ABSTRACT

Patent foramen ovale (PFO) and pulmonary arteriovenous fistula (PAVF) have been both proposed as a mechanism for cerebral infarction. However, there are only a few reports on how to distinguish the role of the two factors in cerebral infarction.

CASE REPORT

A 52-year-old female patient suffered from recurrent cerebral infarction three times. Five years ago, she had sudden syncope with unknown cause, with the loss of consciousness, the disorder of speech, and an inability for physical activity. Brain magnetic resonance imaging (MRI) showed hemorrhagic cerebral infarction in the junctional zone of the left occipital lobe, but had no sequelae after symptomatic treatment. She had left hemianopsia 3 years ago, which was verified by brain MRI indicating hemorrhagic cerebral infarction in the right occipital lobe. She then received symptomatic treatment with no occurrence of sequelae. Additional sudden syncope occurred 3 months ago, with aggravated left hemianopsia, and large-area cerebral infarction at the right side as shown in brain computed tomography (CT). Although receiving symptomatic treatment, she complained of slurred speech and impaired sight, hearing and memory. The patient had a history of stripping for the varicose right great saphenous vein which occurred 10 years ago.

Findings of physical examination were as follows: blood pressure of 120/80 mmHg (1 mmHg = 0.133kPa), clear sound of bilateral breathing, heart rate of 80 beats/min, regular cardiac rhythm, no edema in lower limbs. Findings of neurological examination were as follows: clear consciousness, partial mixed aphasia, the shallow left nasolabial groove, the deviation of tongue, the paresis of right limbs, negative results in the other parts. Findings of other examinations were as follows: normal results in the routine blood test and lipid assay; no atherosclerotic plaque or stenosis found in carotid ultrasound; no artery disease or stenosis found in carotid ultrasound; no artery disease or stenosis found in carotid doppler; no RLS observed in the contrast echocardiography of the left pulmonary artery; and the pulmonary arteriovenous fistula (PAVF) was shown in selective right pulmonary angiography (Figure 1). This suggests a high possibility of recurrent cerebral infarction induced by PAVF. Therefore the procedure...
was suspended for additional evaluation, and afterwards the pulmonary arteriovenous malformation (PAVM) was indicated in the anterior segment of the superior lobe of the right lung through CT pulmonary angiography (CTPA) (Figure 2). For prevention from the recurrence of cerebral infarction in this patient, the percutaneous closure of PAVF was performed by implantation of one 10/12 mm patent ductus arteriosus (PDA) occluder (Figure 3). Furthermore, the findings in selective right pulmonary arteriography included the disappearance of original PAVF, and the non-affected pulmonary artery and its branches; a tiny amount of RLS was indicated in the contrast echocardiography of the right pulmonary artery, after which the occluder was released. Then aspirin 100 mg/d and clopidogrel 75 mg/d were administrated orally after the procedure for 6 months. In the follow-up for 2 years, the patient did not complained of any discomfort.

**DISCUSSION**

The PAVF refers to direct connection of one or more pulmonary arteries with pulmonary veins, forming a fistula or tumor-like lesion and bypassing blood capillaries, and in rare cases direct connection of systemic arteries with pulmonary arteries and/or pulmonary veins with the left atrium. As an uncommon kind of vascular malformation, the disease is congenital in most cases with the incidence of 2-3 per 100,000. With varied clinical symptoms, the disease is identified as single, multiple, or diffuse lung placeholders, and hypoxia caused by the shunt; 47-80% of PAVF patients have hereditary hemorrhagic telangiectasia (HHT), showing the expanding and bleeding capillaries in the skin surface and mucosa and vascular malformations in the lung, brain, and liver. Multiple complications in the central nervous system are common and probably initially manifested in PAVF, including brain abscess, transient ischemic attack (TIA), migraine, and cerebral infarction with the incidence of 10-19% [Cottin 2007].

Paradoxical embolism refers to the embolism caused by a variety of emboli entering from the low-pressure venous system or the right heart into the systemic circulation through intracardiac or abnormal arteriovenous communicating branches, eventually detained in the arterial system of the brain or other organ, provided that the RLS and paradoxical emboli exist. In this patient, paradoxical embolism was mainly responsible for her cerebral infarction, where the shunt pathway for paradoxical embolism was created by blood flowing from pulmonary arteries directly to pulmonary veins without capillary filtration. The thrombosis in the lower limbs or pelvic vein, and even the non-detected thrombosis in the hemorrhoidal vein may be the main source of the emboli. This patient probably had the emboli from the smaller veins of the lower limbs, due to her history of the varicose great saphenous. Unfortunately, no direct evidence for this presumption was obtained in clinical examinations, possibly because of limited testing methods or the dropped emboli. As reported in previous rare cases, the embolism might be caused by local blood stasis in PAVF as well as the formed and dropped primary thrombi [Cohen 2006]; the polycythemia secondary to chronic hypoxia may also facilitate the thrombosis [Cottin 2007].

Currently, PFO is widely recognized as an intracardial shunt pathway. But the extracardial pathway in PAVF, rarely reported, has not been clearly known. Based on positive results in both cTTE and cTCD, PFO was determined as the cause for recurrent cerebral infarction of this patient, which was verified by TEE. From this point, the reasons for missed diagnosis and preventive measures are summarized as following: 1) The characteristics of embolism shown in brain imaging should be primarily investigated, in combination with the patient’s medical history, family history, and physical

(continued)
supposed that the shunt through pulmonary circulation in
lism, but no exclusion of PAVF. Though theoretically, it is
large amount of shunt and clinically suggests a risk of embo
in resting state indicates the exclusion of PAVF that causes a
after VM, PAVF is unlikely developed; a tiny amount of shunt
in resting state and a larger increased amount of shunt exists
pulmonary hypertension. If no shunt or a minor shunt occurs
in large-sized PFO in case of right atrial enlargement and
after VM; the substantial, continuous shunt may be observed
size in the resting state, and a larger amount of shunt occured
amount of shunt or no shunt was found in PFO with a small
pressure gradient, and RLS occurs only when the pressure in
pathway in PFO mainly depends on the size of PFO and the
cause for RLS. RLS is indicated by positive results in cTCD,
including intracardial and extracardial pathways. Intracardial
pathway is mostly common in PFO, also found in atrial septal
defect (ASD); extracardial pathway occurs in intrapulmonary
shunt (e.g., PAVF) and rarely in other channels (e.g., azygos
vein to pulmonary vein fistula [Huang 2010]). For this patient,
the four findings were observed in cTCD and cTTE: continu-
ous RLS (even in resting state), early RLS (upon injection),
a large amount of shunt (curtain microembolic signals), and a
minor effect of VM on RLS. The identification between PFO
and PAVF could not be achieved according to a single one of
the findings, which was nevertheless suggested by compre-
hensive analysis of all the findings. This is because the shunt
pathway in PFO mainly depends on the size of PFO and the
pressure gradient, and RLS occurs only when the pressure in
the right atrium is higher than that in the left atrium. A tiny
amount of shunt or no shunt was found in PFO with a small
size in the resting state, and a larger amount of shunt occurred
after VM; the substantial, continuous shunt may be observed
in the large-sized PFO in case of right atrial enlargement and
pulmonary hypertension. If no shunt or a minor shunt occurs
in resting state and a larger increased amount of shunt exists
after VM, PAVF is unlikely developed; a tiny amount of shunt
in resting state indicates the exclusion of PAVF that causes a
large amount of shunt and clinically suggests a risk of embo-
lism, but no exclusion of PAVF. Though theoretically, it is
supposed that the shunt through pulmonary circulation in
PAVF occurs later than that in PFO. The shunt was observed
within 10 seconds in this patient; also as reported in some
literature the shunt in PFO could occur up to 40 seconds
[Jauss 2000]. Therefore, PFO and PAVF cannot be reliably
identified merely based on the occurrence time of shunt.

This patient had no symptoms before and after the onset
of stroke, which suggests that cerebral infarction was the early
clinical manifestation in PAVF. From this point, PAVF may
occur in patients with cryptogenic stroke. CTPA, a highly
sensitive diagnostic method for PAVF, has obvious advantages
over pulmonary arteriography in the diagnosis of PAVF and
the visualization of anatomy, which is expected in substitu-
tion for arteriography. Considering the patients have a sig-
nificantly increased risk of embolism, with the feeding artery
of a diameter over 3 mm [Sun 2012], active treatments should
be given for them upon diagnosis of PAVF, including surgical
therapy taken as the primary treatment option for PAVF.

Conventional treatment for PAVF by surgical resection
of the affected lobe of lung has some disadvantages, includ-
ing large wounds, more complications, slower recovery, and
partially lost pulmonary functions; surgical procedures are
contraindicated in those with multiple PAVF. Transcath-
eter interventional closure of PAVF, an alternative for sur-
gical procedure, is preferred in the treatment of PAVF with
multiple advantages over surgical approach including simple
operation, small wounds, and safe and effective treatment
[Joseph 2013]. As reported in the literature, the PAVF
occluder is mostly composed of easy-to-shift spring coils
[Abushaban 2004], which probably causes systemic embolism
by transportation, residual shunt, and a high recanalization
rate [Mager 2004]. The occluder device made in China was
chosen for this patient with PAVF through the access vessel
with a larger diameter (5 mm) because a number of coils are
costly if the device is purchased overseas. Similar to the
Amplatzer Plug, the made-in-China PDA occluder device has
some desirable features, including easy-to-use and one-step
operation for complete closure; this recyclable and relocat-
able device has been successfully applied in interventional
treatments of PAVF in patients with the large-sized feeding
artery. The occluder device should be placed on the distal sec-
tion of the feeding artery, with a diameter 2-4 mm larger than
the artery, for prevention from its falling into the cystic neo-
plasm and the closure of normal proximal pulmonary arter-
ies, thus contributing to a far lower incidence of the occluder
shifting and falling-out and a lower possibility of postopera-
tive recanalization compared with the device containing coils.

In conclusion, transcatheter closure of PAVF is a good
interventional treatment ensuring small wounds, high safety,
and exact clinical effects, provided that the indications are
strictly followed. The spring coils could be used for PAVF
closure in the access vessel with a diameter smaller than
5 mm, and Amplatzer Plug or PDA occluder is the preferred
choice for the access vessel with a diameter larger than 5 mm.

Unfortunately, no direct evidence of thrombi in the over-
riding pulmonary arteries and veins was found in this patient,
which only presumptively suggests her recurrent cerebral
infarction induced by paradoxical embolism. Although this
patient had good recovery in the 2-year follow up, the safety
and effectiveness of the closure procedure remains to be determined in the long-term follow up. Using this method of clinical diagnosis and treatment, clinicians have profound insights in the recognition of paradoxical embolism, knowing that PAVF-paradoxical embolism can induce cryptogenic stroke, in addition to the correlation of the embolism with intracardiac abnormal channels. This provides a new basis for the screening of etiological factors in the patient population with cryptogenic stroke.

REFERENCES


