

# Green Teeth Associated with Neonatal Hyperbilirubinemia Caused by Biliary Atresia: Review and Case Report

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*Green pigmentation in teeth is an uncommon condition associated with bilirubin deposits in dental hard tissues. Its occurrence causes anxiety to both child and family. The purpose of this paper is to present a case involving an eleven-year-old girl with green pigmentation of permanent teeth who underwent a liver transplant due to biliary atresia when she was one year old. The reported case confirms the relevance of past medical history in establishing the diagnosis and treatment plan of green teeth.*

**Keywords:** Hyperbilirubinemia, Biliary atresia, Teeth

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## INTRODUCTION

Biliary atresia is a rare, nonhereditary chronic liver disease of unknown origin characterized by hepatic cholangiodestruction of the biliary system.<sup>1</sup> The clinical setting failure of biliary flow may be due to biliary obstruction by mechanical means or by metabolic factors in the hepatic cells.<sup>2</sup> Inflammatory damage to the hepatic bile ducts produces sclerosis and narrowing or even obliteration of the biliary tree.<sup>3</sup> Untreated, this condition leads to cirrhosis and death within the first year of life.

Biliary atresia incidence in the world varies from 5 per 100,000 to 32 per 100,000 live births; it is highest in Asia and girls are affected slightly more often than boys.<sup>4,5</sup> The disease leads to hyperbilirubinemia (HBR), which is characterized by elevated serum levels of bilirubin, a product of hemoglobin degradation. Some potential other causes of HBR include hepatitis, urinary tract infection, cystic fibrosis, sepsis and various metabolic diseases.<sup>1,6</sup>

For clinical purposes, the predominant type of bile pigments in the plasma can be used to classify hyperbili-

rubinemia into two major categories: a) plasma elevation of predominantly unconjugated bilirubin due to the overproduction of bilirubin, impaired bilirubin uptake by the liver, or abnormalities of bilirubin conjugation, and: b) plasma elevation of both unconjugated and conjugated bilirubin due to hepatocellular diseases, impaired canalicular excretion, and biliary obstruction.<sup>7</sup>

Bilirubin is extensively distributed and deposited throughout the body during HBR.<sup>8</sup> In soft tissues, the pigmentation immediately disappears due to the intense cell turnover. However, in mineralized dental tissues, bilirubin is trapped permanently because, after maturation, those tissues lose their metabolic activity resulting in green pigmentation of the teeth.<sup>6-11</sup> Other oral manifestations include various degrees of retardation in the dental and bone development, gingival hyperplasia, higher susceptibility to dental caries and enamel hypoplasia.<sup>6,10</sup>

Intrinsic green discoloration of teeth is considered to be rare and the majority of reports are related to the primary dentition.<sup>9,12-16</sup> When it occurs, however, it is a cause of anxiety to the family, and dental management may be complicated by many factors, such as the difficulty in masking the teeth with restorative materials and the side effects of immunosuppressive drugs in patients with a liver transplant. This study reports an unusual case of a patient who underwent liver transplantation and had green pigmentation of permanent teeth associated with hyperbilirubinemia caused by biliary atresia.

## CASE REPORT

An eleven-year-old girl, accompanied by her mother, was referred to the Dental School of our institution having as the chief complaint the greenish color in her teeth. Oral examination revealed that all permanent anterior teeth and permanent first molars were green in color. Green discoloration was mostly limited to the incisal half of maxillary central

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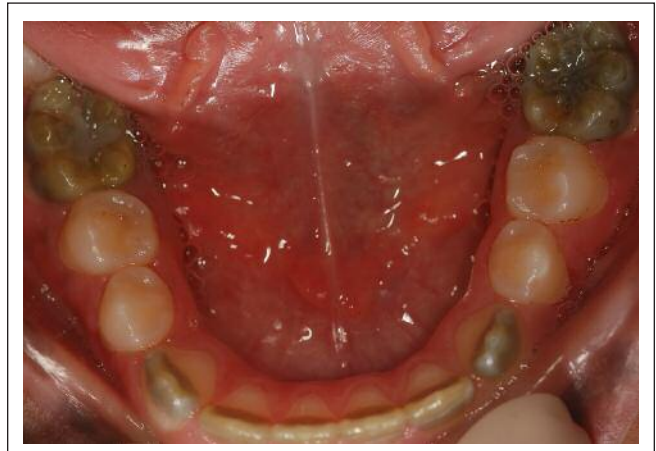
**Figure 1.** Intraoral view showing intrinsic green pigmentation of anterior permanent teeth.



**Figure 2.** Pigmentation of inferior lip.



**Figure 3.** Occlusal view showing green discoloration of permanent maxillary teeth.



**Figure 4.** Occlusal view showing green discoloration of permanent mandibular teeth.

incisor and lower incisors and on the incisal tip of canines and maxillary lateral incisors. The first molars seemed to be more severely affected, with green pigmentation extending over most of the clinical crown. Premolar teeth were not affected. The extent of the dental changes mirrors the period of hyperbilirubinemia, with the deepest discoloration affecting the earliest formed dental hard tissue. The enamel of all erupted teeth showed a smooth and regular surface. The examination of oral soft tissue revealed pigmentation in the inferior lip. Regarding occlusal pattern, the patient had posterior crossbite and anterior open bite (Figures 1, 2, 3, and 4).

Based on the child's dental history, an interview about her medical history was conducted to obtain useful information for a differential diagnosis. The patient was born of normal delivery and had adequate weight and height. In her first week of life, she developed jaundice, and biliary atresia was confirmed through a transoperative cholangiography. A biopsy of the liver confirmed biliary cirrhosis, which was compatible with the diagnosis of biliary atresia.

The child underwent surgery (*Kasai* procedure) to correct the biliary atresia when she was 40 days old; however, the

child's condition developed to a disordered cirrhosis, requiring a liver transplant. The transplant was performed when the patient was one-year-old; at that time, she received an isogroup reduced liver. The immediate post surgical period was satisfactory and the renal deficiency and biliary atresia were resolved.

The primary immunosuppression treatment was conducted using neo-natal *cyclosporine* and *prednisone*. The child exhibited side-effects related to the immunosuppression medication that included arterial hypertension, hirsutism, and severe gingival hyperplasia; as a result, the *cyclosporine* medication was changed to *tracolumus*, an immunosuppressive agent which was better accepted by the patient.

Since then the patient has received medical assistance with periodical evaluations of the immunosuppressant serum level, samples of renal and hepatic function, serum level of glucose and electrolytes, viral serology and abdominal Doppler echography. Currently, the patient's quality of life can be comparable to that of other children at her age group.

The greenish coloration of the permanent teeth is compatible with her medical history. Dental treatment will involve an orthodontic treatment through maxillary expansion (Hass appliance) and a palate grid. After a period of approximately 06 months of contention, an aesthetic treatment will take place with the use of composite or porcelain veneers on the permanent anterior teeth.

## DISCUSSION

Biliary atresia is the most common cause of green pigmentation due to HBR reported in the literature.<sup>8,13,17</sup> If the intrahepatic biliary tree is unaffected, surgical reconstruction by the *Kasai* procedure – hepatopertoenterostomy of the extrahepatic biliary tract – is possible. If the atresia is complete, liver transplantation is the only option.<sup>1</sup>

The first attempted liver transplant for biliary atresia, performed in March 1963 by Starzl, was on a young child.<sup>18</sup> At the Children's Hospital in Pittsburgh, 308 primary liver transplants have been performed between 1995 and 2006, including 103 (33%) for biliary atresia.<sup>1</sup> As a result of the shortage of donor livers, potential transplant patients must often wait for years for a donor liver. There is an urgent need for new technology to support patients with biliary atresia.

During HBR, bilirubin is distributed and deposited in different tissues of the body. The pigmentation disappears from the soft tissues due to high tissue turnover. Hence, the bilirubin is permanently trapped in hard dental tissues leading to intrinsic staining by bilirubin oxidation, which is clinically visible in erupted teeth.<sup>6-10,12,14</sup>

Tank<sup>19</sup> proved that the same pigment deposited in all parts of the body during severe jaundice is also deposited in the enamel organ, resulting in discoloration that may range from yellow to dark shades of green. It has also been reported that pigmentation is brightest when the tooth first erupts, and then it slowly fades with age. A possible explanation for that is the loss of enamel translucency as the child grows older, which interferes in the transmission of the green coloration from the dentin.<sup>8,14</sup> The extent and intensity of dental changes will mirror the period of HBR, with most patients displaying involvement that is limited to primary dentition.<sup>9,12,14</sup>

While end-stage hepatic disease severely affects dental development, dental tissues formed after transplantation can be normal.<sup>10</sup> However, there will be a deeply stained green band within the dentin that separates the pigmented parts from the non pigmented parts.<sup>10,20</sup> Histologically, green circular stripes parallel to the incremental lines of the dentin are observed. Enamel hypoplasia can be caused by changes in the organic matrix of the developing enamel resulted from metabolic disturbances, but it is more likely to be related to the effects of osteopenia and other disturbances of calcium and phosphate metabolism encountered in chronic liver diseases.<sup>6,9,13</sup>

In this case report, the patient presented varying levels of pigmentation in permanent teeth. Premolar teeth were not affected. A possible explanation for the pattern observed is related to the period of exposure to hepatic disease and odontogenesis. Dental changes mirror the period of HBR,

with the deepest discoloration affecting the earliest formed dental hard tissue (central incisors and first molars). The transplant was performed when the child was one year old, and the renal deficiency and biliary atresia were resolved. While end-stage hepatic disease severely affects dental development, dental tissues formed after transplantation can be normal (premolars, second and third molars).

Pigmentation of soft tissues was observed in the inferior lip. Immunosuppressive therapy with either *tacrolimus* or *cyclosporine* may lead to the presence of typical hyperpigmented patches on the gingival margin, on the internal surfaces of the cheeks, and on the surfaces of the lips.<sup>21</sup> There was no delay in the eruption of permanent teeth, which is commonly observed in pediatric patients with chronic liver diseases.<sup>6</sup>

The appearance of a child's first tooth is often a developmental milestone for the family, and the appearance of a discolored tooth can be disturbing and a cause for anxiety.<sup>6</sup> As the child grows older and starts to attend school, the presence of discolored teeth can cause difficulties with her peers.<sup>10,16</sup>

Green pigmentation is visible through the translucent enamel and can be very difficult to mask with restorative materials. There are various treatment options, including composite veneers or crowns and possibly bleaching for the permanent dentition.<sup>6,14</sup>

Dental management of those children may be complicated by many factors, such as excessive bleeding and the inability to metabolize routine anesthetics.<sup>6</sup> The high predisposition to dental caries may be associated with the continuous necessity of feeding to compensate for the low intestinal absorption of nutrients.<sup>8,22</sup> Moreover, patients with a liver transplant require lifelong immunosuppressive therapy and the side effects of these drugs include an increased susceptibility to infections, growth disturbances in children, and gingival hyperplasia.<sup>10,23</sup> The high risk of infection dictates a need for antibiotic cover for more invasive dental procedures.<sup>6</sup>

As the pediatric care of infants and young children improves, it is likely that more children with life threatening illnesses will survive. For this reason, physicians caring for children with a history of HBR should be aware of the risk of green pigmentation in the primary and permanent dentition and should advise parents about the potential risk. As the child grows older, cosmetic treatment of those teeth becomes a priority in order to improve their self-esteem and to collaborate in their social integration.

## CONCLUSIONS

Aesthetics has a very important role in current pediatric dentistry. In this case report, we describe an uncommon form of tooth pigmentation caused by serum bilirubin deposition during dental formation. Intrinsic green discoloration of teeth is considered to be rare and the majority of reports are related to the primary dentition. The present case report supports the importance of using a patient's medical history to determine the etiology of the dental staining. Regular

dental care is also necessary to discuss the cosmetic treatment available.

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