



# A Case of Atypical and Silent Stroke: In an Era of Technological Evolution, Simple Diagnostic Tests and Instruments Remain Valid

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**Keywords:** Newborn; Red reflex test; Stroke; Brain ultrasound; Cerebral magnetic resonance.

**Abbreviations:** ETF: Transfontanellar ultrasound; MRI: Brain Magnetic Resonance; RETCAM: Retinal camera instrument.

## Background

The American Academy of Pediatrics currently recommends red reflex assessment as a component of eye evaluation in the neonatal period and during all subsequent routine health supervision visits [1]. The red reflex in all newborns has become a screening test for the early diagnosis of congenital cataracts in the Emilia Romagna Region since 2018 [2]. The examination appears useful in the early diagnosis of ocular diseases (cataracts, glaucoma, retinoblastoma, retinal abnormalities), but also as the first sign of dysfunction of neurogenic origin and

## Abstract

In this case report we describe how an asymptomatic stroke was diagnosed from the detection of the presence of heterochromia on the red reflex. The newborn was in full health and showed no evident neurological symptoms. On examination of the red reflex, mandatory screening in Emilia Romagna, pallor of the retina associated with anisocoria appeared. The investigations made it possible to diagnose a stroke in an unusual location, involving the temporal lobe and the insula, and a thrombosis of the retinal vein. After one year the newborn had no ocular damage, no altered instrumental examinations, and normal psychomotor development. The diagnosis of stroke in the neonatal population can be complicated by the absence of localization signs, especially if the location is atypical. The red reflex test is a screening test for eye diseases, but it can be very useful for the early recognition of neurological pathologies involving the eye. The screening should be promoted in collaboration between ophthalmologists and pediatricians. In a first-level hospital, good training on all clinic screening and the possibility of performing an ultrasound examination of the brain is essential for good assistance to newborns.

diseases with ocular manifestations [3]. In a first-level hospital, good training and the possibility of performing an ultrasound examination of the brain are essential for good assistance to newborns.

## Material and methods

We perform by holding a direct ophthalmoscope close to the examiner's eye with the ophthalmoscope lens power set at "0". In a darkened room, the ophthalmoscope light is projected onto both eyes of the child from approximately 45 cm away. A red



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reflex should emanate from both eyes to be considered normal, and symmetric. We perform the ETF with a General Electric Voluson ultrasound with a 10 Hz probe.

### Case presentation

C.A., first-born, male, was born from spontaneous delivery at 37 weeks + 4 days, weighing 2740 g, and without malformations. The mother had hypothyroidism of pregnancy under treatment, thrombocytopenia (anti-PLT antibodies negative), and was a smoker of 5-6 cigarettes a day. Maternal tests for HIV, HCV, HBV, CMV, and toxoplasma were negative, the vaginal swab was negative for *Streptococcus Agalactiae*. Labor went smoothly. However, at birth the newborn required ventilation with NeoPuff (FiO<sub>2</sub> 0.21) for 1 minute (Apgar at 1'= 5, 5'= 7, 10'=9) with normalization of all its functions. There were no criteria for Hypoxic-Ischemic Encephalopathy. He was roomed in by his mother. At about 24 hours of life, in a state of apparent well-being and the absence of evident neurological symptoms, the newborn showed an ocular reactive asymmetry: in the right eye a bright red reflex and normal reactivity to light stimuli, instead in the left eye a dull red reflex and a fixed pupil unresponsive to light stimuli. Transfontanellar ultrasound showed a hemorrhagic hyperechoic area of the brain parenchyma involving the right temporal lobe and insula (Figures 1 and 2). Transferred to a second-level hospital, the ophthalmological and RETCAM examination identified signs of thrombosis of the retinal vein. MRI and MRI angiography diagnosed edema of the optic nerve in the left hemisphere and the alteration of the flow of the arterial segment operculum temporal-insular in the right hemisphere and associated venous stasis. The EEG showed no alterations consistent with seizures. There were no coagulation disorders in the newborn.

### Discussion

The case can highlight how screening practices can have a higher value than the purpose for which they are implemented. In our case, there is a link between red reflex screening and the diagnosis of a rare event such as an asymptomatic thrombotic stroke. New-borns have the highest risk ratio: 1 in 4000 live births [4]. There are different ways of characterizing pediatric stroke. One is by age. From the 28<sup>th</sup> week of gestation until the 28<sup>th</sup> day of postnatal life, the stroke is classified as a perinatal stroke [5]. The stroke can also be classified according to whether the underlying cause is ischemic or hemorrhagic [6]. Most newborns have seizures in the first few days of life or symptoms such as encephalopathy, lethargy, hypotonia, apnea, and poor feeding [7]. A small minority of newborns have no overt or subclinical clinical signs, making early diagnosis difficult [8]. Some authors use the term silent stroke when asymptomatic infarcts are only found on neuroimaging or when the diagnosis is made at later ages [9]. The red reflex test is a mandatory newborn screening test in Emilia Romagna in all newborns before discharge from the neonatal nursery and during all subsequent pediatric checks. Various courses were held in the province of Parma involving hospital and territorial assistance pediatrics figures to disseminate the correct execution practice and make screening effective. The primary purpose is the early diagnosis of ocular malformations and congenital cataract. A crucial aspect of our case was the potential missed diagnosis due to atypical and unexpected clinical signs. This can have a major impact on the quality of life of the child and family members. The case described was asymptomatic, in well-being, and there was no suspicion of a neurological disorder among Nursery staff or family members. The only clinical manifestation identified

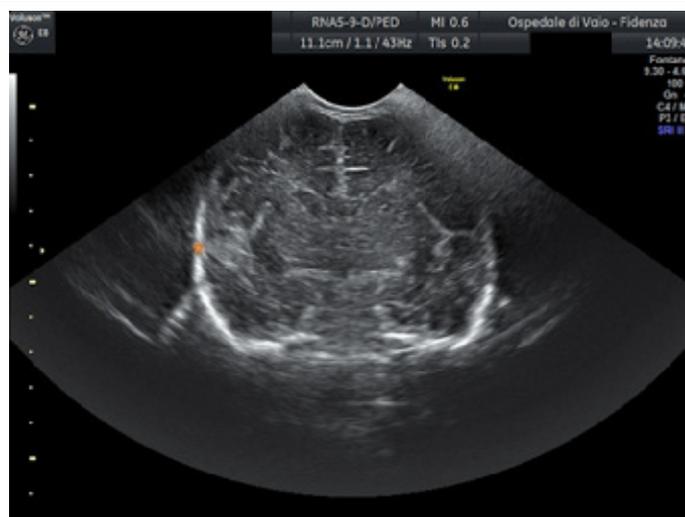


Figure 1



Figure 2

was an asymmetric staining between the eyes on red reflex assessment and an asymmetric response to light stimulus. The location of the stroke is also unusual and it is rare the simultaneous presence of two thrombotic-hemorrhagic lesions in different sites. Indeed, a temporo-insular cortical hemorrhage in the right hemisphere and a thrombosis in the left ophthalmic vein were diagnosed. A possible hypothesis regarding the origin of the stroke may be in the physiologically increased hematocrit of the blood of the newborn and the association with the mother's cigarette smoking. These factors increase blood viscosity and are causes of platelet activation and coagulation. The increased adherence of platelets and macrophages induced by smoking results in the development of a procoagulant and inflammatory environment [10,11].

### Conclusions

The diagnosis of stroke in the neonatal population can be complicated by the absence of localization signs especially if the location is atypical. The red reflex test is a screening test for eye diseases. Still, it can be very useful for the early recognition of neurological pathologies involving the eye. The screening should be promoted, including through courses in collaboration between ophthalmologists and pediatricians. The diagnostic gold standard for ischemic or hemorrhagic stroke is MRI. However, transfontanellar ultrasound remains valid, as an exam that is easily performed, has good sensitivity, can be repeated in the

short term, and has early identification at least as regards hemorrhagic lesions [12,13]. Delays in diagnosis of stroke could be reduced by increasing the use of brain ultrasound among medical staff members in the first-level hospital, where magnetic resonance imaging is not immediately available, and where, even in countries with the highest per capita income, at least a third of births take place.

#### Supplementary material

Figures 1 and 2 show the ultrasound images of the stroke in the temporal hemisphere and insula.

#### Declarations

**Funding:** No funding was received for the paper.

**Ethics approval and consent to participate:** Not applicable to this study. The typology of the study (case report) does not require the local ethics committee's approval. All procedures performed in this study were followed with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Appropriate written informed consent was obtained from the parent of the patient.

**Conflict of interests:** Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/ licensing arrangement, etc.) that might pose a conflict of interest in connection with the submitted article.

**Authors' Contribution:** PL Bacchini and S Monaco collected the data, conceptualized and wrote the manuscript, and contributed to the manuscript; All authors read and approved the final manuscript.

**Consent for publication:** We confirm that written informed consent was obtained from the patient's parent for the publication of this case report. The manuscript follows the Italian Privacy Law.

**Availability of data and materials:** All relevant data are within the paper. All data supporting information are available from the corresponding author, and from Sara Monaco, U.O. of Paediatrics, Vaio Hospital, AUSL of Parma, Italy, mail: smonaco@ausl.pr.it., according to Italian Privacy Law.

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