Scimitar syndrome consists of a constellation of findings related to a congenital anomalous connection of the right pulmonary veins through the inferior vena cava. The anomalous vein is referred to as the “scimitar,” because it resembles a Turkish sword on chest radiography (Figure 1). The incidence of scimitar syndrome is approximately 2 in 100,000 live births, with female predominance. There are several reports of familial occurrence of this syndrome.

The main features include partial anomalous pulmonary venous connection of the right lower and sometimes middle and upper veins to the inferior vena cava or to the junction of the right atrium and the inferior vena cava. Frequently associated with these characteristics are hypoplasia of the right lung and hypoplasia of the right pulmonary artery. The bronchial supply to the right lower lobe may also be sequestered, and there may be an anomalous arterial supply to the right lower lobe from the aorta. Because of the reduced volume in the right thorax, dextroposition of the heart occurs frequently. “Approximately 25% of patients with scimitar syndrome also have other forms of congenital heart disease, most commonly a secundum atrial septal defect,” according to Frank Cetta, MD, chair of the Division of Pediatric Cardiology at Mayo Clinic Rochester. Ventricular septal defect, patent ductus arteriosus, tetralogy of Fallot, and aortic arch anomalies have also been reported.

There is a spectrum of clinical presentation. Infants may present at less than 1 year of age and usually are severely affected with pulmonary hypertension caused by extreme hypoplasia of the right lung. The prognosis for these patients frequently is poor. The “adult form” diagnosis usually occurs after 1 year of age and is not associated with severe pulmonary hypertension. The clinical features and presentation resemble those of an atrial septal defect. If the anomalous venous return involves only the right lower lung and the lung is hypoplastic, very little volume overload may occur on the right side of the heart and intervention may not be necessary. However, if the arterial supply to the right lung is normal and the lung is not hypoplastic, a left-to-right shunt may occur through the anomalous scimitar vein, causing associated right atrial and right ventricular volume overload. Patients may present with progressive exercise intolerance and dyspnea on exertion similar to adults who present with left-to-right shunt from atrial septal defects. Characteristics found on physical examination also mimic those of an atrial septal defect (systolic ejection pulmonic outflow murmur associated with a widely split and fixed second heart sound) if shunting through the scimitar vein is extensive.

This congenital cardiac anomaly is corrected surgically. “One technique creates a baffie from the orifice of the anomalous scimitar vein to the left atrium,” says Joseph A. Dearani, MD, a cardiovascular surgeon at Mayo Clinic Rochester. “If there is an atrial septal defect, the hole actually may be used to help insert the baffie, thus rerouting the scimitar vein flow into the left atrium.” An alternative surgical technique is reimplantation of the scimitar vein into the wall of the right atrium with creation of a baffie to communicate with the left atrium. Most recently, direct reimplantation of the scimitar vein into the left atrium via a right thoracotomy has also been described. Part of the right lung may be sequestered, and frequently, anomalous systemic arteries course from the celiac axis or abdominal aorta to the sequestration. The right thoracotomy approach allows easy identification of anomalous arteries, and these can be ligated before repair. In addition, a pulmonary sequestration, if present, can be resected by the thoracotomy approach.

Surgical Outcomes
In a large long-term outcome study of surgical treatment of scimitar syndrome, 122 patients with scimitar
syndrome were analyzed from 22 university centers in Canada and Europe between 1960 and 1990. This study indicates that the vast majority of patients with scimitar syndrome probably do not require intervention; only 30% required surgical repair. “Intervention is warranted only for select patients with a large left-to-right shunt and signs of right-sided volume overload or infants who are critically ill,” says Dr Dearani.

A more recent study that assessed the long-term follow-up of the more novel surgical approach (direct reimplantation of the scimitar vein into the left atrium without cardiopulmonary bypass) demonstrated good surgical outcome in 9 patients during postoperative follow-up that ranged from 6 to 130 months.

**Important Imaging Features of Scimitar Syndrome**

As with all cases of anomalous pulmonary venous connection, meticulous echocardiographic imaging from all planes is essential. The subcostal view offers the best image of the entrance of the scimitar vein into the left atrium or into the junction of the right atrium and the inferior vena cava. In addition, the suprasternal notch view is important, even in large patients, to assess the “crab” view of the left atrium (Figure 2). This view ensures that the remainder of the pulmonary venous connections are normal. Parasternal short-axis imaging at the level of the pulmonary artery bifurcation is also important because it allows assessment of the relative size of the right pulmonary artery. In cases of scimitar syndrome with hypoplasia of a portion of the right lung or sequestration of that lung, the right pulmonary artery may be small.

Other useful imaging techniques include transesophageal echocardiography, which may offer improved imaging of the pulmonary venous connections in larger patients with poor surface windows. Magnetic resonance imaging, magnetic resonance angiography, and computed tomography accurately define the course of the pulmonary vein (Figure 3). The role of cardiac catheterization may be to quantify the amount of pulmonary flow and to measure the pressure in the scimitar vein and the respective pulmonary wedge pressures. There are reports of scimitar vein stenosis, and therefore measurement of the pressure in the scimitar vein may prove helpful in the overall management of this syndrome. Angiographically, the scimitar vein is usually entered easily just at or below the diaphragm and can be visualized easily with a hand injection. Angiography and the descending thoracic aorta also identify collateral vessels that may be feeding the portion of the right lung that supplies the scimitar vein. In older patients, coronary angiography may also be important if surgical intervention is considered.

**Case Report**

A 56-year-old woman was referred to Mayo Clinic for refractory, recurrent atrial fibrillation and atrial flutter. Thirty years earlier, she had undergone surgical repair of a secundum atrial septal defect via a midline sternotomy. Chest radiography showed mild cardiomegaly with dilation of the main pulmonary artery and a diffuse infiltrate in the right middle and lower lobe. Transsthoracic echocardiography showed moderate right atrial and right ventricular enlargement and anomalous connection of the right pulmonary veins to the inferior vena cava.
Subsequent cardiac catheterization showed that the main pulmonary artery pressure was 46/22 mm Hg with a mean of 31 mm Hg. Her calculated pulmonary vascular resistance was 3.26 units/m². The calculated QP/QS ratio was 2.54. Chest CT clearly showed that the vast majority of the pulmonary venous supply from the right lung entered the scimitar vein, which then in turn entered the inferior vena cava just below the junction of the right atrium and the inferior vena cava (Figure 4). The left pulmonary veins connected normally to the left atrium.

The patient was advised to consider surgical repair, including repeated sternotomy, baffling of the scimitar vein to a surgically created atrial septal defect, and a maze procedure. The objective of operation would be to eliminate the large (QP/QS ratio, 2.5) left-to-right shunt that had caused considerable right-sided cardiac chamber enlargement and also to perform a maze procedure to eliminate or limit development of chronic atrial tachyarrhythmias. The right thoracotomy approach is less appealing in this situation because of the inability to do a complete maze procedure.

“Most adult patients were not cured by the surgery that they had when they were young and require meticulous lifelong follow-up,” says Dr Cetta. “When these patients present with new-onset arrhythmia, they need first to have a thorough evaluation to ensure that no serious anatomic or hemodynamic abnormality is present. Only after all anatomic and hemodynamic issues have been addressed should invasive treatment to correct the rhythm abnormalities occur.”

Scimitar syndrome should always be considered in patients with secundum atrial septal defects. “Anomalous pulmonary veins should always be sought when any type of atrial septal defect is diagnosed,” says Dr Dearani. “The availability of percutaneous septal occluder devices makes it important to confirm normal pulmonary venous anatomy before placing a device.”

**UNDER THE STETHOSCOPE**

by Clarence Shub, MD

**Atrial Septal Defect**

- Wide, “fixed” splitting of S2, although typical, occurs in only about 70% of patients. Persistent, expiratory splitting of S2 is found in the vast majority of patients, even if not uniformly “fixed.”
- “Fixed” splitting of S2 should be verified with the patient in the upright position; normal subjects occasionally have “fixed” splitting in the supine position.
- In normal adults, S2 is single at the apex (A2). A split S2 at the apex indicates a pulmonic component suggesting the possibility of atrial septal defect.
- A pulmonary systolic ejection murmur, typically located at the upper left sternal border and augmenting with inspiration, is frequently present and is related to increased pulmonary blood flow.
Endothelial dysfunction of coronary or peripheral arteries is an independent predictor of future cardiac events. Until now, assessment of endothelial function has been difficult to implement clinically, because functional determination requires invasive studies that are operator dependent. Less invasive techniques have been used for research purposes, but they have not been adopted in clinical practice, again because of complexity of the tests and operator dependency.

Mayo Clinic Rochester has participated in clinical trials of reactive hyperemia peripheral tonometry (RH-PAT) for the noninvasive measurement of microvascular endothelial function. Digital reactive hyperemia is partly mediated by endothelium-derived nitric oxide; nitric oxide is responsible for endothelium-mediated vasodilation. Therefore, the magnitude of reactive hyperemia serves as a proxy for the degree of peripheral vascular endothelial dysfunction. The test measures changes in digital pulse volume during reactive hyperemia; patients with coronary microvascular endothelial dysfunction have a less robust hyperemic response than those with normal coronary endothelial dysfunction. “There is an excellent correlation between abnormalities in peripheral vascular function and coronary vascular function,” says Amir Lerman, MD, director of the Chest Pain and Coronary Physiology Clinic (CPCPC) at Mayo Clinic Rochester. “There is a strong relationship between coronary blood flow response to acetylcholine (a measure of coronary endothelial dysfunction) and peripheral microvascular endothelial function.”

The test requires about 45 minutes to perform. A finger probe is placed to measure digital volume changes that accompany pulse waves (Figure). The measure of reactive hyperemia is the RH-PAT index, which is the ratio of the average amplitude of the PAT signal over a 1-minute interval (starting 1 minute after cuff deflation), divided by the average amplitude of the PAT signal for 3.5 minutes before cuff inflation. The RH-PAT index is reported as normal (>2.1), borderline (1.7-2.1), or abnormal (<1.7). An RH-PAT index less than 2.0 has high sensitivity and specificity for coronary endothelial dysfunction. “Studies have revealed an excellent correlation between results of invasive measures of endothelial function and reactive hyperemia,” says Dr Lerman.

Physicians in the CPCPC, who have performed invasive endothelial function studies in more than 900 patients, provide consultation, diagnostic testing, and treatment recommendations for patients with chest pain who do not have any obstructive disease or patients with severe coronary artery disease who are not candidates for conventional medical or interventional approaches. In addition to invasive and noninvasive assessment of endothelial function, they offer physiologic and ultrasound assessment of indeterminate coronary lesions. Innovative treatment of patients with chronic coronary artery disease includes new medications, angiogenesis, spinal cord stimulation, and enhanced external counterpulsation.
In the past, the overall outcome for patients who have an out-of-hospital cardiac arrest (OHCA) due to ventricular fibrillation has been dismal. Historically, the overall hospital survival of these patients has been approximately 10%. Isolated examples of improved outcomes with 20% to 30% survival have been reported, generally only as the result of intensive educational efforts in communities in the practice of basic life-support resuscitation and rigorous training of emergency service personnel. The survival among witnessed cardiac arrests secondary to ventricular fibrillation has usually been slightly higher than for unwitnessed cardiac arrests.

The relatively recent introduction of automated electronic defibrillators (AEDs) represents an important contribution to improved outcomes in OHCA patients. Since the early 1990s, the overall survival among OHCA patients with ventricular fibrillation as the initial rhythm has increased to approximately 40% (44% if the arrest is witnessed) in Olmsted County, Minnesota, where Mayo Clinic Rochester is located. “This improved observed survival has been attributed primarily to the provision of AEDs to local police officers, which has resulted in short call-to-shock times,” says Roger D. White, MD, Mayo Clinic Rochester anesthesiologist, director of the Rochester City and Olmsted County Early Defibrillation Program, and medical codirector of Gold Cross ambulance services. “The long-term survival of these patients has generally been excellent and similar to that expected in a matched population.” However, among survivors of OHCA, the biggest concern is possible temporary or permanent neurologic injury attributable to cerebral anoxia at the time of cardiac arrest, despite resuscitative efforts.

“The use of therapeutic active cooling–induced hypothermia—was proposed many years ago as a method to reduce the risk of neurologic injury related to cerebral anoxia in this situation,” says Malcolm R. Bell, MD, director of the Mayo Clinic Rochester Cardiac Care Unit. Experimental data have demonstrated improved neurologic recovery with induced hypothermia, as have anecdotal instances of accidental hypothermia in humans (for example, cold water drowning). Two recent landmark clinical trials, one from Europe and the other from Australia, randomized OHCA patients to induced hypothermia for 24 hours or normothermia and showed that patients in the induced hypothermia group had better outcomes. In each study, the major differences in outcome were improved cerebral performance and survival in the hypothermia-treated patients. Target temperatures were 32°C to 34°C.

Therapeutic hypothermia was introduced into the Coronary Care Unit at Mayo Clinic Rochester in 2005. “It is important to stress that this clinical protocol begins in the field. The attending local ambulance crews begin the cooling process with application of ice packs for any OHCA patient who has a ventricular fibrillation cardiac arrest and who remains comatose after the initial resuscitation effort. The ice packs are left in place during transport to the emergency department,” says Dr White.

Patients eligible for therapeutic cooling include the following:
- Patients with witnessed or unwitnessed OHCA secondary to ventricular fibrillation
- Patients in a comatose state or with impaired
consciousness immediately after restoration of normal rhythm

- Patients with stable hemodynamic values after return of normal cardiac rhythm
- Patients for whom the cooling process is initiated within 4 hours of the event

The hypothermia protocol is divided into 2 parts: 1) induction and maintenance of hypothermia and 2) an antishivering regimen. Hypothermia is induced with a noninvasive therapeutic temperature management system (Arctic Sun 2000, Medivance Inc, Louisville, Colorado) using adhesive gel pads placed on the patient’s torso and lower limbs. Cooled water is then circulated through this system, cooling the patient via the principle of heat/energy exchange. Using this system, patients can be cooled to 33°C to 34°C within 4 to 6 hours. This target temperature, controlled via the module, is maintained for 24 hours, after which the patient is gradually rewarmed using the same system. During this time, the patient is cared for as would be any OHCA patient, including administration of antiarrhythmic agents to maintain stable normal rhythm, ventilatory and circulatory support, and coronary angiography and percutaneous coronary intervention if appropriate.

“Prevention of shivering is an important component of this hypothermia protocol,” says Dr Bell. “Shivering leads to patient discomfort and is a reflex mechanism to overcome hypothermia and must therefore be avoided.” The current protocol includes routine use of midazolam and fentanyl while patients are also paralyzed using pancuronium. After active rewarming at 24 hours, these drugs are withdrawn. Careful neurologic assessment by neurology critical care colleagues is performed after 24 hours and daily thereafter to accurately assess for any residual neurologic impairment.

All 7 patients treated thus far have been successfully cooled to a target temperature range of 33°C to 34°C with no complications attributable to the cooling or the antishivering regimen. The patients whose initial rhythm was ventricular fibrillation were all discharged home, one with mild neurologic impairment and the others with full recovery. While occasional patients without ventricular fibrillation as their initial event have been subjected to hypothermia, their outcomes have not been as good as those in the ventricular fibrillation group. This difference highlights the uncertainty of applying hypothermia to patients without ventricular fibrillation as the cause for their OHCA, because limited or no data exist for these patients. Further research needs to be conducted to examine the role of hypothermia in these patients, and it will be the focus of ongoing investigations at Mayo Clinic Rochester.

Genetic Mutation Responsible for Some Forms of Atrial Fibrillation Discovered

Investigators at Mayo Clinic Rochester have identified a gene mutation responsible for atrial fibrillation. “This discovery underscores the importance of heritable factors in the development of atrial fibrillation,” says Timothy M. Olson, MD, director of the Cardiovascular Genetics Laboratory and first author on the study. The multidisciplinary team identified a genetic mutation of the ion channel gene KCNA5, responsible for the atrial-specific potassium ion channel. “Identification of a new molecular basis for atrial fibrillation provides a critical step toward individualized diagnosis and treatment of arrhythmias,” says Andre Terzic, MD, PhD, director of the Marriott Heart Disease Research Program at Mayo Clinic Rochester and a senior author of the study.

Genomic DNA scanning revealed a nonsense mutation in the KCNA5 gene. This gene encodes Kv1.5, a voltage-gated potassium channel found in human atria; loss of Kv1.5 function as a result of this mutation produced action potential prolongation and early after-depolarization in atrial myocytes. “This channelopathy provides a substrate for atrial fibrillation in a manner similar to ventricular torsades de points; chaotic atrial activity results from ‘atrial torsades,’” says Dr Olson. Treatment of affected atrial cells in vitro with the aminoglycoside gentamicin overrides the defect, resulting in structurally and functionally normal Kv1.5 potassium channels.

The defect was identified in a family with early-onset lone atrial fibrillation. The role of genetic mutations in the etiology of atrial fibrillation in other patients and families, particularly those who lack traditional risk factors for arrhythmia, is under intense ongoing investigation.
The Mayo Clinic Rochester Cardiovascular Health Clinic provides a comprehensive program of risk assessment and risk reduction for patients who have heart disease or, by virtue of their family history, lifestyle, or both, may develop heart disease. The Cardiometabolic Program is a new multispecialty collaborative program designed to help patients with metabolic syndrome reduce their cardiovascular risk by implementing intensive lifestyle modification. The program is aimed to meet the growing need for management techniques for these patients.

“The program is cardiometabolic, but the consequence we fear the most is cardiovascular,” says Francisco Lopez-Jimenez, MD, program director and associate director, research.

Metabolic syndrome is diagnosed when 3 of the following 5 criteria are met:

1. Central obesity (waist circumference >40 inches in men and >38 inches in women or body mass index >30)
2. Impaired fasting glucose (fasting glucose >100 mg/dL)
3. Low high-density lipoprotein cholesterol (HDL <40 mg/dL in men or <50 mg/dL in women or either sex on treatment for low HDL cholesterol)
4. High triglycerides (fasting triglycerides >150 mg/dL or on treatment for hypertriglyceridemia)
5. Hypertension (systolic blood pressure >130 mm Hg or diastolic blood pressure >85 mm Hg or treated hypertension)

Nearly 40% of individuals seen in the outpatient setting have metabolic syndrome, and these patients are 2 to 4 times more likely to have a cardiovascular event or die from a cardiovascular condition than those without metabolic syndrome. Exercise, diet, and appropriate medical management of hyperlipidemia and hypertension are all helpful in treating this syndrome.

The Mayo Clinic Cardiometabolic Program combines strategies for diet and exercise with behavior modification techniques to help patients most effectively manage metabolic syndrome and thus reduce their risk of cardiovascular disease. The core program consists of 2 hours once a week for 6 weeks. During these sessions, the following areas are addressed:

**Nutrition**
- Specific recommendations for caloric intake and changes to diet
- A teaching kitchen where participants learn in a hands-on setting to prepare healthy, tasty foods
- Ongoing cognitive/psychological assessment of eating habits and how to change unhealthy eating behavior

**Exercise**
- On-site exercise instruction by Mayo Clinic exercise specialists
- Exercise with support groups to provide motivation
- Cardiac stress testing to assess patient risk and formulate recommendations

**Follow-up**
All patients undergo measurement of metabolic syndrome components at the beginning of the program and periodically during the program to provide patients with feedback to track their progress. After leaving the formal 6-week program, a long-term follow-up program is implemented to support and track patients ongoing success.

“Identification and intervention can reduce the risk of diabetes and cardiovascular disease in patients with metabolic syndrome,” says Randal J. Thomas, MD, director of the Mayo Clinic Rochester Cardiovascular Health Clinic. “Our goal is to develop an individualized long-term plan for each patient to minimize his or her risk of developing cardiovascular disease.”

The Mayo Clinic Cardiovascular Health Clinic offers thorough risk assessment and risk reduction assessment in addition to the Cardiometabolic Program. Specialized diagnostic testing and comprehensive recommendations are provided, including exercise, nutrition, dietary supplement and vitamins, smoking cessation, and relaxation techniques. In addition to the 6-week program, an intensive 2-day program will be implemented in the near future for patients unable to complete the 6-week program.
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