Neurological Consequences of Atrioesophageal Fistula After Radiofrequency Ablation in Atrial Fibrillation

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Background: Radiofrequency ablation for atrial fibrillation (RAF) is an increasingly performed procedure. It is performed during cardiac surgery or percutaneously by catheter. A dangerous complication of RAF is atrioesophageal fistula (AEF), which predominantly manifests neurologically owing to food embolism. Because neurologists may not be familiar with AEF and the prognosis is dependent on a prompt diagnosis, awareness of AEF by the neurologist may play a crucial role.

Objective: To summarize for the neurologist the knowledge about fistula between the left atrium and esophagus occurring after RAF.

Design, Setting, and Patients: Using a MEDLINE search, we collected reports about AEF after RAF in 28 patients.

Main Outcome Measures: From the collected reports, the description of symptoms, diagnostic investigations, therapy, and outcome of the 28 patients were summarized.

Results: In 28 cases, AEF developed 3 to 38 days after RAF. Confusion, grand mal seizures, meningitis, focal cortical signs, and postprandial transient ischemic attacks associated with fever were the leading manifestations in 21 of 28 patients. Blood tests showed leukocytosis, elevated serum C-reactive protein levels, and thrombocytopenia. Blood cultures were frequently positive for bacteria. Lumbar puncture revealed pleocytosis, elevated protein levels, increased lactate levels, and bacteria. Diagnosis was established by thoracic contrast computed tomography. Endoscopy, insertion of nasogastric tubes, and transesophageal echocardiography were detrimental, leading to an increase in fistula size and food or air embolism. Therapy comprised surgery (n=11) or temporary esophageal stenting (n=1). The remaining patients died before attempted surgery or confirmation of the diagnosis. A neurological deficit persisted in 3 of the 9 surviving patients.

Conclusions: In patients with meningitis, stroke, seizures, or impaired consciousness and fever, it should be determined whether they have had a previous RAF. In cases with a history of recent RAF, AEF should be strongly considered, especially if there are also symptoms such as dysphagia or chest pain. After RAF, the patient, his or her family, and his or her treating physicians should be informed about the signs of AEF, which may occur even weeks after RAF.

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Radiofrequency ablation for atrial fibrillation (RAF) is an increasingly performed procedure, applied especially in patients with paroxysmal atrial fibrillation who are classified as refractory to antiarrhythmic drug therapy. Radiofrequency ablation for atrial fibrillation is performed either during cardiac surgery as an additional procedure or as a percutaneous catheter intervention. It is associated with various complications such as pericardial effusion, pericardial tamponade, pulmonary vein stenosis or thrombosis, and left atrial wall hematoma.1

Probably the most dangerous, life-threatening complication of RAF is the development of a fistula between the left atrium and the esophagus. The fistula may initially and predominantly manifest with neurological abnormalities, and neurological abnormalities are the main cause for hospitalization of patients with this complication (Table). Neurologists may not be familiar with the clinical presentation of this rare complication. However, the prognosis of patients with a fistula is highly dependent on prompt and appropriate diagnosis and therapy. Thus, awareness of atrioesophageal fistula (AEF) by the neurologist may play a crucial role in the survival of patients with this life-threatening disease.

The aim of this review is to summarize for the neurologist the knowledge about fistulas occurring between the left atrium and esophagus after RAF.
METHODS
Using a MEDLINE search, we collected reports about fistulas between the left atrium and esophagus. We noted this in general and especially as a complication after RAF. In the search, we found 28 cases of AEF that developed after RAF.

ETIOLOGY OF FISTULA BETWEEN ESOPHAGUS AND LEFT ATRIUM
Depending on the site of the primary lesion, esophagial fistula (EAF) and AEF must be differentiated.

Esophagial fistula may be due to esophageal injuries such as perforation with feeding tubes, esophageal biopsies, esophageal surgery, erosion of an esophageal diverticulum into the left atrium, and carcinoma.14-21 Rheumatic mitral valve disease with an enlarged left atrium and esophageal compression in association with the intake of potassium chloride tablets has been reported as a further cause of EAF.

Atrioesophageal fistula has been described as induced by trauma such as after a gunshot wound of the chest.23 Atrioesophageal fistula after RAF may develop owing to the proximity between the left atrium and esophagus.24 Myocardial injury during RAF may also affect the esophageal wall.25 Whether reflux esophagitis, which

Table. Patients With Atrioesophageal Fistula After Surgical or Interventional Therapy of Atrial Fibrillation

<table>
<thead>
<tr>
<th>Source</th>
<th>Age, y/ Sex</th>
<th>Procedure</th>
<th>Time After Procedure, d</th>
<th>Symptoms and Findings</th>
<th>Cerebral Imaging</th>
<th>Therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preis et al.²</td>
<td>56/M</td>
<td>PRFA</td>
<td>38</td>
<td>Fever, bilateral arm weakness</td>
<td>Multiple foci of restricted diffusion</td>
<td>Surgery</td>
<td>Survived, expressive aphasia</td>
</tr>
<tr>
<td>Cummings et al.⁶</td>
<td>NR=M=4, F=5</td>
<td>PRFA</td>
<td>10-16</td>
<td>Sepsis, embolic strokes (n=8), angina pectoris (n=2), gastrointestinal bleeding (n=3)</td>
<td>Intravascular air (n=2)</td>
<td>NR</td>
<td>Died</td>
</tr>
<tr>
<td>Sommex et al.⁴</td>
<td>58/F</td>
<td>SRFA</td>
<td>22</td>
<td>Fever, numbness of right arm</td>
<td>Ischemic lesions</td>
<td>Surgery</td>
<td>Died on 20th postoperative day</td>
</tr>
<tr>
<td>Schley et al.⁵</td>
<td>37/M</td>
<td>PRFA</td>
<td>25</td>
<td>Fever, grand mal seizure, status epileptic</td>
<td>NR</td>
<td>Surgery attempted</td>
<td>Died during preparation for surgery</td>
</tr>
<tr>
<td>Scavanacca et al.⁶</td>
<td>72/M</td>
<td>PRFA</td>
<td>22</td>
<td>Dysphagia, fever, loss of consciousness after eating, tonic-clonic seizures, hematemesis</td>
<td>NR</td>
<td>Gastroesophageal endoscopy</td>
<td>Died</td>
</tr>
<tr>
<td>Pappone et al.⁷</td>
<td>36/M</td>
<td>PRFA</td>
<td>3</td>
<td>Fever, pleuritic chest pain, convulsions</td>
<td>Bilateral ischemia</td>
<td>Surgery</td>
<td>Survived, left hemiparesis</td>
</tr>
<tr>
<td>Pappone et al.⁷</td>
<td>59/M</td>
<td>PRFA</td>
<td>21</td>
<td>Fever, grand mal seizure</td>
<td>Cerebral emboli</td>
<td>Antibiotics</td>
<td>Died</td>
</tr>
<tr>
<td>Ouchikhe et al.⁸</td>
<td>58/M</td>
<td>PRFA</td>
<td>21</td>
<td>Fever, confusion, meningitis</td>
<td>Bilateral hyperdense lesions (frontal, occipital, parietal, and temporal)</td>
<td>NR</td>
<td>Died</td>
</tr>
<tr>
<td>Doll et al.⁹</td>
<td>42/M</td>
<td>SRFA</td>
<td>10</td>
<td>Fever, postprandial transient ischemic attack Hematemesis</td>
<td>NR</td>
<td>Surgery</td>
<td>Survived</td>
</tr>
<tr>
<td>Doll et al.⁹</td>
<td>62/F</td>
<td>SRFA</td>
<td>6</td>
<td>Fever, neurological symptoms</td>
<td>NR</td>
<td>Endoscopy</td>
<td>Died</td>
</tr>
<tr>
<td>Doll et al.⁹</td>
<td>59/M</td>
<td>SRFA</td>
<td>12</td>
<td>Fever, neurological symptoms</td>
<td>NR</td>
<td>Surgery</td>
<td>Survived</td>
</tr>
<tr>
<td>Doll et al.⁹</td>
<td>36/M</td>
<td>SRFA</td>
<td>11</td>
<td>Chest pain</td>
<td>NR</td>
<td>Surgery</td>
<td>Survived</td>
</tr>
<tr>
<td>Dagres et al.¹⁰</td>
<td>Mean, 51</td>
<td>SRFA (n=4), PRFA (n=1)</td>
<td>8-28</td>
<td>Fever (n=3), chest pain (n=2), hemiparesis (n=3), grand mal seizure (n=1), aphasia (n=1)</td>
<td>NR</td>
<td>Surgery (n=3), attempted surgery (n=2)</td>
<td>Survived (n=3), died (n=2)</td>
</tr>
<tr>
<td>Bunch et al.¹¹</td>
<td>48/M</td>
<td>PRFA</td>
<td>14</td>
<td>Fever, chest pain, dysphagia</td>
<td>NR</td>
<td>Temporary stenting</td>
<td>Survived</td>
</tr>
<tr>
<td>Malanis et al.¹²</td>
<td>59/M</td>
<td>PRFA</td>
<td>35</td>
<td>Fever, altered mental state, multiple petechiae</td>
<td>Negative for ischemic changes</td>
<td>Surgery</td>
<td>Died during surgery</td>
</tr>
<tr>
<td>Borchert et al.¹³</td>
<td>59/M</td>
<td>HIFU</td>
<td>10</td>
<td>Fever, chest pain, ventricular fibrillation, generalized seizures</td>
<td>Multiple ischemic lesions</td>
<td>Surgery</td>
<td>Died on fifth postoperative day</td>
</tr>
</tbody>
</table>

Abbreviations: HIFU, percutaneous high-intensity focused ultrasound ablation; NR, not reported; PRFA, percutaneous radiofrequency ablation; SRFA, surgical radiofrequency ablation.
has been reported to be associated with paroxysmal atrial fibrillation, favors the development of AEF has not yet been investigated to our knowledge.26 To reduce radiofrequency-induced tissue damage, alternative ablation techniques have been developed. However, AEF has also been reported as a complication of ablation using high-intensity focused ultrasound (Table).13

**PATHOLOGIC CONSEQUENCES OF THE FISTULA**

A fistula between the left atrium and esophagus may lead to severe bleeding and food emboli. One might expect hemorrhage to be more common than food emboli because at rest, left atrial pressure exceeds esophageal pressure. The lower viscosity of blood as compared with the viscosity of food would further increase the likelihood of gastrointestinal bleeding.21 However, gastrointestinal bleeding is only rarely reported (Table) and severe bleeding has not been reported in AEF.

There is a high incidence of food emboli in AEF leading to life-threatening and mostly fatal “meat and vegetable” systemic emboli and septicemia.14 Esophageal atrial fistula as a cause of embolic meningocencephalitis was first described in 1970.32 Those patients who present with more insidious symptoms likely possess the anatomical equivalent of a single-way valve, allowing esophageal contents to enter the heart while preventing blood entry into the esophagus. Further cerebral manifestations of AEF and EAF comprise abscesses as well as cerebral air and food embolism.15,17,20

**EPIDEMIOLOGY**

The incidence of AEF after surgical RAF is reported to be 1%.9,10 The incidence of AEF after percutaneous RAF is unknown and has been estimated to be between 0.05% and 0.2%.7,10 It is probably markedly underreported. Among the 28 reported cases listed in the Table, the mortality of patients with EAF was 68%. The mortality was 40% after surgical RAF and 80% after percutaneous RAF, and persisting neurological deficits are reported in 3 of the 9 surviving patients.2,7,10

**NONNEUROLOGICAL MANIFESTATIONS**

The clinical presentation of AEF includes lethargy, general weakness, fever, chest pain, dysphagia, melena, hematemesis, and sepsis (Table). The interval between the ablation procedure and the clinical manifestation of AEF varies from 3 to 38 days.

**NEUROLOGICAL MANIFESTATIONS**

Neurological abnormalities occur frequently in AEF (Table). They comprise confusion, grand mal seizures, meningitis, focal cortical signs, and postprandial transient ischemic attacks. These abnormalities are most frequently associated with fever. They are unspecific and may not lead the neurologist to consider a cardiac cause for the patient’s symptoms, especially if there are no findings such as scars from surgery indicating a recent invasive procedure. In patients who develop neurological signs, delays in the diagnosis probably contribute to the high mortality.10

**LABORATORY FINDINGS**

Blood tests show leukocytosis, elevation of serum C-reactive protein levels, thrombocytopenia, and an elevated erythrocyte sedimentation rate. Blood cultures are frequently positive for bacteria. Lumbar puncture may reveal pleocytosis, elevated protein levels, increased lactate levels, and bacteria.8

**DIAGNOSIS**

Chest radiography or computed tomography of the chest may be diagnostic if air is visualized within the cardiac cavities or in the mediastinum, or if intravenous contrast medium enters the esophagus from the left atrium.5 Furthermore, a contrast esophagogram may show extravasation of water-soluble contrast material in communication with a pulsating chamber.24 Unfortunately, not all of these signs may be present in each patient and different diagnostic investigations have to be carried out in suspected cases. Application of a barium swallow study should be avoided because barium entering the circulation has detrimental consequences. Furthermore, endoscopy, insertion of nasogastric tubes, and transesophageal echocardiography should not be carried out as they may lead to an increase in fistula size as well as possible food or air embolism from inflation of air during the procedure.9,6,7,10

**DIFFERENTIAL DIAGNOSIS**

Endocarditis is frequently suspected in cases with signs of infection and positive blood cultures after an invasive cardiac intervention.2 Indeed, infective endocarditis at the left atrial appendage entrance, most likely induced by endocardial damage during RAF, has been described recently as a further complication of RFA and thus renders the situation even more complicated.20 It seems reasonable to consider endocarditis as a differential diagnosis and to perform transesophageal echocardiography only after AEF has been definitively excluded.

Meningitis is a further differential diagnosis. In fact, meningitis and pathologic findings of cerebrospinal fluid have been reported as a manifestation of AEF.8 These findings suggest that in patients with meningitis, the neurologist must always ask for a history of RFA. If there is a history of RFA, AEF should be strongly considered.

Embolic stroke due to recurrent atrial fibrillation may frequently be a differential diagnosis because atrial fibrillation after RAF may recur, and a fistula between the esophagus and left atrium may induce atrial fibrillation.3,19 Patients with AEF frequently present with transient ischemic attacks or stroke. Atroesophageal fistula should be strongly considered if the events are associated with fever or occur after meals.

Epileptic seizures and confusion are frequent manifestations of AEF (Table) but may also occur simply because of fever due to other causes. Thus, in patients with seizures and confusion associated with fever, it should always be determined whether they have a history of RFA.
TREATMENT

Therapy of AEF comprises surgical resection of the necrotic parts of the esophagus and closure of the left atrium. Atrial laceration may be treated with a bovine pericardial patch, and the esophageal laceration may be treated with a purse-string suture. Stenting of the esophagus is an established procedure for interventional closure of esophageal leakages. It was reported to have been successful in a single patient with AEF. However, the safety of this procedure has to be further evaluated because endoscopy with its inherent risk of air embolism is necessary for appropriate positioning of the stent. Furthermore, with an esophageal stent, only 1 side of the fistula is closed while the left atrial side remains open.

PROGNOSIS

Atrioesophageal fistula as a complication of RAF has a high mortality. According to the published cases (Table), patients with AEF after surgical RAF have a higher chance of survival than patients with AEF after percutaneous RAF. This difference may be owing to the higher awareness of patients with AEF after surgical RAF have a higher chance of survival than patients with AEF after percutaneous RAF. A complication may occur even weeks after RAF.

In patients with meningitis, stroke, seizures, or impaired consciousness and fever, it should be determined whether they have a history of RAF. In cases with RAF, AEF should be strongly considered, especially if there are also symptoms such as dysphagia or chest pain. The diagnosis of AEF should be immediately confirmed or ruled out. Such patients are at high risk for experiencing fatal complications by investigations such as endoscopy, transesophageal echocardiography, or a barium swallow study, which is frequently done after admission to an intensive care unit.

If RAF is carried out, the patient, his or her family, and his or her treating physicians should be informed about the signs of the life-threatening complication of AEF, which may occur even weeks after RAF.

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REFERENCES


