Efficacy of Intravenous Propranolol for Life-threatening Diffuse Neonatal Hemangiomatosis

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Abstract

Oral propranolol is recommended as the first-line agent for infantile hemangioma requiring systemic treatment. Life-threatening complications such as obstructive infantile hemangioma of the airway or infantile hepatic hemangioma associated with high-output congestive heart failure are major indications for the consideration of early treatment. We present the case of an infant with life-threatening diffuse neonatal hemangiomatosis including airway obstruction due to subglottic hemangioma, heart failure due to multiple hepatic hemangiomas with portohepatic venous shunts and severe anemia due to continuous gastrointestinal bleeding, in which treatment with intravenous propranolol proved successful.

Introduction

Diffuse neonatal hemangiomatosis (DNH) is an uncommon disease that can rarely be life-threatening (1). Severe cases warrant immediate therapeutic intervention (2). While oral propranolol is recommended for infantile hemangiomas (IH), few reports have described the use of intravenous propranolol for DNH (3, 4). We present an infant with life-threatening DNH in which intravenous propranolol proved successful.

Case Report

A 6-week-old boy was admitted for respiratory distress, difficulty feeding, and bloody stools. He had been delivered at a private hospital. At birth, multiple cutaneous IH had been identified. He was discharged home at 5 days old, but at 3 weeks of age presented with gradually worsening bloody stools and respiratory distress. On admission, multiple generalized IH were observed (**Figure 1A**). Physical examination revealed a systolic murmur at the right sternal border and the liver was palpable 4 cm below the right costal margin. Upper airway endoscopy demonstrated mucosal blush and swelling in the subglottis (**Figure 1B**). Contrast-enhanced computed tomography (CT) showed hepatomegaly with multiple intrahepatic nodular structures with portohepatic venous shunting (**Figure 2A**). Abdominal CT and cranial magnetic resonance imaging demonstrated multiple IH in the pancreas, spleen, bladder, rectum, right testis, and cerebellar hemispheres. Skin biopsy revealed pathology consistent with IH, with positive reactivity for glucose transporter-1 in endothelial cells (**Figure 2B)**. These findings confirmed the diagnosis of DNH. Echocardiography showed

enlargement of the left ventricle and severe pulmonary hypertension.

The day after admission, oral propranolol (4.28 mg/mL) was initiated at 1.0 mg/kg/day divided twice daily and increased to 2.0 mg/kg/day on day 3. However, the patient's clinical condition worsened, necessitating mechanical ventilation, administration of diuretics, and a single transfusion of red blood cells. Four days after admission, he was transitioned from oral to continuous intravenous propranolol and the dose was increased from 1.0 to 3.0 mg/kg/day. No significant complications were observed immediately after the start of intravenous propranolol, except for temporary, asymptomatic hypotension (64/35 mm Hg). His cardiovascular parameters and subglottic hemangioma improved, and the patient was extubated at 9 weeks of age. Bloody stools resolved and the patient was discharged on 3 mg/kg/day of oral propranolol divided twice daily at 16 weeks old.

Discussion

Given the lack of response to oral propranolol, we hypothesized that our patient's gastrointestinal bleeding was preventing adequate intestinal absorption of the drug. While consensus remains lacking regarding the optimal dose of intravenous propranolol for IH, previous reports have used doses ranging from 0.5 to 2 mg/kg/day (3) (4). In one case, similar to our patient, an infant with a large cervicofacial IH and necrotizing enterocolitis failed to respond adequately to oral propranolol and was transitioned to intravenous propranolol due to concern for inadequate gastrointestinal absorption. In the other case, the reason for intravenous propranolol administration was not stated. We administered intravenous propranolol with continuous electrocardiography and heart rate and blood

pressure monitoring, as recommended for acute cardiac treatment with intravenous propranolol (5). Earlier evaluation and initiation of oral propranolol may have prevented the progression of subsequent complications in our patient. Screening hepatic ultrasonography is recommended in infants showing 5 or more cutaneous IH, since high-output heart failure can be a rare complication (2). Further studies are warranted to evaluate intravenous propranolol in the setting of life-threatening DNH, especially with gastrointestinal involvement.

Data availability statement

Data available on request from the authors.

Ethics statement

Written informed consent was obtained from parents of this minor patient, for the publication of any potentially identifiable images and data included in this article.

Conflict of interest

The authors declare no conflicts of interest in association with the present study.

Author contributions

All coauthors read and met the *Pediatric Dermatology* criteria for authorship. TI drafted the initial manuscript. KS and HU have made substantial, direct, and intellectual contributions to the work, and

approved it for publication.

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Figure Legends

Figure 1. A) On admission, multiple generalized cutaneous infantile hemangiomas are present. **B)** Laryngoscopy and bronchoscopy demonstrate subglottic infantile hemangiomas (black arrowheads).

Figure 2. A) Contrast-enhanced computed tomography reveals multiple diffuse intrahepatic nodular structures showing dense enhancement in the right hepatic lobe. **B)** Positive glucose transporter-1 immunostaining in the endothelial cells and erythrocytes.

Figure 1A

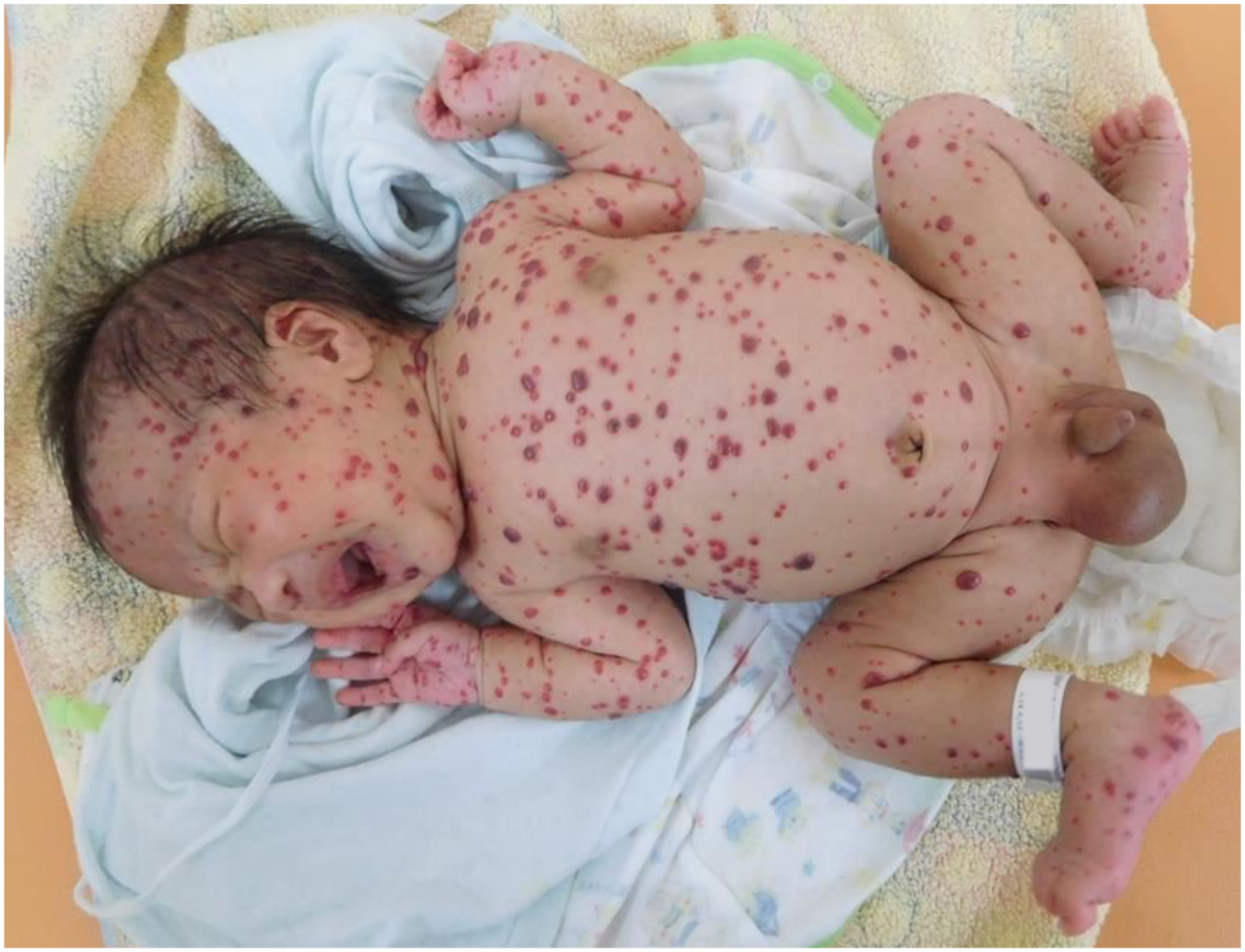

Figure 1B

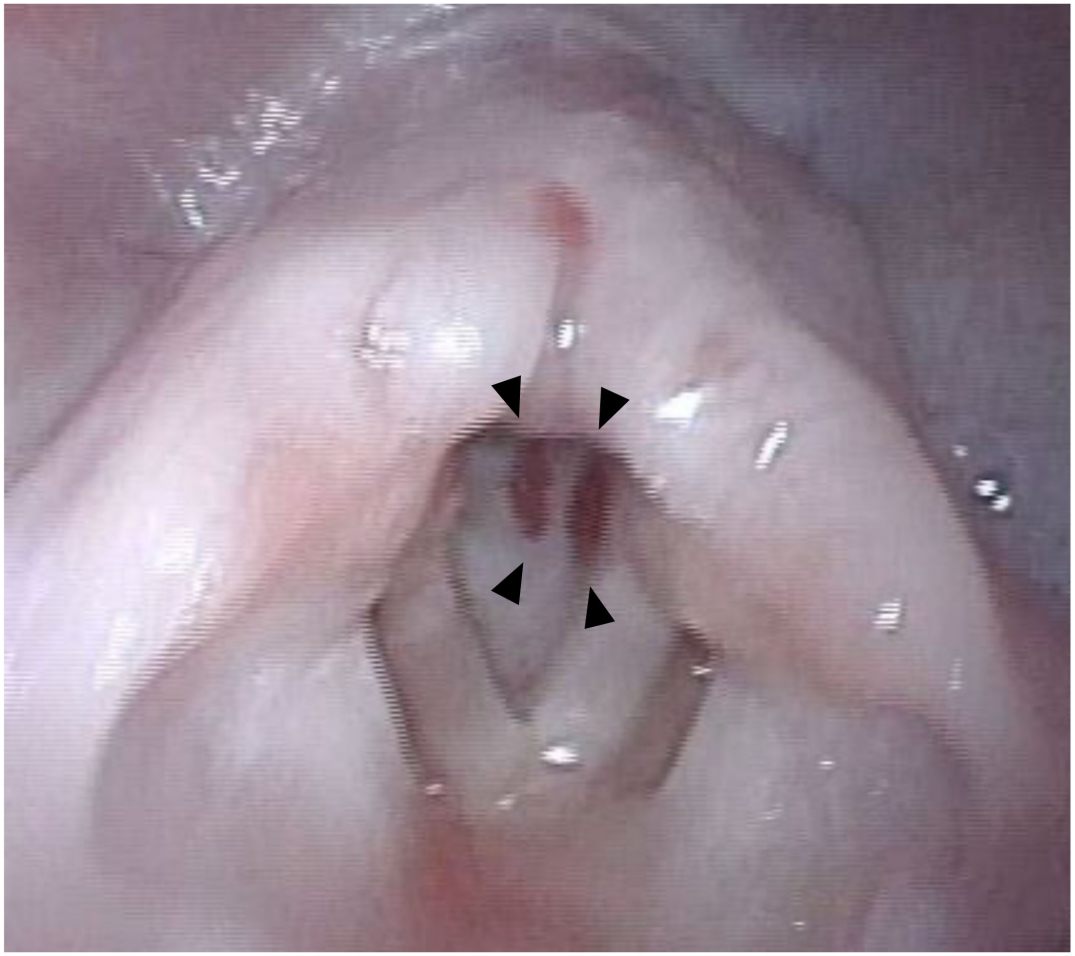

Figure 2A

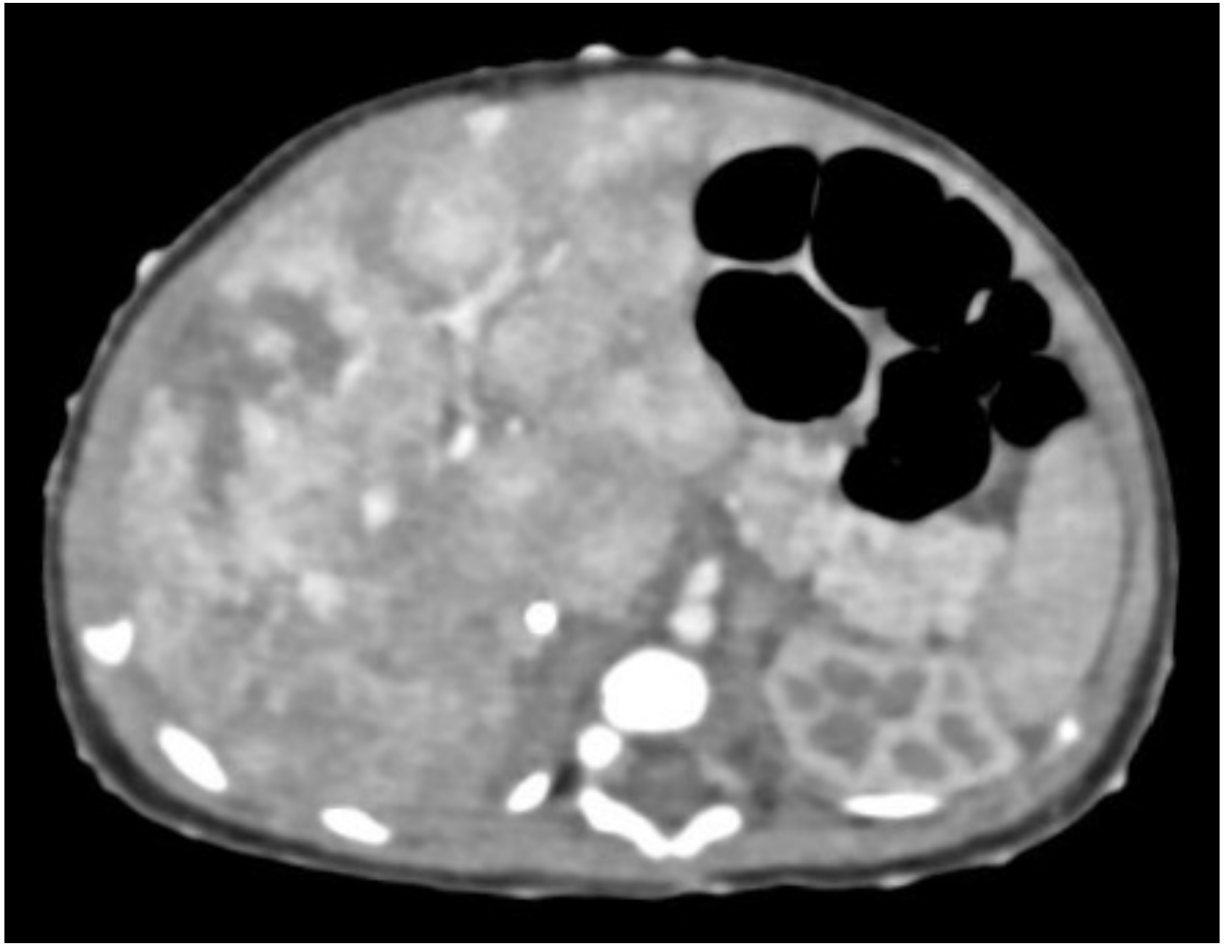

Figure 2B