Oral Findings in Alagille Syndrome

A Case Report

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Key Words

Alagille syndrome • Liver disease • Dentition • Hypoplasia, dental

Abstract

Objective: To highlight the role of dental practitioners in the management of children with liver diseases. **Clinical Presentation:** A 13-year-old girl with Alagille syndrome presented with oral manifestation of end-stage liver disease that needed liver transplant. The dentition showed hypoplastic lesions and severe discoloration. The gingiva was inflamed and edematous due to poor oral hygiene and possibly to the medication the child was placed on to reduce graft rejection. **Conclusion:** Dental considerations should be incorporated in the overall management of children with liver disease and transplant. Consultation with a dental practitioner should be sought before, during and after treatment of such cases.

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Introduction

Alagille syndrome is a condition that can lead to end-stage liver disease, usually requiring treatment by a liver transplant. As with any transplant, the greatest complication is the possibility of rejection. One of the major causes of rejection apart from incompatibility of the tissues is preoperative and postoperative infection. The oral cavity has been shown to harbor many pathogenic bacteria that

could produce bacteremia with the potential of causing severe and acute infection in other organs of the body.

Alagille syndrome is a genetic disorder that is inherited as an autosomal dominant trait located on chromosome 20p [1]. A deletion or mutation of a single copy of the human gene Jagged 1 has been shown to be the underlying genetic defect in the syndrome [2, 3]. Alagille et al. [4] in 1975 first described this disease as a syndrome characterized by hepatic hypoplasia, associated with characteristic facies, vertebral malformations, and retardation of physical, mental and sexual development as well as cardiac murmurs. Since then, many more in-depth studies have been published on the various characteristics of the syndrome. Emerick et al. [5] studied 92 patients with Alagille syndrome to determine the frequencies of clinical manifestations and to correlate such findings with the outcome of the disease. They showed that 85% of the patients had paucity of interlobular ducts, 96% cholestasis, 97% cardiac murmur, 51% butterfly vertebrae, 78% posterior embryotoxon and 96% characteristic facies. Other features included renal disease as well as intracranial bleeding and stroke (49 and 14%, respectively).

Pediatric liver transplant has now become an accepted therapy for end-stage liver disease [6] although children with Alagille syndrome may or may not require liver transplantation. The most common factors contributing to the decision for transplantation are complications such as bone fracture, pruritus and severe xanthoma [7].

In this paper we present the role of the dental practitioner in the overall management and oral findings in a child with Alagille syndrome.

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Fig. 1. Intrinsic discoloration and hypoplasia of the dentition.

Fig. 2. Severe intrinsic discoloration and enamel hypoplasia of the anterior teeth.

Case Report

A 13-year-old girl presented for dental treatment at the school dental clinic for checkup. Medical history revealed that she was jaundiced at birth and at 60 days after, she underwent laparotomy, intra-operative choleogram and a liver biopsy. The result of the biopsy revealed paucity of interlobular bile ducts. An echocardiogram also showed the presence of peripheral pulmonary artery stenosis. She also presented with hepatosplenomegaly but without ascites and edema. Otherwise, all other vital signs were normal. At age 3, she had pain in her right hip with an accompanying limp of the right foot. There was no history of trauma or fever. She was put on a waiting list for a liver transplant. Prior to her transplant, she developed severe rickets with extensive bowing of the tibias and suffered a fracture of the right femur. At age 11, she underwent an orthotopic liver transplant. She was placed on cyclosporin, prednisolone, Zestril and multivitamins.

Her dental development was normal for her chronological age. The maxillary lateral incisors were conically shaped (fig. 1). All her teeth showed a grayish intrinsic discoloration with focal areas of white and yellow patches and enamel hypoplasia with pronounced horizontal and vertical developmental lines (fig. 1). The discoloration, however, was more severe in the maxillary and mandibular anterior teeth (fig. 2) than others. There was no carious lesion and with the exception of the maxillary lateral incisors, all the teeth had normal morphological characteristics. Although the oral mucosa was normal with no evidence of discoloration, the gingivae, especially around the anterior teeth, showed evidence of inflammation and mild gingival swelling (fig. 1, 2). The oral hygiene was fair.

Her dental management so far has involved improving of oral hygiene and placing fissure sealant on the molars. She is to have treatment to improve the aesthetics of the maxillary anterior teeth as soon as she is disposed to such treatment.

Discussion

The major complications after liver transplantation are related to graft rejections, immunosuppression, side effects of the agent used for immunosuppression, and excessive bleeding after injury resulting from poor liver function and/or the effects of anticoagulation medication [8]. One of the causes of graft rejection and early death after liver transplantation is infection from a variety of sources. The oral cavity harbors numerous pathogenic and opportunistic species which, when out of their normal environment, can cause serious infections [9]. In fact, oral bacteria have been incriminated in systemic diseases such as pneumonia, gastritis, peptic ulcers and infective endocarditis [10–13].

Dental infections, therefore, may pose great risks for patients especially after liver transplant. Consequently it is recommended that dental examination and consultation should be carried out at different management phases to evaluate the oral health status of such patients (table 1). Preoperatively, all carious teeth should be restored or extracted; the periodontal tissue should be healthy and the oral hygiene should be improved. All dental treatment should be carried out in collaboration with the physician who will advise on drug selection, the use of antibiotic prophylaxis and control of bleeding in cases requiring tooth extraction or surgery.

Postoperatively, patients also require regular dental checkups because of the continuous use of immunosuppressive drugs. One of the side effects of these immunosuppressive agents is the suppression of bone marrow, which may result in leukopenia, thrombocytopenia or

Table 1. Dental procedures and rationale for patients with end-stage liver disease before transplantation

Procedure	Rationale
<i>Before transplantation</i>	
Medical investigation	Bleeding tendencies, medication type could affect oral health and dental procedures
Oral hygiene instruction	Reduction of oral bacterial load
Professional prophylaxis	Treatment and prevention of plaque-related disease
Chlorhexidine mouthwash	Clinical antiplaque and antibacterial agent
Extraction of all grossly carious teeth	Reduction of foci of infection in the oral cavity
Antibiotic cover for invasive dental procedures	Reduction of bacteremia
<i>After transplantation</i>	
Oral hygiene instruction	Reduction of oral bacterial load
Professional prophylaxis	Reduction of oral bacterial load/oral health maintenance
Restorative and cosmetic dental treatment	Improvement of aesthetics and function
Medical consultation	Monitoring medication and general health

anemia, any of which may predispose patients to excessive bleeding tendencies and opportunistic infections such as candidiasis.

Cyclosporin has also been associated with increased incidence of drug-induced gingival overgrowth, which may not only impair oral aesthetics but may also lead to gingival inflammation and periodontal tissue damage [14]. Regular dental prophylaxis and drug modulation, in consultation with the physician, can prevent the development of this condition.

Conclusion

Dental consultation, examination and treatment should be required for patients being prepared for liver transplant or having end-stage liver disease. The dentist should institute an aggressive preventive regimen and consult with the transplant surgeon before performing any invasive dental procedures. After transplantation, a regimen of regular dental visits is essential to monitor patients' oral health status and possible adverse effects of the immunosuppressants.

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