Abnormal extrapulmonary accumulation of $^{99m}$Tc-MAA during lung perfusion scanning

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We present fourteen patients with an abnormal extrapulmonary accumulation on lung perfusion scintigraphy with $^{99m}$Tc-macroaggregated albumin (MAA), who were examined during the last decade. These included six patients with lung cancer, four with pulmonary arterio-venous fistula, two with congenital heart disease, one with inferior vena cava (IVC) syndrome and one with congenital bronchogenic cyst. All six patients with lung cancer had superior vena cava (SVC) syndrome, and the tumor invaded the thoracic wall.

As causes of abnormal accumulation, fourteen patients had a right-to-left shunt, and one patient with IVC syndrome had a systemic vein-to-portal vein shunt, and one patient with lung cancer associated with superior vena cava (SVC) syndrome had both right-to-left and systemic vein-to-portal vein shunts. In the two patients with systemic vein-to-portal vein shunts, a hot spot was observed at the hepatic hilum, and radionuclide venography revealed remarkably developed collateral pathways to the portal vein. An extrapulmonary accumulation seen on $^{99m}$Tc-MAA lung perfusion scan therefore indicates the existence of unusual hemodynamics with a shunt. We should therefore be careful not to overlook this peculiar finding.

Key words: $^{99m}$Tc-MAA lung scan, right-to-left shunt, superior vena cava syndrome, inferior vena cava syndrome, pulmonary arteriovenous fistula

INTRODUCTION

Following intravenous injection of $^{99m}$Tc-macro-aggregated albumin (MAA) in normal subjects, large particles (10–60 μm) are micro-embolized in the pulmonary arteries and pre-capillaries in accordance with pulmonary arterial blood flow, and only 2–5.7% of these agents transfer to the systemic circulation. Thus, activity in other organs is rarely seen on $^{99m}$Tc-MAA lung perfusion scan.

Nevertheless, an extrapulmonary abnormal accumulation of $^{99m}$Tc-MAA is seen in certain situations, for example: (a) when this agent bypasses the lungs due to a right-to-left cardiac or pulmonary shunt, (b) when it is shunted to the portal vein before reaching the right atrium and ventricle of the heart, and (c) when this agent is degraded to a submicron-particulate size. Therefore, except for situations involving a radiopharmaceutical problem (c), visualization of organs other than the lungs or demonstration of extrapulmonary hot spots suggests the existence of unusual hemodynamics with a shunt.

In this study, we review fourteen patients with extrapulmonary abnormal accumulation on $^{99m}$Tc-MAA lung perfusion scans during the past ten years, and clarify the mechanism of these abnormal accumulations.

SUBJECTS AND METHODS

$^{99m}$Tc-MAA lung scans were performed in a total of 378 patients between April, 1981 and April, 1991. During this period, 14 patients with an extrapulmonary abnormal $^{99m}$Tc-MAA accumulation were encountered. Table 1 summarizes the clinical data on these patients, including 6 patients with lung cancer, 4 with pulmonary arteriovenous fistula, 2 with congenital heart disease, 1 with inferior vena cava (IVC) syndrome, and 1 with congenital bronchogenic cyst. All six patients with lung cancer also had superior vena cava (SVC) syndrome, and were diagnosed by angiography and chest X-ray CT. $^{99m}$Tc-MAA...
Table 1  Diagnoses of 14 cases with extrapulmonary \(^{99m}\text{Tc-MAA}\) uptake sites

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung cancer (SVC syndrome)</td>
<td>6</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>3</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Large cell carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Pulmonary arteriovenous fistula</td>
<td>4</td>
</tr>
<tr>
<td>Left lower field (5 × 6 cm in diameter)</td>
<td></td>
</tr>
<tr>
<td>Right lower field (4 × 5 cm)</td>
<td></td>
</tr>
<tr>
<td>Left lower field (1 × 1 cm)</td>
<td></td>
</tr>
<tr>
<td>Left lower field (5 cm)</td>
<td></td>
</tr>
<tr>
<td>Congenital cardiac disease</td>
<td>2</td>
</tr>
<tr>
<td>Single ventricle</td>
<td></td>
</tr>
<tr>
<td>VSD</td>
<td></td>
</tr>
<tr>
<td>IVC syndrome (thrombophlebitis)</td>
<td>1</td>
</tr>
<tr>
<td>Congenital bronchogenic cyst</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
</tr>
</tbody>
</table>

Figure 1  A. Posteroanterior chest X-ray showing a mass lesion adjacent to the SVC in the right upper lobe (→). B. Radionuclide venography visualized the collateral pathways, the superficial veins of the thorax (→) and IVC (←), immediately after depicting the left subclavian vein. C. \(^{99m}\text{Tc-MAA}\) lung perfusion scan showing a reduced perfusion in the right upper lung field and an intense uptake in the left upper thoracic wall (→). And a “hot spot” in the hepatic hilus was noted (←). D. An intense uptake in both kidneys was seen (→). Compared with the activity of \(^{99m}\text{Tc-MAA}\) in the kidneys, that of the liver was lower (←) (posterior view).

Lung scan was performed 2 min after intravenous injection of 111–185 MBq (3–5 mCi) of \(^{99m}\text{Tc-MAA}\) in the supine position, with a gamma camera (TOSHIBA, GCA 901-A) equipped with a low energy collimator, at an energy window of 140 keV, 20%. Six projecting images (anterior, posterior, right and left lateral, and bilateral posterior oblique images) were obtained. In two patients, radionuclide venography was performed to search for an obstruction site in the veins (Cases 1 and 3).

CASE REPORTS

Case 1:  Lung cancer (adenocarcinoma) with SVC syndrome and tumor invasion to the thoracic wall
A 53-year-old male was hospitalized with dizziness and facial edema. The chest radiograph showed a mass lesion adjacent to the SVC in the right upper lung (Fig. 1-A). Chest X-ray CT showed tumor invasion in the mediasti-
revealing complete obstruction of the left subclavian vein, and the superficial veins of the left thoracic walls were depicted as collateral pathways (Fig. 1-B). The subsequently obtained 99mTc-MAA lung perfusion scan showed a reduced uptake in the right upper lung field, and additionally demonstrated an abnormal uptake in both kidneys and a hot spot in the hilar region of the liver (Fig. 1-C,1-D). Angiography performed via both antecubital veins demonstrated severe stenosis of the SVC and markedly developed collateral veins in the thoracic wall.

**Case 2: Pulmonary arteriovenous fistula**
A 54-year-old male was referred to our hospital for the evaluation of an abnormal shadow in the chest radiograph, which had grown gradually during the last decade. A chest radiograph on admission showed a well-defined oval lesion 5–6 cm in diameter in the left lower lung field (Fig. 2-A). 99mTc-MAA scan showed accumulation in the brain, parotid glands, thyroid gland, spleen and kidneys, indicating the presence of a right-to-left shunt. The urinary bladder activity was probably due to free pertechnetate released from 99mTc-MAA (Fig. 2-B). The degree of right-to-left shunt was measured by Sty’s method by obtaining whole body imaging, revealing a degree of 6.5%. Pulmonary angiography revealed pulmonary arteriovenous fistula (Fig. 2-C). At surgery, a large pulmonary arteriovenous fistula was found in the left lower lobe.

**Case 3: IVC syndrome due to thrombophlebitis**
A 24-year-old male complained of edema and pain in the left leg. To investigate whether pulmonary thromboembolism had occurred, radionuclide venography with 99mTc-MAA via both pedal dorsal veins was carried out before obtaining a 99mTc-MAA lung scan. No segment of the inferior vena cava was visualized and prominent collateral vessels toward the liver were demonstrated (Fig. 3-A). Obstruction of the inferior vena cava and/or bilateral iliac veins might have been present, but it was not directly demonstrated. These collaterals might have been due to the increased pressure gradient between the inferior epigastric vein and portal venous system.

99mTc-MAA lung scan revealed no evidence of pulmonary thromboembolism, and the scan did show an abnormal uptake in the left hepatic lobe and a hot spot in the hepatic hilum (Fig. 3-B).

**DISCUSSION**

On 99mTc-MAA lung perfusion scan, extrapulmonary accumulation of this agent is infrequently encountered. Extrapulmonary accumulation was noted in only 14 of 378 patients (3.7%) studied during the past 10 years at our institution. Radionuclide venography before 99mTc-MAA lung perfusion scan may provide more detailed hemodynamic information related to a shunt. In the present report, we classified the 14 cases with extrapulmonary
innominate, vertebral, intercostal, lumbar and sacral veins to the aygos and internal mammary venous pathways. All these collateral pathways can cause an abnormal extrapulmonary accumulation of $^{99m}$Tc-MAA, because it will become stagnant in such collateral veins, as shown in Case 1.

And as a fifth collateral pathway, in addition to the pathways cited above, Kobayashi et al. reported the route of a systemic vein-to-pulmonary venous shunt (right-to-left shunt) between the venous plexus of the thoracic wall and the pulmonary vein in a patient with lung cancer complicated by SVC syndrome with tumor invasion of the thoracic wall. In that case, abnormal uptake of $^{99m}$Tc-MAA was observed in the brain, thyroid, and kidneys. By conventional venography obtained by injecting contrast material into both antecubital veins, shunt formations between the venous plexus of the right thoracic wall and the right pulmonary vein were verified. The shunt probably developed due to tumor invasion of the thoracic wall. The blood pressure of the venous plexus in the thoracic wall was increased by obstruction of the SVC, and venous blood drained into the pulmonary veins.

All cases of lung cancer in our report had SVC syndrome with tumor invasion of the thoracic wall similar to the case reported by Kobayashi et al. To date, we have carried out $^{99m}$Tc-MAA lung scan for many other patients with lung cancer, but no abnormal extrapulmonary accumulation has been seen in patients without SVC syndrome or tumor invasion of the thoracic wall. The abnormal uptake is therefore considered due to a right-to-left shunt formation as reported by Kobayashi et al. For this reason, we should be careful not to overlook a right-to-left shunt on $^{99m}$Tc-MAA lung scan in patients with SVC syndrome. Moreover, Case 1 showed a hot spot in the hepatic hilum, although our remaining patients except Case 3 (IVC syndrome) did not show any sign of such a hot spot. This hot spot is probably due to a shunt between the systemic vein and portal vein. Previous reports have demonstrated various routes for this shunt. The degree and/or duration of the stenosis in the SVC may contribute to the manifestation of this kind of shunt.

**Pulmonary arteriovenous fistulae**

A pulmonary arteriovenous fistula is a well-known disease showing a right-to-left shunt, and this disease occasionally produce cyanosis, secondary polycythemia and complications such as bacterial endocarditis, cerebral embolism and cerebral abscess.

A right-to-left shunt was detected by the abnormal accumulation of $^{99m}$Tc-MAA in the liver, kidneys, spleen and parotid glands, as shown in Case 2. The urinary bladder activity was probably due to free pertechnetate released from $^{99m}$Tc-MAA.

Activity of the liver was lower than that of the kidneys, because $^{99m}$Tc-MAA in the hepatic artery is diluted by the tracer-free portal vein flow. This finding was also noted in

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**Fig. 3**  
A. Radionuclide angiography using $^{99m}$Tc-MAA revealed extensive collateral formation toward the liver from both thighs (→). Collaterals of the left side were visualized second to those of the right. The inferior vena cava was not identifiable.  
B. $^{99m}$Tc-MAA lung perfusion scan showing an abnormal uptake in the left hepatic lobe (→) and a hot spot in the hepatic hilar region (←).
the right-to-left shunt in Case 1 which involved lung cancer.

Furthermore, \(^{99m}\)Tc-MAA lung scan is useful in quantifying the degree of right-to-left shunt noninvasively. Transcatheter embolization of the pulmonary artery has recently been performed for this condition. Follow-up \(^{99m}\)Tc-MAA lung scan may also be useful in evaluating the hemodynamics after embolization.

**IVC syndrome**

In patients with IVC syndrome, liver visualization on radionuclide venography after injecting \(^{99m}\)Tc-MAA into lower limb veins was reported in the literature. The venous collateral pathways in IVC obstructions were described by Ferris et al. as follows: (a) the central channels, consisting of the ascending lumbar, vertebral venous plexuses and the azygos-hemiazygos venous system, (b) the intermediate channels, composed of the ureters, the gonadal and the renal-azygos venous system, (c) the portal venous system via the inferior-mesenteric vein, and (d) the superficial routes, including the inferior and superficial epigastrics and the circumflex iliac veins. There are usually various degrees of contributions from these pathways.

Such a systemic vein-to-portal vein shunt (d) is considered the cause of the liver visualization. In Case 3, occlusion of the IVC and/or bilateral iliac veins would encourage the development of superficial abdominal collaterals and thus possibly the development of paraumbilical shunting to the liver. A paraumbilical vein, and occasionally a persistent umbilical vein, it is said, join the left main branch of the portal vein. Lin et al. said that the nonuniformity and various patterns of abdominal left-lobe uptake in SVC or IVC syndrome suggested a few possibilities. First, paraumbilically shunted \(^{99m}\)Tc-MAA that entered the left main branch of the portal vein could be subject to a streaming effect within the left main branch. Second, there may be places other than the left main branch where paraumbilically shunted \(^{99m}\)Tc-MAA could enter the left-branch system, and these entry sites could vary from one patient to another.

In Case 3, in addition to this abnormal accumulation of \(^{99m}\)Tc-MAA in the left hepatic lobe, a hot spot in the hilus of the liver was noted. This hot spot may also be related to the blood flow of the umbilical or paraumbilical vein toward the liver as collaterals for the systemic venous return. Thus, abnormal accumulation of \(^{99m}\)Tc-MAA in the liver could identify collateral pathways between the systemic vein and portal venous system.

**Others**

In patients with congenital shunt heart disease, we usually detect right-to-left shunt on \(^{99m}\)Tc-MAA lung scan. Previous investigators demonstrated a good correlation between quantitative assessment of the degree of shunt on \(^{99m}\)Tc-MAA perfusion scan and those obtained by catheterization. The remaining case showing abnormal extrapulmonary uptake of \(^{99m}\)Tc-MAA in this study involved congenital bronchogenic cyst. To the author's knowledge, there are no reports of this manifestation in these disorders. In our case of congenital bronchial cyst, multiple cysts involving the entire right lower lobe were demonstrated, and the pulmonary artery of the lower lobe was poorly developed with a very thin wall at surgery. Shunt formation within the lesion might be related to the poorly developed pulmonary artery.

Recent investigations demonstrated abnormal pulmonary vascular channels, dilated alveolar capillaries and small arteriovenous shunts in the lungs of patients with liver cirrhosis. Several cases showing an extrapulmonary abnormal accumulation on \(^{99m}\)Tc-MAA lung scan were reported. Especially in cirrhotic patients with severe hypoxemia, \(^{99m}\)Tc-MAA lung scan should be performed to detect such a micro-vascular shunt in the lungs, because this shunt is difficult to detect by other imaging methods.

In conclusion, we presented 14 unusual patients with an extrapulmonary abnormal accumulation on \(^{99m}\)Tc-MAA lung perfusion scan, and stressed the existence of abnormal hemodynamics such as right-to-left shunt with collateral pathways. We therefore have to be careful not to overlook this abnormal finding on lung perfusion scan. And radionuclide venography may provide a detailed assessment of abnormal hemodynamics in patients with SVC or IVC syndrome.

**REFERENCES**

