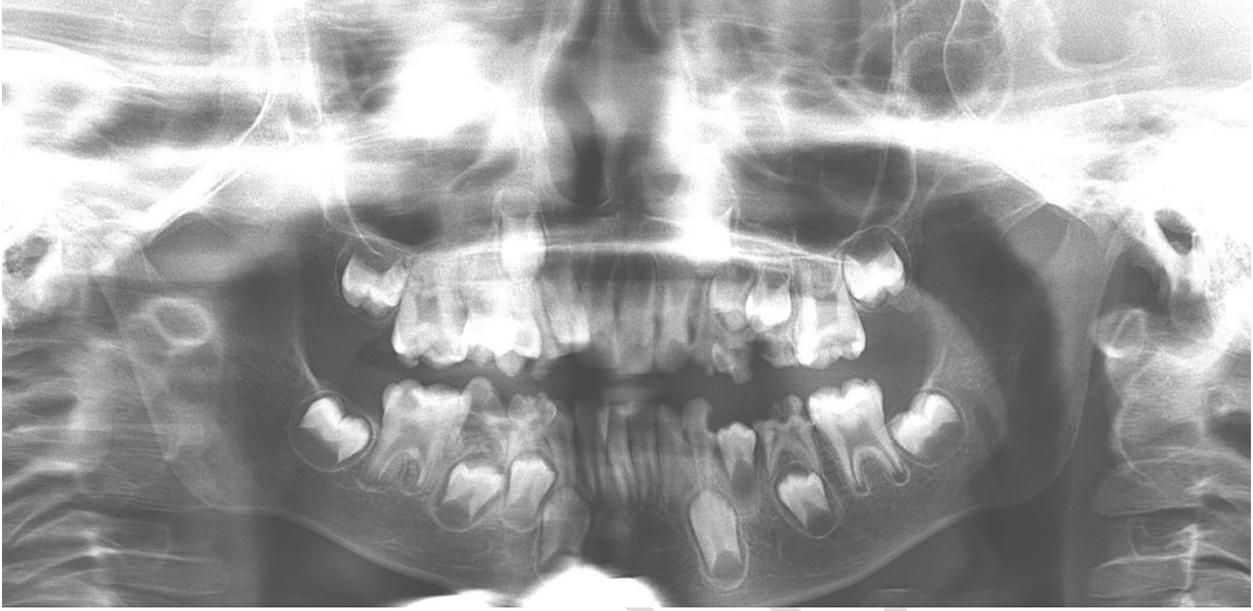
	Teeth extractions	Restorations	Pulpal treatments
Case 1	51, 52, 61, 62, 64, 74, 84	53, 63, 73, 83	55, 65, 75, 85
Case 2	51, 52, 53, 54, 55, 63, 64, 65, 74, 75	36, 46, 73, 83	16, 26

Teeth were numbered according to International Dental Federation Classification

**Table 2.** The preoperative blood panels of 2 cases

	International Normalizing Ratio	Prothrombin Time (second)	Activity	Thrombocyte count (10 <sup>3</sup> cells/ ml)
Case 1	1.53	47.5	56.7	116
Case 2	1.66	20.9	55.8	449

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**Figure 1.** Preoperative radiography of case 2

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