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Distinct Clinical Presentations of Vein of Galen Aneurysmal Malformation: A Case Series

Toktam Sheykhian[1] | Behzad Mohammadpour Ahranjani[1] | Saghi Elmi[2] | Mohammadamin Parsaei[3]

[1]Maternal, Fetal and Neonatal Research Center, Family Health Research Institute, Tehran University of Medical Sciences, Tehran, Iran | [2]Pediatric Department, Shepparton, Victoria, Australia | [3]Breastfeeding Research Center, Family Health Research Institute, Tehran University of Medical Sciences, Tehran, Iran

Correspondence: Mohammadamin Parsaei (amin.parsaei890@gmail.com)

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ABSTRACT

We present two cases of vein of Galen aneurysmal malformation, detected in early life, with differing outcomes. This suggests that early detection of this malformation in fetuses or neonates does not necessarily indicate a poor prognosis, highlighting the need for vigilant monitoring and timely intervention to optimize outcomes.

1 | Introduction

The Vein of Galen Aneurysmal Malformation (VGAM) is an extremely rare arteriovenous malformation originating in the embryonic choroidal system between the sixth and eleventh gestational weeks [1, 2]. This condition is characterized by abnormalities in the choroidal plexus, which drains into the median prosencephalic vein of Markowski [3]. During the embryonic period, the median prosencephalic vein functions as a prominent midline venous collector and serves as the precursor to the vein of Galen in later development [3]. Abnormal arterial shunting from the anterior and posterior circulations leads to dilation of the median prosencephalic vein, which leads to the development of VGAM [4]. Recent advances in ultrasonography practice have significantly increased the antenatal detection of VGAM, with diagnosis rates reaching up to 73% of cases, the majority of which are identified during the third trimester [5]. VGAM is typically diagnosed through direct visualization of the vein via ultrasonography; however, in rare instances, the detection of cardiac anomalies may precede the identification of VGAM by several weeks [5].

VGAM comprises two distinct types: choroidal and mural [2]. Choroidal VGAM predominates in neonates presenting with a low clinical score attributed to cardiac failure [2]. The condition is sustained by the entirety of the choroidal arteries and their corresponding branches, which converge into an enlarged venous pouch [2]. In this condition, volume overload prevails, leading to increased cardiac output, tachycardia, cardiac enlargement, cardiac failure, pulmonary hypertension and edema, respiratory distress syndrome, and multiple organ failure [6]. Conversely, mural VGAM exhibits enhanced tolerance and manifests in infants devoid of cardiac symptoms [2]. This variant arises from the presence of singular or multiple direct arteriovenous fistulae within the wall of the VGAM [2]. There is also a proposed criterion, known as the Bicêtre clinical score, to evaluate prognosis and guide management for neonates diagnosed with VGAM. This 21-point scale assesses the severity of cardiac, pulmonary, neurological, hepatic, and renal symptoms using both clinical and laboratory values. Lower scores on the Bicêtre scale are indicative of poorer outcomes in these patients [7].

In this study, we present two cases of VGAM with distinct clinical presentations by following the Clinical Case Reporting Guideline Development (CARE) guidelines [8].

2 | Case Presentation

2.1 | Case 1

2.1.1 | Case History/Examination

A male neonate delivered at full term (39 weeks of gestation, G_2L_1) via vaginal delivery exhibited a 5-min Apgar score of 8 and a birth weight of 3240 g. The mother, aged 33, had an unremarkable pregnancy without specific medical history or medication use.

During the initial postnatal physical assessments, no anomalies were detected. However, a few hours after birth, the neonate was subsequently admitted to the Neonatal Intensive Care Unit (NICU) due to respiratory distress, necessitating ventilatory support. Manifestations included tachypnea, severe Congestive Heart Failure (CHF), and mild cyanosis within the first few days of life.

In subsequent physical examinations, a grade III/VI murmur was identified at the left lower sternal border, indicative of Tricuspid Regurgitation (TR). The murmur was accompanied by a pronounced S_2, a blood pressure of 68/32 mmHg with a wide pulse pressure, and an oxygen saturation level of 94% in venous blood gas analysis. Peripheral pulses were noted to be bounding in all four extremities, and a cranial bruit was deliberately sought and detected.

2.1.2 | Management and Clinical Course

Electrocardiography (ECG) revealed a normal sinus rhythm, extreme right axis deviation, and no ST-T changes. The chest x-ray findings indicated cardiomegaly with heightened pulmonary vascularity (Figure 1). Moreover, transthoracic echocardiography revealed severe systemic pulmonary hypertension, dilated right heart chambers, severe TR, as well as a moderate-sized Patent Ductus Arteriosus (PDA) with right-to-left shunting. Transcranial ultrasound and contrast-enhanced Computed Tomography (CT) scan of the brain revealed a VGAM (Figure 2). According to color Doppler ultrasound, severe dilatation of the internal cerebral, Galen, and straight sinus veins was seen (diameter: 13 mm) (Figure 3). Collectively, a Bicêtre evaluation score of 7 to 8 was calculated, suggesting a poor prognosis for the neonate.

Given the Bicêtre score and the severe hemodynamic instability of the patient, in consultation with the neurosurgical team, we prioritized intensive medical interventions to stabilize CHF and provide comprehensive neonatal care. These measures were intended to optimize the patient's condition for subsequent endovascular treatment, thereby minimizing procedure-associated morbidity and mortality. The therapeutic protocol included the administration of inotropic agents, such as dopamine and dobutamine (up to 10 μg/kg/min), along with milrinone (0.4–0.75 μg/kg/min). The effectiveness of these interventions was assessed through serial transthoracic echocardiographic evaluations. Additionally, mechanical ventilation was required to manage respiratory acidosis and cyanosis.

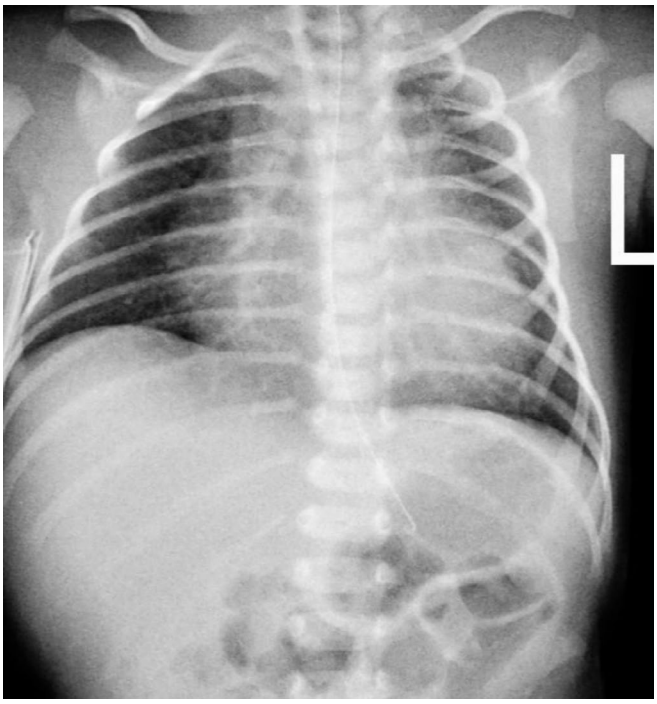


FIGURE 1 | Anteroposterior chest x-ray of Case 1, illustrating cardiomegaly.

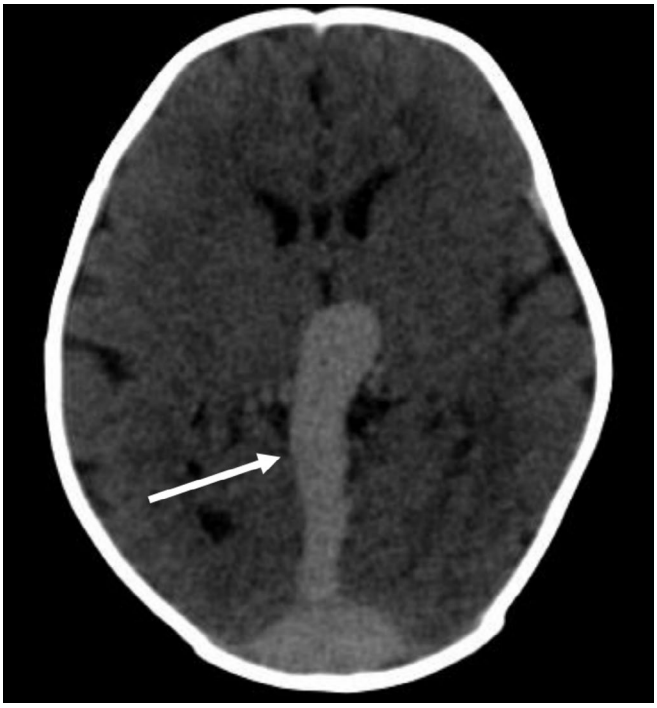
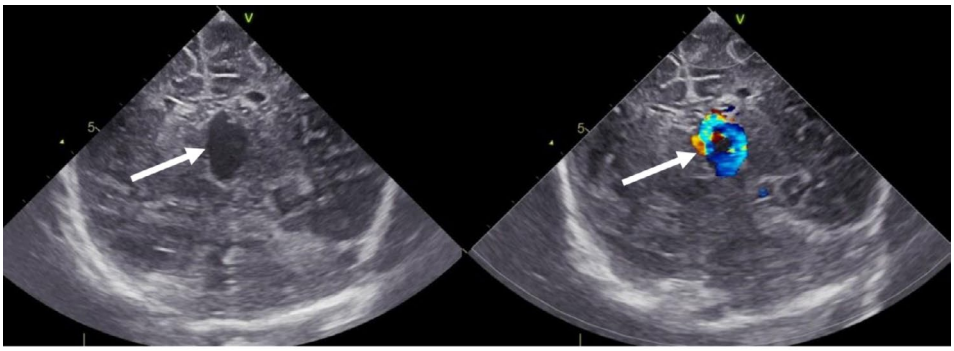


FIGURE 2 | Plain and contrast-enhanced view of a brain CT scan for Case 1, revealing the dilated vein of Galen (white arrow).

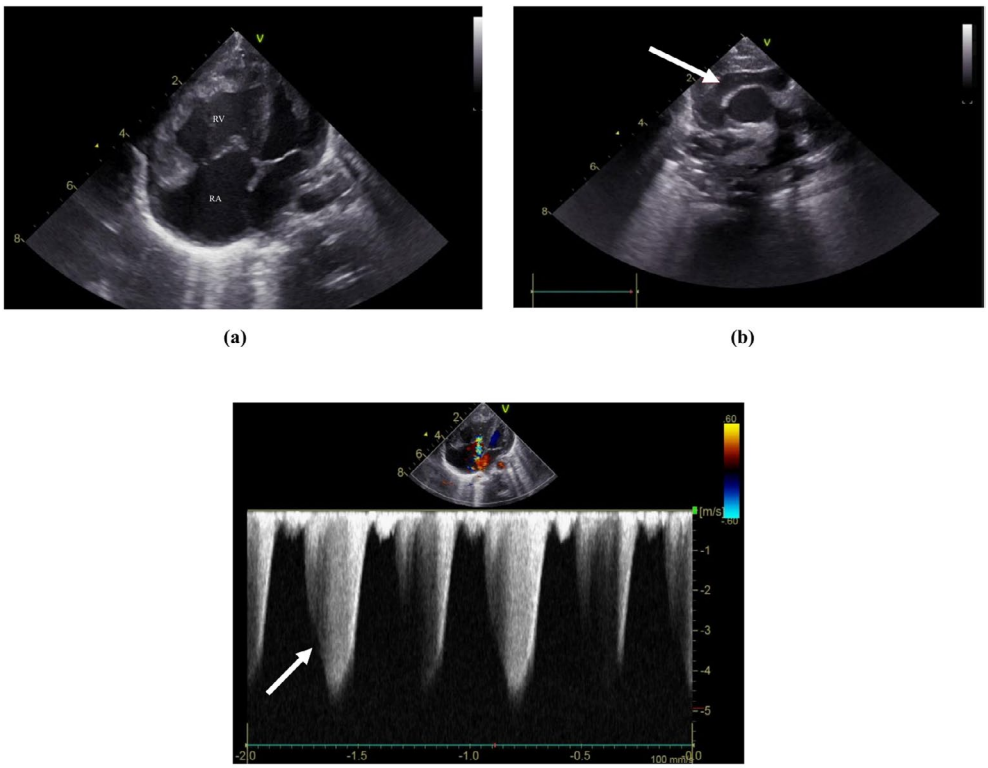
2.1.3 | Outcomes

The infant remained hospitalized for 25 days. A pre-discharge echocardiogram indicated Right Atrial Enlargement (RAE) and Right Ventricular Enlargement (RVE), normal Ejection



(a) (b)

FIGURE 3 | (a) Axial bran sonogram of Case 1 showing a cystic intracranial echo-free area (dilated vein of Galen) and (b) Doppler assessment revealing prominent turbulent blood flow with a low resistance waveform.



(a) (b)

(c)

FIGURE 4 | Echocardiography examination of Case 1, representative of (a) right atrial enlargement and right ventricular enlargement, (b) dilated superior vena cava (white arrow), and (c) tricuspid regurgitation in the Doppler view (white arrow). RA = right atrium; RV = right ventricle.

Fraction (EF), moderate TR, mild pulmonary hypertension, and closure of PDA (Figure 4). These findings indicated a partial resolution of the CHF symptoms and clinical stabilization. Consequently, the patient was deemed suitable for the planned embolization procedure. However, the parents declined consent for the procedure, leading to discharge with intensive medical therapy, including diuretics, and a structured follow-up program with plans for future endovascular surgery to address the vascular malformation. Regrettably, post-discharge, the parents failed to adhere to the prescribed medical regimen and follow-up plan. This noncompliance ultimately led to the patient's demise a few months later, prior to undergoing the embolization procedure.

2.2 | Case 2

2.2.1 | Case History/Examination

This case involved the admission of a 3600 g, full-term, female neonate to the NICU. Born to a 25-year-old mother (G_1, 40 weeks of gestation) with an uneventful pregnancy, the fetal diagnosis occurred relatively late in gestational age, at 32 weeks. Subsequently, the neonate's diagnosis of VGAM was established through echocardiography and brain sonography.

Upon admission, the newborn exhibited mild tachypnea (47 breaths per minute). Her systemic blood pressure was measured at

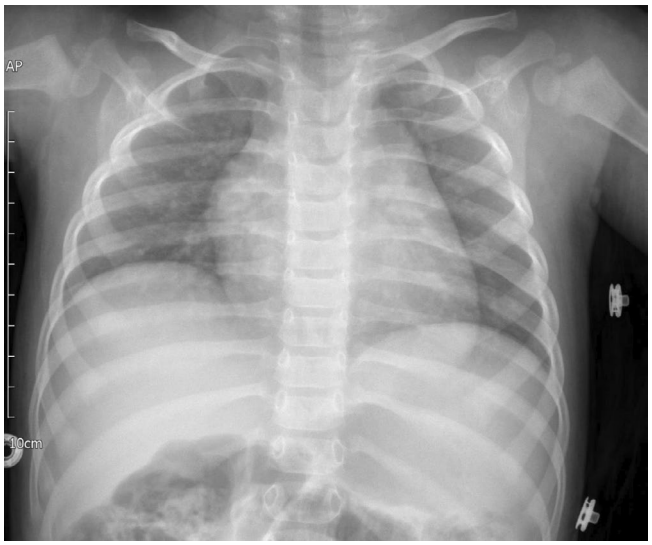


FIGURE 5 | Anteroposterior chest x-ray of Case 2, suggestive of mild cardiomegaly.

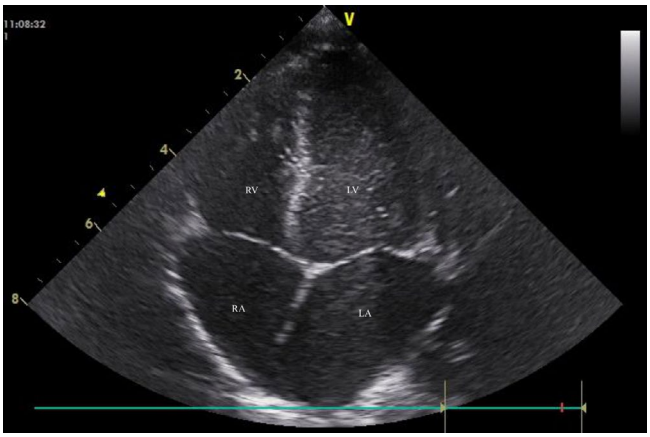


FIGURE 6 | Normal echocardiographic view of Case 2 in her latest examination. LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

70/40 mmHg, with a normal pulse pressure. She displayed a heart rate of 140 beats per minute and an oxygen saturation level of 94%.

2.2.2 | Management and Clinical Course

The initial echocardiography, conducted after 24 h, disclosed mild RAE/RVE, mild TR, mild pulmonary hypertension without reversal flow in the descending aorta, and a Patent Foramen Ovale (PFO) with a right-to-left shunt. Chest x-ray findings indicated mild cardiomegaly (Figure 5).

Furthermore, the first brain sonography identified a cystic region with turbulent flow, located posteriorly and in the midline, confirming the presence of VGAM. The patient was discharged after 5 days, receiving a low diuretic dose, and maintaining stable general health. Cumulatively, a Bicêtre evaluation score of 18 was computed, indicative of a favorable prognosis.

2.2.3 | Outcomes

In the subsequent post-discharge follow-up session, the neonate exhibited minor symptoms. Notably, her most recent transthoracic echocardiography at the age of 1 year demonstrated normal cardiac chambers, normal pulmonary artery pressure, mild TR (Figure 6), and an oxygen saturation of 98%. Presently, she is deemed eligible for interventional endovascular treatment.

3 | Discussion

VGAM represents a venous ectasia secondary to an arteriovenous fistula, potentially leading to CHF [9]. Although VGAM is an exceedingly rare congenital disorder, occurring in fewer than 1 in 25,000 births [10], it remains the most common symptomatic cerebrovascular malformation in neonates, accounting for approximately 30% of all pediatric vascular malformations [11]. The development of VGAM occurs between the sixth and eleventh weeks of gestation, arising from arteriovenous connections between primitive choroidal vessels and the median prosencephalic vein of Markowski [2, 12]. VGAM frequently results in high-output heart failure due to increased preload resulting from the intracranial vascular anomaly, leading to significant dilation of the superior vena cava [1, 2].

As the disease progresses, heart failure becomes a typical manifestation, accompanied by dilation of the fetal right-side heart, attributed to the arteriovenous shunt's capacity to divert 80% or more of the cardiac output [1, 2]. In the neonatal period, the predominant presentation is high-output congestive cardiac failure and multiorgan dysfunction [13]. The VGAM can also cause a mass effect leading to progressive neurological impairments [14]. It can also present with intracranial hemorrhage, cerebral ischemic changes, and seizures, or lead to hydrocephalus due to the obstruction of cerebrospinal fluid flow [14, 15].

Neonatal diagnosis of VGAM is made by transfontanelle Doppler ultrasonography, CT scan, angiography, and Magnetic Resonance Imaging (MRI) [15]. Historically, neonates with VGAM and heart failure faced a poor prognosis, with a mortality rate of 100% [16]. However, contemporary medical advancements have introduced endovascular treatment as the preferred approach for such cases [16, 17]. Early presentation of VGAM in the neonatal period is associated with a poor outcome and neonatal mortality rates of 8%–63% and > 90% in the case of the provision of treatment and the lack of treatment, respectively [9]. However, this rate is 10% in children with late presentation [9]. This approach prominently involves the embolization of either feeding arteries or draining veins, leading to a reduction in blood flow and an increased survival rate in infants diagnosed with VGAM [18]. By implementing this strategy, the cessation of excessive blood flow through VGAM contributes to enhanced cardiac function and the prevention of brain injury [18].

When a neonate receives a diagnosis of VGAM, the prognostic outcome is ascertained through the Bicêtre neonatal evaluation score [7]. This scoring system primarily relies on clinical observations, with scores below 8 indicating a poor prognosis. Such patients are often too unstable to undergo embolization

treatment due to the extensive risk of mortality [7]. Scores ranging between 8 and 12 indicate an imperative need for prompt embolization intervention [7]. In cases with scores between 12 and 21, a comparatively stable condition is discerned, permitting the deferment of endovascular treatment until the age of 5 months [7]. The administration of treatment at this juncture is associated with improved tolerance, and the attendant risk of impeding brain maturation remains relatively low [7].

In this investigation, we present two cases diagnosed with VGAM by Bicêtre scores of 7–8 and 18 in the early stages of life, revealing distinctly different clinical trajectories. The neonate exhibiting more severe symptoms succumbed within months of birth, while the latter demonstrated a significantly better clinical course, evidenced by favorable echocardiography findings, and underwent subsequent endovascular embolization interventions. Upon scrutiny of the clinical courses of these two cases, Case 1 appears consistent with a choroidal VGAM subtype, while Case 2 is suggestive of a mural VGAM.

These observations challenge the conventional understanding, derived from prior research, that neonatal diagnosis of VGAM is associated with poor outcomes, whereas symptom onset beyond the neonatal period correlates with more favorable prognoses [17]. Both cases, diagnosed during the neonatal period, displayed markedly different trajectories, underscoring that the age of diagnosis alone may not reliably predict VGAM outcomes. Instead, other factors, such as specific imaging findings—including prenatal detection of cerebral anomalies or cardiac dysfunction—may serve as more accurate predictors of clinical progression and could better inform treatment and management strategies [5].

This study highlights the distinct clinical courses and prognoses of VGAM in early life while acknowledging several limitations. The markedly different outcomes in the two cases underscore the critical role of imaging modalities and the Bicêtre scale in prognosis prediction, independent of symptom detection timing. However, inconsistencies in imaging techniques and diagnostic work-ups reveal a lack of standardized guidelines, necessitating further research to address this gap. Recent studies have also questioned the reliability of the Bicêtre clinical score for newborns [19], emphasizing the need for a more structured and effective decision-making tool to reduce misdiagnosis and mismanagement. Robust neuroradiological evaluation remains essential for accurately assessing the hemodynamic impact of VGAM. Emerging neonatal brain MRI studies have identified potential biomarkers for neonatal outcomes, including the maximal mediolateral diameter and the cross-sectional area at the narrowest point of the straight or falcine sinus [20], as well as the presence of middle cerebral arterial pseudofeeders [21]. These findings underscore the growing utility of MRI in diagnosing and prognosticating VGAM, highlighting the need for further research to establish optimal diagnostic and prognostic criteria.

However, limitations at our center precluded the acquisition of brain MRIs, which provide a more detailed and comprehensive assessment of cerebral vascular formations and significantly aid in determining the optimal management approach. As a result, we relied solely on brain CT scans, potentially introducing bias into our decision-making process. This reliance on CT imaging also restricted the application of newer criteria, such as those proposed by Mortazavi et al. [22], which incorporate neonatal brain MRI features and have been suggested to outperform the conventional Bicêtre clinical score. Future research is required to systematically examine and compare the advantages and limitations of various diagnostic and prognostic criteria for VGAM, with the aim of improving outcomes for affected neonates.

Furthermore, we opted not to perform emergent embolization for Case 1 by following the Bicêtre recommendations. This decision was compounded by the parents' refusal to consent and their noncompliance with the prescribed management plan, ultimately leading to the tragic demise of the infant. However, alternative guidelines suggest that in the presence of severe CHF, immediate endovascular embolization may be a more favorable option [5, 22]. While these cases carry a poor prognosis, the procedure could potentially be life-saving. Our findings indicate that although the Bicêtre criteria may provide valuable guidance for treatment management in cases with better prognostic indicators, their precision may be insufficient for very high-risk cases. This underscores the need for a more nuanced approach in such scenarios. Additionally, effective communication with the parents of high-risk infants is crucial. Clinicians must emphasize the critical nature of the situation and the potential benefits of interventional procedures to ensure timely consent and facilitate life-saving treatments.

Collectively, our findings indicate that, contrary to earlier research emphasizing a strong association between early-presenting VGAM and poor outcomes, the clinical trajectory of such patients can exhibit significant variability. The paramount objective in managing this life-threatening condition is its timely detection—ideally during antenatal ultrasonographic examinations—followed by prompt postnatal diagnostic evaluation and treatment. Achieving these goals necessitates the integration of advanced neuroimaging modalities, the adoption of more refined diagnostic and prognostic criteria, and the involvement of multidisciplinary specialist teams to optimize outcomes.

Author Contributions

Toktam Sheykhian: conceptualization, data curation, investigation, project administration, resources, supervision, validation, writing – review and editing. **Behzad Mohammadpour Ahranjani:** validation, writing – original draft. **Saghi Elmi:** writing – review and editing. **Mohammadamin Parsaei:** investigation, validation, visualization, writing – original draft.

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The authors have nothing to report.

Ethics Statement

We strictly adhered to the principles of the Declaration of Helsinki throughout the whole study process. Also, this study was approved by the Research and Ethics Committee of the Tehran University of Medical Sciences.

Consent

Written and formal consent for data publication was obtained from the parents of both patients.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors have nothing to report.

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