Abnormal brain perfusion demonstrated by Tc-99m MAA total-body scan in two children with complex congenital heart disease

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This paper describes abnormal brain perfusion unexpectedly demonstrated by Tc-99m MAA total-body imaging in two children with intracardiac right-to-left shunt (RLS) associated with complex congenital heart disease. One child was a 12-year-old girl with asplenia cardiac syndrome and multiple cerebral infarctions caused by thromboembolism in the internal carotid artery, and the other child was a 6-month-old boy who developed focal cerebral infarction following shunt operation. In both children, the total-body imaging depicted the brain due to RLS, where radioactivity decreased unilaterally in the cerebral hemisphere. In the first patient, radioactivity also decreased in the contralateral cerebellum, suggesting the crossed cerebellar diaschisis phenomenon. These abnormalities in brain perfusion were confirmed by Tc-99m HMPAO brain SPECT. Careful review of the distribution of the radiotracer in the depicted brain on Tc-99m MAA total-body imaging may provide important information regarding brain perfusion in some patients with a high risk of stroke complication associated with RLS.

Key words: Tc-99m MAA perfusion scan, congenital heart disease, crossed cerebellar diaschisis, right-to-left shunt

INTRODUCTION

PARADOXICAL EMBOLISM CAUSING STROKE is a serious complication in patients with intracardiac right-to-left shunt (RLS).[1-3] Lung and total-body imaging with Technetium-99m-macroaggregated albumin (Tc-99m MAA) has been used to elucidate pulmonary perfusion and/or systemic circulation, and to estimate the magnitude of intracardiac RLS in cyanotic children with complex congenital heart disease.[1-10] In the presence of RLS, MAA particles reach the systemic circulation to lodge in the capillary beds of the end extrapulmonary organs,[1,4-6,8,10] and distribution of these radioparticles therefore supposedly reflects normal or abnormal perfusion in the depicted organs. In this paper, we described unusual or unexpected abnormalities in cerebral perfusion demonstrated by Tc-99m MAA total-body scanning in two children with complex con-

genital heart disease and cerebral infarction associated with intracardiac RLS.

CASE REPORTS

Case 1:

A 12-yr-old girl weighing 28 kg with asplenia cardiac syndrome (asplenia with abdominal heterotaxy, dextrocardia, double outlet right ventricle with pulmonary arterial atresia, common atrioventricular valve, right aortic arch, and pulmonary perfusion supply via the collaterals of the thoracic aorta) presented with sudden onset of right hemiparesis, left facial nerve paralysis, and aphasia.[11-13] Previous cardiac catheterization soon after birth confirmed that these complex cardiac anomalies were contraindicated for surgical correction. She also had a history of brain abscess in the left cerebrum at the age of 3 years. Laboratory data showed polycythemia (hemoglobin, 19 g/dl and hematocrit, 70%) and low PaO$_2$ saturation, 60–65%. On the second day of the onset of the symptoms, brain CT showed low density areas of infarctions in the left basal ganglion and in the ipsilateral temporal and
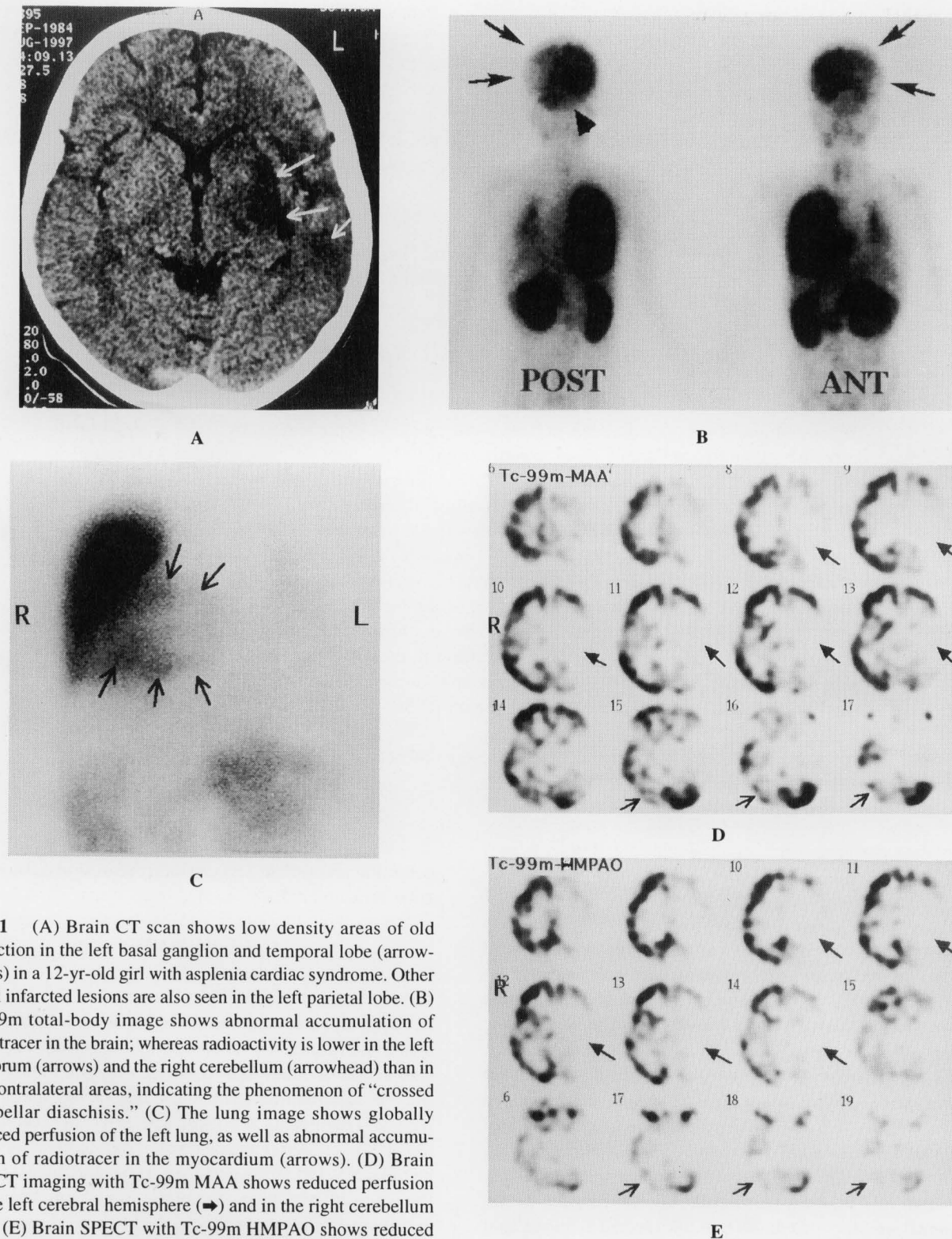
Fig. 1 (A) Brain CT scan shows low density areas of old infarction in the left basal ganglion and temporal lobe (arrowheads) in a 12-yr-old girl with asplenia cardiac syndrome. Other small infarcted lesions are also seen in the left parietal lobe. (B) Tc-99m total-body image shows abnormal accumulation of radiotracer in the brain; whereas radioactivity is lower in the left cerebrum (arrows) and the right cerebellum (arrowhead) than in the contralateral areas, indicating the phenomenon of "crossed cerebellar diaschisis." (C) The lung image shows globally reduced perfusion of the left lung, as well as abnormal accumulation of radiotracer in the myocardium (arrows). (D) Brain SPECT imaging with Tc-99m MAA shows reduced perfusion in the left cerebral hemisphere (➡) and in the right cerebellum (→). (E) Brain SPECT with Tc-99m HMPAO shows reduced perfusion areas in the left cerebral hemisphere (➡) and in the right cerebellum (→), which nearly match those on Tc-99m MAA SPECT.

occipital lobes, and magnetic resonance (MR) angiography disclosed a blockade due to thromboembolism in the left internal carotid artery. She then received administration of heparin, and the thrombolized artery was recanalized one week later. Thereafter she received five months of rehabilitation for hemiparesis and aphasia, resulting in gradual improvement in her symptoms; but the infarction sites demonstrated as low density areas were persistent on the brain CT scan (Fig. 1-A). A Tc-99m MAA perfusion study was requested because of the high risk of pulmonary thromboembolism, and because of the evaluation of the presence of the left superior vena cava, which had not been confirmed by previous catheterization. Anterior and posterior dynamic flow imaging was first acquired with a dual-head detector scinticamera (GCA 901 A/W2, Toshiba Medical, Tokyo, Japan) following bolus injection of 2 MBq/kg body weight of Tc-99m MAA (approximately 2000 MAA particles/MBq, particle size, 10–60 μm > 90%, MAA weight, less than 0.15 mg) into the left antecubital vein while the patient was in the supine position.[5,6,8] Pulmonary perfusion was supplied by the systemic artery, which was identified by radioactivity in the left ventricle and thoracic aorta prior to lung perfusion. Anterior and posterior total-body imaging was subsequently obtained at a speed of 10 cm/minute. This image showed extrapulmonary radioactive accumulation in the brain, kidneys, spleen, liver and myocardium consistent with the presence of RLS (Fig. 1-B). In the brain, radioactivity of Tc-99m MAA was decreased in the left cerebral hemisphere as well as in the contralateral cerebellum, suggesting the phenomenon of "crossed cerebellar diaschisis (CCD)" (Fig. 1-B).[14,15] Spot imaging of the chest obtained by means of a 500,000 count frame showed global reduction in perfusion of the right lung (R = 86%, L = 14%), and showed abnormal accumulation of radiotracer in the myocardium more clearly (Fig. 1-C). Brain SPECT imaging was also performed with a three-head detector (GCA 9300 A/HG, Toshiba Medical) to confirm the abnormal distribution of radiotracer in the brain (Fig. 1-D). Data were acquired in a 128 × 128 matrix, 60 steps (6° each) per detector for 40 seconds per angle. After preprocessing data with the ramp filter set to a cutoff frequency of 0.75/cm and order no. 8, the filtered back projection method was used for image reconstruction. This image showed hypoperfused areas in the left cerebral hemisphere and in the right cerebellum. The RLS ratio estimated on the total-body image by the Gates method[5,6] was 68.7%, and the radioactive ratio of the brain to total body was 7.8%. Chest spiral CT scan did not show any evidence of pulmonary thromboembolism, showing only increased peripheral vascular marking in the right lung. Seven days later, Tc-99m HMPAO brain SPECT was performed by standardized techniques to investigate perfusion abnormalities in the brain observed in the Tc-99m MAA study. The hypoperfused lesions detected by technetium-99m-hexamethyl-propylene amine oxime (Tc-

99m HMPAO) SPECT nearly matched those on Tc-99m MAA (Fig. 1-E). Two months later, Tc-99m MAA lung scan was performed because of occasional chest pain, after injecting the same dose of Tc-99m MAA as used in the previous study into the right antecubital vein, but the status of pulmonary perfusion was unchanged from that in the previous perfusion study. There were no clinically detectable neurological changes following the two perfusion studies.

Case 2:
A cyanotic one-month-old boy weighing 3,200 g underwent a modified right Blalock-Taussig shunt for his complex congenital cardiac anomalies of pulmonary arterial atresia with intact ventricular septum (IVS), patent ductus arteriosus (PDA), atrial septal defect (ASD), tricuspid regurgitation, tricuspid valve stenosis/hypoplastic right ventricle, patent foramen ovale.[11] This procedure connected the left subclavian artery arising from the innominate artery to the ipsilateral pulmonary artery with synthetic graft material.[13] Before surgery, the lungs had been perfused only via PDA. Postoperatively, both severe cyanosis (PaO2 saturation of 19.7 mmHg, PaCO2 saturation of 51.6 mmHg, and low PaO2 saturation of 65%) and polycythemia (hemoglobin of 17 g/d*l* and hematocrit of 70%) persisted. Ten days after the surgery, the infant showed intermittent spasm of the right hand, which occurred one or two times every one or two hours. Brain CT scan was immediately performed, but there were no abnormal opacities seen in the brain. He was followed up conservatively. On the fifth day after the onset of seizure, brain CT scan was again performed and revealed a low density infarcted area localized in the left parietal lobe (Fig. 2-A). After the brain CT scan, a Tc-99m MAA lung perfusion study was performed on the same day, with the same scinticamera and techniques as used in Case 1. This study had been previously scheduled to investigate the presence of pulmonary thromboembolism for his still low PaO2 saturation of 70–80% after surgery and to evaluate the magnitude of RLS. A 20 MBq dose (less than 0.15 mg) of Tc-99m MAA was injected with the patient in the supine position. Compared with preoperative lung perfusion imaging, which had shown nearly even perfusion in both lungs (R = 53%, L = 47%), the lung image at this time showed global reduction in perfusion of the left lung (L = 28%, R = 72%). The total-body image showed radioactive accumulation in extrapulmonary organs including the brain, whereas the radioactivity was focally decreased in the left cereberal hemisphere (Fg. 2-B). MAA particles had distributed nonuniformly in the soft tissues of the extremities. The estimated RLS ratio was 40.8%, and the radioactive ratio of the brain to the whole body was 1.7%.[1,5,6] There were no clinically detectable neurological changes after the injection of MAA. Tc-99m HMPAO SPECT was performed two weeks after the perfusion study, and it revealed hypoperfused areas in the left

A

B

C
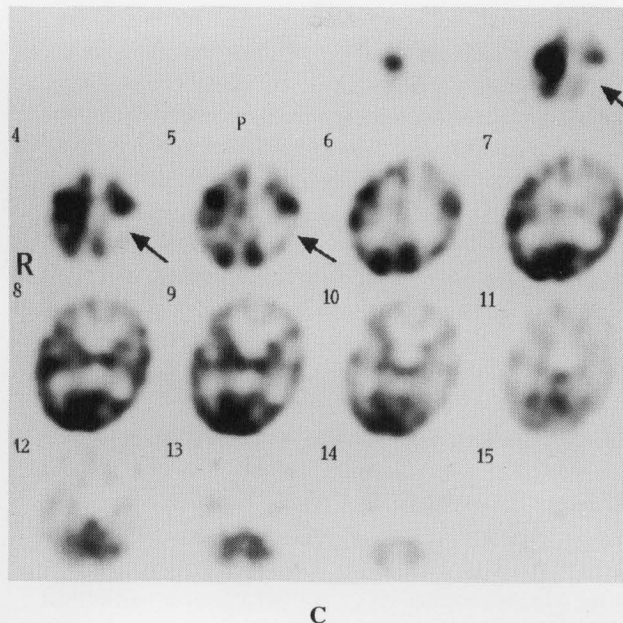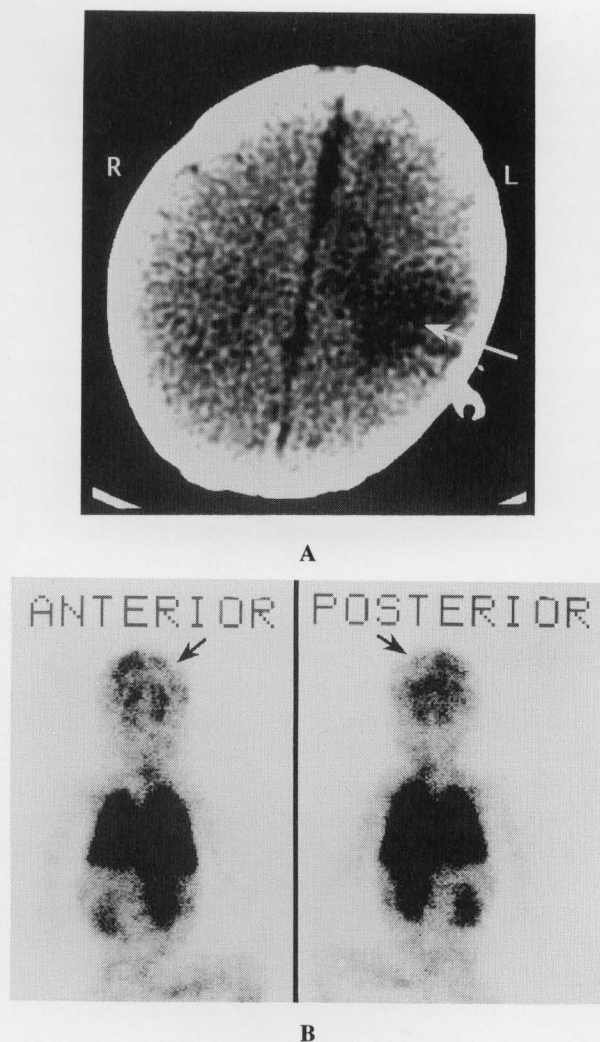
Fig. 2 (A) Brain CT scan in a one-month-old boy with complex congenital heart disease shows a low density area of localized infarction in the left parietal lobe. (B) Tc-99m MAA total-body imaging shows abnormal accumulation of radiotracer in the brain, whereas the radioactivity is focally decreased in the left cerebral hemisphere (arrows). MAA particles distribute nonuniformly in the soft tissues of the extremities, indicating a "quantum mottling" pattern. (C) Brain SPECT with Tc-99m HMPAO reveals hypoperfused areas in the left parietal lobe (arrows).

parietal lobe (Fig. 2-C). Thereafter, brain CT or MR scans were repeated several times and confirmed regression of the infarction, and cardioangiography revealed a stenotic change in the left pulmonary artery at the distal portion of the previous modified-Blalock-Taussig shunt, causing reduced perfusion of the left lung.

DISCUSSION

As demonstrated in the two children reported, the feasibility of Tc-99m MAA perfusion study including dynamic and total-body imaging for elucidating pulmonary perfusion or systemic circulation and for quantifying the magnitude of intracardiac RLS in cyanotic patients with congenital heart disease has been well recognized.[3–6,9,10] In our patients, Tc-99m MAA total-body imaging also provided important information regarding abnormal brain perfusion. A child with cardiac RLS greatly risks the serious complication of stroke due to paradoxical embolism and easy thrombus formation.[1–4] For that reason, the distribution of this radioparticle in the brain must be carefully investigated in the imaging study. Since non-

invasive Tc-99m MAA perfusion scanning is usually repeated for follow-up studies instead of cardiac catheterization in cyanotic patients with congenital heart disease,[3,6] total-body imaging may be useful for detecting the presence of abnormal brain perfusion associated with thrombotic complication.

MAA particles bypassing the lungs via intracardiac RLS enter the systemic circulation and become impacted in the capillary beds of the end organs embolized,[1,5,6,8] so that the distribution of these radioparticles in the brain is supposedly proportional to perfusion in the capillary beds, and can reflect abnormal perfusion when thrombotic complication is present. The accord between the distribution of Tc-99m MAA and Tc-99m HMPAO on SPECT images in our first patient provides evidence in support of this hypothesis. Although microembolization of the brain microvasculature with MAA particles occurs in patients with RLS, cerebral toxicity levels are considered negligible with administration of an adequate dose of this radiotracer.[6,16–20] Previous studies proved that brain scan after intravenous injection of Tc-99m MAA is a safe technique for investigating brain perfusion.[16,17] Direct

carotid or vertebral artery injection of Tc-99m MAA has also been used in humans to obtain brain perfusion scans.[18,19] A continuing process of fragmentation in the brain tissue may move the aggregated particles down the vascular tree and will prevent prolonged blockage of any single vessel.[16] The evidence of collateral circulation within the cerebral microcirculation was demonstrated in a previous animal study, and this may also act as an additional safety factor in preventing areas of ischemia.[17] Rosenthall et al.[18] and Kanafani et al.[19] reported that direct carotid or vertebral arterial injection of Tc-99m-MAA did not induce any untoward neurological sequelae or complications in their patients, and the latter group did not find any evidence of microembolization in postmortem examination of brain tissues in their patients. Gates et al.[5,6] also reported that there was no evidence of cerebral microembolization at autopsy in some of the children who died of cardiac disease and had been previously examined by Tc-99m MAA perfusion scanning. According to the investigations of Kennady et al.[16,17] relating to the threshold of cerebral toxicity, the injected dose of radiolabeled-MAA accumulating in the brain has a safety factor of 6 mg per 100 g brain tissue. Therefore, we consider that Tc-99m MAA perfusion study can be safely performed with an appropriately reduced dose in patients with RLS.[1,5,6,8,20] Furthermore, intravenous injection of Tc-99m MAA or appropriately sized particle matter labeled with radionuclides has been performed in a great number of cyanotic neonates or children by many other investigators without any reported complications.[1-8,20]

The finding in our first patient is, to our knowledge, the first description of the phenomenon of CCD appearing on Tc-99m MAA total-body imaging. It is a well-recognized phenomenon on brain imaging with other perfusion agents including Tc-99m HMPAO in patients with supratentorial infarction or hemorrhage, and it can often persist for a long time after the onset of infarctions, as seen in this patient.[11] The most likely mechanism of CCD is the interruption of the corticopontocerebellar pathway at the supratentorial level, causing deafferentation and transneuronal metabolic depression of the contralateral cerebellar hemisphere.[11,12] Reduced activity of Tc-99m MAA particles in the contralateral cerebellum in our patient indicates that depression of blood flow may occur even in relatively large capillary beds measuring 10–60 μm in diameter, most of which are located proximally to the blood-brain barrier.

The nonuniform tissue distribution of MAA particles in the extrapulmonary soft tissues in the second patient may be consistent with a "quantum mottling" pattern, which has recently been described as a new pictorial indicator of RLS by Dogans et al.[10] The speculative explanation of this phenomenon is related to a small number of MAA particles that embolize the systemic circulation.[1,10] This pattern can also be seen in the brain,[10] and this random or heterogeneous distribution of discrete clumps of radioac-

tivity may disturb the detection of abnormal perfusion on total-body imaging, but it seems to occur rarely.[20] The reported patient is the first case demonstrating this pattern among our studies of over 30 patients with documented RLS. Meins et al.[20] did not find this phenomenon in the observation of 150 children with intracardiac RLS, and they indicated that the radioactivity appeared to be homogeneous in the brain in all patients. And, other investigators could not find this pattern of heterogeneous distribution of radiotracer in their scintigraphies in patients with RLS either.[1,5,6] In our opinion, therefore, quite large hypoperfused brain areas will be noticeable on total-body imaging. Furthermore, SPECT scan will facilitate the recognition of abnormal brain perfusion, as shown in our first patient.

Abnormal radioactivity of Tc-99m MAA in the myocardium in our first patient may be related to a fairly high RLS ratio. As a pictorial indicator of RLS, this finding has rarely been described.[8] Reduced perfusion of the entire left lung in this patient is considered to be due to uneven flow in the right and left pulmonary arteries supplied by the thoracic aorta. In patients with complex congenital cardiac anomalies, a knowledge of anatomy is important in order to avoid false-positive diagnosis of pulmonary embolism.[3,12] The injection sites should be changed for accurate assessment of lung perfusion in some patients, since the lung distribution of a perfusion agent can differ according to the site of injection.[3]

We described unusual or unexpected abnormalities in cerebral perfusion demonstrated by Tc-99m MAA total-body imaging in two patients with congenital heart disease with RLS. In such patients, this imaging is often performed repeatedly to assess lung perfusion, the magnitude of RLS, and therapeutic effects.[1,4,7] Therefore, careful review of the distribution of radiotracer in the depicted brain may also provide critical information regarding brain perfusion in some patients with a high risk of stroke associated with RLS.

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