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Autopsy Techniques in Patients With History of Radiofrequency Ablation for Atrial Fibrillation

Why En Bloc Letulle Technique of Dissection Is Preferred

Bindu Challa, MD; Keluo Yao, MD; Patricia Allenby, MD; Charles L. Hitchcock, MD, PhD; Youri Ivanov, MD; Sergey V. Brodsky, MD, PhD

Context.—Esophageal fistula formation is one of the most feared complications of radiofrequency catheter ablation. This procedure and its many variations, such as the “maze,” are becoming the mainstream treatment for atrial fibrillation owing to limitations of antiarrhythmic drugs. The incidence of this complication rate has been reported to be from 0.01% to 1%.

Objective.—To delineate the importance of using the en bloc Letulle method of dissection for identifying esophageal fistulas for cases with a history of radiofrequency catheter ablation.

Design.—Six autopsy cases with a history of radiofrequency catheter ablation for atrial fibrillation were selected from 1736 autopsies performed between 2009 and 2020.

Results.—The initial presenting symptoms included neurologic symptoms, chest pains, epigastric discomfort, and sepsis. Transesophageal echocardiogram of 4 cases showed no evidence of thrombus or vegetation, however, 2 cases had evidence of atrial esophageal fistula. The autopsy findings included 5 atrial esophageal fistulas and 1 esophagopericardial fistula. Atrial esophageal fistulas were small and could be detected without difficulty when the en bloc Letulle technique was used and would have been easily missed by the Virchow method. The immediate causes of the deaths were myocardial ischemia, septic emboli to brain and heart, hypovolemic shock secondary to exsanguination, stroke, and coagulopathy.

Conclusions.—To date, this is the largest collection of autopsy cases showing esophageal fistula associated with prior radiofrequency catheter ablation. The Letulle dissection method is preferable in this setting.

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Esophageal fistula (EF) is one of the most serious complications of Cox Maze and left atrial pulmonary venous ablation procedure. As atrial fibrillation arises from ectopic foci, destruction of these foci can limit episodes of atrial arrhythmias. Using this principle, cut-and-sew Maze procedure was developed by Dr J. Cox in 1987 in which multiple incisions are made in the left and right atria in a maze-like fashion. Once these incisions heal and form scar tissue, they block the ectopic foci or reentrant circuits. The development of alternative energy sources has enabled surgeons to create lines of ablation to replace incisions of original Cox Maze procedure. Evolution of epicardial ablation tools created the ability to access portions of the left atrium either through mini-thoracotomies or by using thoracoscopic tools, thus leading to development of total thoracoscopic Maze procedure. In 1998, Haissaguerre et al recognized pulmonary vein foci as initiators of atrial fibrillation, which currently forms the cornerstone of most interventional treatments of atrial fibrillation. This led to the development of left atrial pulmonary venous ablation procedure where ablation of cardiac/vascular tissue is performed most commonly with radiofrequency energy to induce a transmural heat injury, which later scars to isolate the electrical propagation of impulses. Catheters are typically introduced into the right atrium from the femoral vein up the iliac vein and vena cava. Catheters are guided by fluoroscopy, intracardiac echocardiography, and with the assistance of various mapping systems that help locate the ectopic foci, identify the depolarization pattern, position the ablation catheter, and evaluate ablation results. The ablation of cardiac tissue is performed most commonly with radiofrequency (microwave) energy to induce a transmural heat injury (60°C–70°C at the catheter tip) that scars to isolate the electrical propagation of impulses. Nowadays, it has become the mainstream treatment for atrial fibrillation owing to limitations of antiarrhythmic drugs. However, these procedures are associated with complications especially the development of EF. The incidence of this complication rate has been reported to be 0.01% to 1% with a high mortality rate (~55%). At least 120 cases have been reported in the literature at the time of this report.
Autopsy is the diagnostic tool that allows detection and confirmation of EF. There are several methods that can be used for organ evisceration. The Virchow method (organ removal one by one), Rokitansky technique (in situ dissection combined with en bloc removal), Ghon technique (en bloc removal), and en bloc Letulle technique are among the most commonly used methods.\(^5\)\(^6\) Advantage of the Virchow method is that organs can be studied in detail but anatomic relations of organs are not preserved. Rokitansky technique is preferred to limit the spread of infectious diseases like HIV infection, hepatitis B, among others. Disadvantage of the Ghon technique is that interrelationships between different organ systems are not preserved. In en bloc Letulle method, cervical, thoracic, abdominal, and pelvic organs are removed “en masse” and subsequently dissected as organ block. This technique is best for preservation of relationships between organs and organ systems.\(^7\)

METHODS

This study was exempt from the regulatory requirements of the National Institutes of Health regarding studies on deceased human subjects, as determined by the Institutional Review Board of The Ohio State University Wexner Medical Center (OSUWMC), Columbus, Ohio. Consecutive autopsy cases between January 2009 and December 2020 with the history of the radiofrequency catheter ablation for atrial fibrillation were identified from the autopsy pathology database at the OSUWMC. Clinical presentation of one of these cases has been previously reported\(^7\)\(^8\) and some clinical data are used here for comparison.

RESULTS

There were 1736 complete adult autopsies performed at the OSUWMC between 2009 and 2020. Among those, we identified 6 cases (0.35%) on decedents with the history of atrial ablation and a fistula between esophagus and atrium (5 cases) and esophagus and pericardial space (1 case).

Clinical Presentation

Demographic data for the 6 cases are shown in the Table. Three females and 3 males underwent either a thoracoscopic Maze procedure (4 cases) or left atrial pulmonary venous ablation (2 cases). Maze procedure included surgery with chest incisions, and a femoral vein catheter access was used for the left atrial pulmonary venous ablation procedure. All patients developed clinical symptoms that included altered mental status (2 patients), fever (3 patients), nausea, and chest pain or epigastric discomfort (4 patients). Three patients had positive blood cultures for microorganisms (streptococcal species). Patients died on average 34.2 ± 18.6 days (range, 20–69 days) after the surgical procedure. The findings of the imaging studies were suggestive of EF in 3 of 6 patients.

Summary of the Autopsy Findings

All 6 cases showed a fistula between the esophagus and other organs. The fistula connected a mid-portion of the esophagus with the posterior wall of the left atrium in 5 cases and with the left posteriolateral pericardial space in 1 case. All fistula tracts were small and were detected after using the en bloc Letulle technique during autopsy (Figure, A and B). Microscopically, fistula tracks were inflamed and were partially necrotic (Figure, C). The fistula tracts would be easily missed or damaged by other methods of evisceration, such as the Virchow method. The immediate causes of the deaths were multifocal myocardial ischemia (1 case), hypovolemic shock due to exsanguination (1 case), acute infarcts in the brain (3 cases), and an antemortem coagulopathy (1 case).

Postmortem neuropathologic examination also revealed significant findings in the brain. Thus, in 4 of 6 cases significant ischemic changes of embolic origin were found, consistent with the neurologic deficits presented during admissions. None of the 4 cases with neuropathology findings had documented history of neurologic deficit before the complication. Additionally, ischemic changes in the myocardiun were present in 3 of 6 cases. The pathologic mechanism of these ischemic changes in the brain and heart may include direct embolization of air through the fistula, embolization of esophageal contents, and thromboembolization secondary to coagulopathy. Indeed, evidence of intravascular thrombi in small vessels were found in 3 of 5 cases. The embolic-driven mechanism is consistent with the findings from prior case reports.\(^7\)\(^8\)

DISCUSSION

Fistula formation after atrial ablation is a rare but fatal complication. We identified EF in 6 of 1736 autopsy cases that were performed at our institution, or 0.35%. Despite advances in medical imaging, autopsy remains an important tool in investigating causes of death, such as investigating potential EF formation. Several autopsy techniques are in use by pathologists, including the Virchow, Letulle, and Ghon methods. We believe that the Letulle method, which uses en bloc organ removal and visualization of organ relationships, is preferable to use in patients with a known history of atrial ablation in order to properly visualize the anatomic defect that is otherwise easily missed owing to their small sizes.\(^9\) The Virchow method is not recommended, because of lower emphasis on organ relationships. The Ghon method is more applicable to restricted autopsy and in the facilities with a limited staff. In addition to the right technique, special attention is needed to the several anatomic areas, including esophageal mucosa, the lining of the major vessels in the vicinity of the surgical site, and the atrial endothelium.

We recommend detailed examination of the esophageal mucosa after longitudinal opening in situ of the esophagus. Fistula, if present, is easily visualized by esophageal wall defect and inflammatory reaction surrounding it; this will help to differentiate it from an incidental wall cut during the autopsy. The common location of the fistulae is consistent with previous case reports, likely due to the close proximity of the esophagus to the posterior wall of the left atrium, corresponding to the atrial ablation sites.\(^7\)\(^8\)

### Demographic Data of Patients Involved in the Study

| Demographic Data | Value |
|------------------|-------|
| Sex, M:F (%:%)    | 3:3 (50:50) |
| Age, mean ± SD (range), y | 60 ± 5.8 (50–65) |
| Race, W:AA (%:%)  | 6:0 (100:0) |
| Weight, mean ± SD (range), kg | 87.8 ± 17.9 (73.5–111.2) |
| Height, mean ± SD (range), cm | 173 ± 11 (160–187) |
| BMI, mean ± SD (range), kg/m² | 29.2 ± 3.4 (24.2–33.1) |
| Time between the procedure and death, mean ± SD (range), d | 34.2 ± 18.6 (20–69) |

Abbreviations: AA, African American; BMI, body mass index; SD, standard deviation; W, White.
The clinical symptoms demonstrated in all 6 cases are broad and include altered mental status, neurologic changes, fever, and hypotension. Similar presentations were found in reported cases that led to hospital admission. In all cases, death occurred within 2 months after the procedure (mean, 34.2 ± 18.6 days). The rapidly developing nature of this complication requires a high level of clinical suspicion after patients undergo a Maze procedure given the array of medical and surgical interventions that can be offered. Computed tomography of the chest and abdomen appears to be sensitive and specific for detecting the complication after admission, based on our findings, and is consistent with previously reported cases. Many patients in the reported cases also developed positive blood culture for mixed bacterial species.

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8. Nair GM, Nery PB, Redpath CJ, Lam BK, Birnie DH. Atrioesophageal fistula in the era of atrial fibrillation ablation: a review. Can J Cardiol. 2014;30(4):388–395.

9. Connolly AJ, Finkbeiner WE, Ursell PC, Davis RL. Autopsy Pathology: A Manual and Atlas. 3rd ed. Dublin, Ireland: Elsevier Health Sciences; 2015.

10. Rajapaksha WR, Cunningham KS, Rose TH. A fatal case of atrioesophageal fistula following radiofrequency ablation of left atrium and pulmonary veins for atrial fibrillation. Cardiovasc Pathol. 2014;23(4):238–240.

11. Tan C, Coffey A. Atrioesophageal fistula after surgical unipolar radiofrequency atrial ablation for atrial fibrillation. Ann Thorac Surg. 2013;95(3):e61–e62.

12. Halm U, Gaspar T, Zachaus M, et al. Thermal esophageal lesions after radiofrequency catheter ablation of left atrial arrhythmias. Am J Gastroenterol. 2010;105(3):551–556.

13. Yamasaki H, Tada H, Sekiguchi Y, et al. Prevalence and characteristics of asymptomatic excessive transmural injury after radiofrequency catheter ablation of atrial fibrillation. Heart Rhythm. 2011;8(6):826–832.