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"Branch retinal artery occlusion in a sixteen-year-old girl with patent foramen ovale"☆

Barbara Casarini [a], Margherita Burani [b,c], Stefano Meletti [b,c], Guido Bigliardi [d], Livio Picchetto [d], Tommaso Verdina [a,*]

[a] Institute of Ophthalmology, AOU Policlinico di Modena, 41121, Modena, Italy
[b] Neurology Department, AOU Policlinico di Modena, 41124, Modena, Italy
[c] Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, 41121, Modena, Italy
[d] Stroke Unit – Neurology Clinic, Department of Neuroscience, 220340, Ospedale Civile di Baggiovara, AOU di Modena, Italy

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ABSTRACT

Introduction: The etiology and risk factors of the extremely rare retinal artery occlusion (RAO) in pediatric patients are poorly understood. We report a case of transient branch RAO (BRAO) patent foramen ovale (PFO)-related left circulation thromboembolism.

Observations: A healthy sixteen-year-old female presented with painless decreased vision in her left eye. Examinations revealed ischemic edema of a localized sector of the macular area and delayed artero-venous blood transit. Following neurological, cardiological and genetic examinations, a diagnosis and subsequent treatment for PFO were undertaken.

Conclusions and importance: This rare case shows that a PFO should be always considered as a potential etiology of RAO in young patients, thus highlighting the importance of investigating all potential sources of embolisms to prevent further ischemic events.

1. Introduction

Branch retinal artery occlusion (BRAO) is defined as decreased blood flow in a branch of the central retinal artery, which leads to hypoperfusion of retinal tissue causing vision loss.

BRAO is considered an extremely rare condition in pediatric patient populations[1] and a patent foramen ovale (PFO) should be considered among the potential causes of BRAO, especially in young patients.[2] PFO is a congenital defect in the septum separating the two atrial chambers, which usually closes at birth, although it can remain patent in approximately 27 % of the general population.[2] Recent evidence suggests that PFO may play a role in cryptogenic stroke.[3]

We report the case of a 16-year old female with a transient BRAO PFO-related thromboembolism, treated with PFO transcatheter closure and prescribed antiaggregant therapy for 6 months.

2. Case description

A 16-year-old caucasian girl presented to the Eye Clinic of the University Hospital of Modena (Italy) with a sudden central scotoma and painless decreased vision in her left eye. The patient had no medical history of infectious diseases, trauma, malignancies or other systemic complaints and did not report any scotoma-associated symptoms (e.g. floaters, flashes). Best corrected visual acuity (BCVA) revealed 20/20 in her right eye and 20/32 in her left eye.

Goldmann applanation tonometry measured the intraocular pressure of 14 mmHg in both eyes. There was no evidence of relative afferent pupil defect (RAPD) in either eye: pupils were round and reactive. Biomicroscopy of the anterior segment was unremarkable in both eyes. Dilated fundus examination in the right eye was within normal limits and in the left eye revealed an ischemic edema in the superior part of the posterior pole with normal vessels and no evidence of embolism. Standard automated perimetry with Humphrey field analyzer (HFA II 740, Carl Zeiss Meditec, Jena, Germany) and program test 30-2 showed a

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* Corresponding author. Institute of Ophthalmology, AOU Policlinico di Modena, via del Pozzo 71, 41121, Modena, Italy.
E-mail addresses: tommaso.verdina@gmail.com, verdina.tommaso@aou.mo.it (T. Verdina).

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normal visual field in the right eye and a visual field defect in the inferior macular area corresponding to the affected area in the left eye. Fundus fluorescein angiography (FA) (Spectralis, Heidelberg Engineering, Heidelberg) showed a delayed artero-venous transit time in the left eye throughout the examination [Fig. 1] and optical coherence tomography (OCT) (Canon OCT HS100, Canon New Zealand Ltd.) showed retinal thickening associated with hyper reflectivity of the inner retina in the left eye [Fig. 2]. Buried drusen of the optic nerve were excluded by ultrasonography examination in both eyes.

The patient was then admitted to the neurology clinic for stroke risk assessment. Her Body Mass Index (BMI) was 22.86, within the healthy weight range (18.5–24.9). Full blood investigations (complete blood count with erythrocyte sedimentation rate, platelet count), protein C and S, activated partial thromboplastin time, serum homocysteine and serum autoimmunity markers were examined and were within normal ranges. Her lipid panel was within normal limits: total cholesterol 128 (normal range <200 mg/dL), LDL-cholesterol 70 mg/dL (optimal range <200 mg/dL) and triglycerides 46 mg/dL (normal range <150 mg/dL). Screening for congenital metabolic diseases and infectious diseases (Venereal Disease Research Laboratory, Quantiferon, antibodies for viral retinitis) was negative. Prothrombin time was slightly above range (1.23, range 0.80–1.20). Genetic examinations reported heterozygosity for factor V Leiden mutation (R506Q), the most common inherited thrombophilia in the unselected white population (prevalence 1 %–7 %), and for thermolabile methylene tetrahydrofolate reductase mutation (MTHFR C677T).[4]

No abnormalities were observed with cerebral magnetic resonance imaging (MRI).

Positivity for a moderate right-to-left shunt was reported with a transcranial color-coded duplex, raising the suspicion of paradoxical embolization. Echo-doppler evaluations of the supra-aortic and lower limb confirmed no stenosis or peripheral embolic thrombosis. Transthoracic echocardiography (TTE) was unremarkable.[6]

Subsequent transesophageal echocardiography (TEE), the gold standard diagnostic tool to identify PFO,[5] revealed a left -to-right shunt at rest through a tunneled defect 13 mm long and 2 mm wide [Fig. 3] and a bubble study confirmed the presence of PFO.

The patient was treated immediately with aspirin 100 mg daily and after a month a PFO transcatheter closure with a traditional Amplatzer Multifenestrated Septal Occluder (Abbott Laboratories, Chicago, IL, USA) was successfully performed as previously described.[7–10] Aspirin 100 mg daily and clopidogrel 75 mg daily were prescribed for 6 months.[11] At 6 months follow up visit visual acuity improved to 20/25 in her left eye and fundus examination showed a reduction of the ischemic edema of the posterior pole with normal vessels.

3. Discussion

The association of retinal artery occlusion (RAO) in individuals with PFO has already been reported in several case reports, although misunderstood. The mechanisms which have been proposed are emboli formation within the atrial septum, arrythmias and emboli originating from the venous system which end up occluding branches of the ophthalmic artery.[12] RAO is an extremely rare retinal condition in pediatric population (1:50.000 in patients under the age of 30). Risk factors that should be considered in a child include mitral valve prolapse, subacute bacterial endocarditis and rheumatic heart disease, atrial mixoma[13] and hyperhomocysteinemia.[14] Children can also develop a hypercoagulable state secondary to autoimmune diseases, such as Susac Syndrome, Antiphospholipid Syndrome and Behcet disease.[14] Less commonly, BRAO has been associated to infections, traumas[15] and neoplastic disorders.[16]

In our case, heterozygosity for both factor V Leiden and MTHFR mutations were discovered along with PFO, without any sign of acute venous thrombosis. Heterozygosity for both mutations cannot be held alone to be the cause of her BRAO, as well explained in a previous review that listed all the other risk factors increasing the risk of venous thromboembolism if associated with factor V Leiden heterozygosis, such as PG20210G > A double heterozygosity, hyperhomocysteinemia, obesity, oral contraceptives, hormone replacement therapy, air travel, minor injury and malignancy.[17] Nevertheless, our patient presented with a PFO, which is a common anomaly found in about 25–30 % of adults during autopsies.[3] Some studies indicate a higher occurrence of PFO (40 %) in adult patients over 55 years old who have experienced embolic strokes, compared to a 10 % occurrence in control subjects.[3] This correlation between PFO and strokes is consistently supported, particularly in individuals under 55 years old.[18] PFO closure has demonstrated a low complication rate (<1 %) and was initially reported to reduce the recurrence of cryptogenic strokes in PFO patients.[19]

In the presented case, the presence of a PFO was discovered through an accurate diagnostic work-up carried out after an ocular thromboembolic event. To reduce the risk of stroke and potential loss of vision in both eyes, the PFO was then closed through a surgical procedure.

In conclusion, this case underscores the significance of conducting

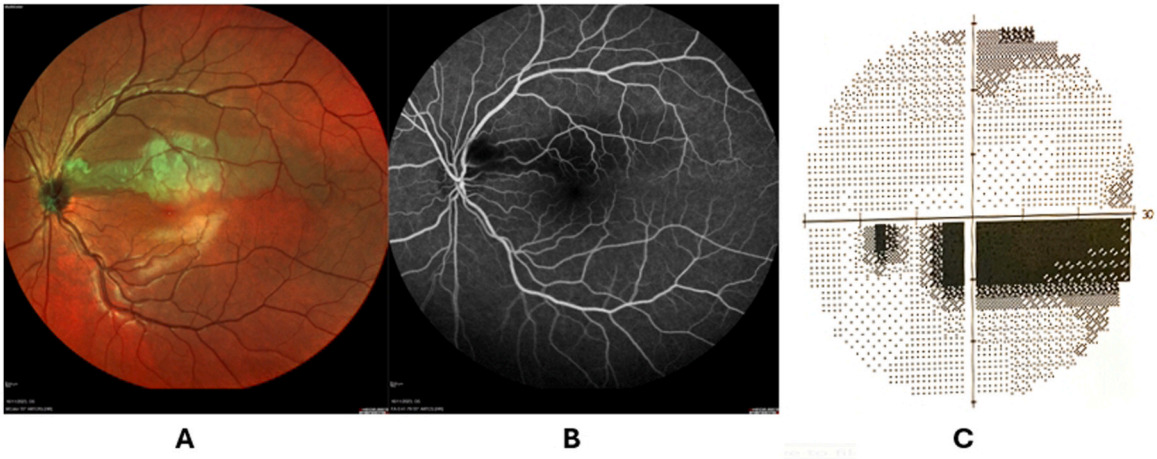

Fig. 1. A 16-year-old caucasian girl presented to Modena Hospital Eye Clinic with a sudden central scotoma and painless decreased vision in her left eye. Fundus colour photograph of the macula was performed (A) showing ischemic edema in the superior part of the posterior pole of the left eye. Fundus fluorescein angiography (B) (taken at 50 seconds from fluorescein intravenously injection) showed a delayed arterovenous blood transit in the same area with a darker choroidal signal, consistent with branch retinal artery occlusion. Standard automated perimetry (C) showed a central inferior scotoma in the left eye. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

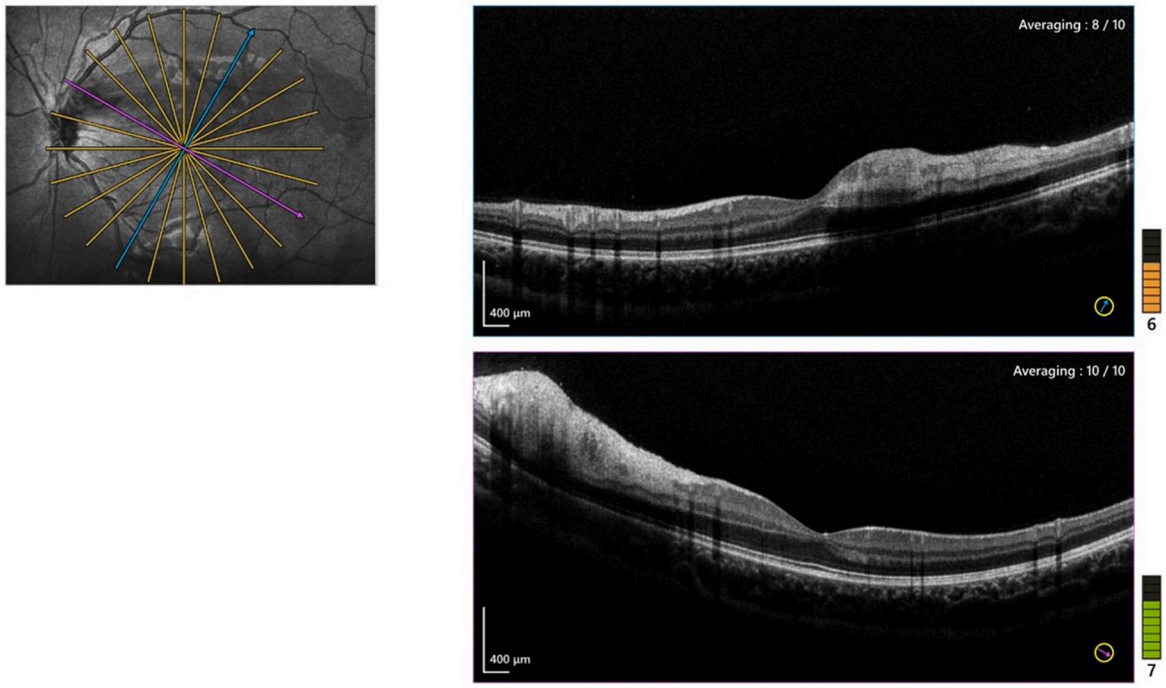

Fig. 2. A 16-year-old caucasian girl with branch retinal artery occlusion in the left eye. Optical Coherence Tomography scan of the macular area of her left eye showing retinal thickening associated with hyper-reflectivity of the inner retina with shadowing of photoreceptor and retinal pigment epithelial layer.

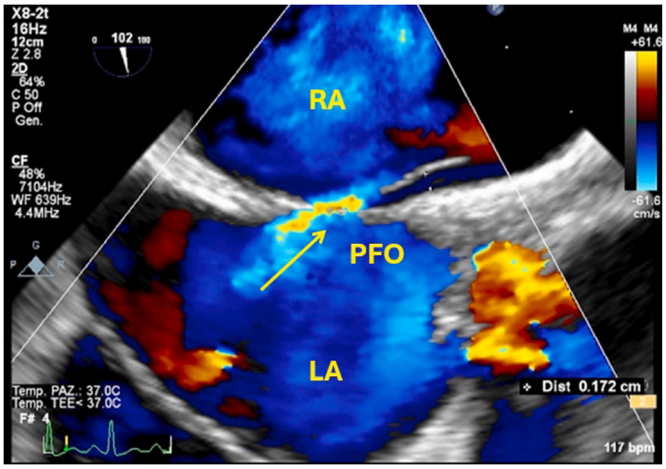

Fig. 3. A transesophageal echocardiogram of a 16 year old girl with a branch retinal artery occlusion in the left eye shows blood flow (arrow) through a patent foramen ovale (PFO) with a shunt from left atrium (LA) to right atrium (RA).

thorough multidisciplinary investigations into all potential sources of embolisms in cases of RAO, especially in young individuals, to identify treatment options aimed at reducing the risk of further embolic events.

CRediT authorship contribution statement

Barbara Casarini: Writing – original draft, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Margherita Burani:** Writing – original draft, Visualization, Data curation. **Stefano Meletti:** Writing – review & editing, Visualization, Validation, Supervision. **Guido Bigliardi:** Writing – original draft, Visualization. **Livio Picchetto:** Writing – original draft, Visualization, Supervision. **Tommaso Verdina:** Writing – review & editing, Validation, Supervision, Conceptualization.

Patient consent

Written consent to publish this case report has been obtained from the patient. This report does not contain any personal identifying information.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Data availability statement

All data are available on a reasonable request to the corresponding author.

Statement of ethics

The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The patient has given a written informed consent to publish the case (including publication of images).

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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