Arrhythmogenic Right Ventricular Dysplasia: A Possible Cause of Sudden Incapacitation

Alon Grossman, Erez Barenboim, Bella Azaria, Yaniv Sherer, and Liav Goldstein

Arrhythmogenic right ventricular dysplasia (ARVD) is an important cause of sudden death in young people. Awareness of this condition is essential so that it may be diagnosed as soon as possible. Early diagnosis may enable prompt treatment and allow screening of family members, since in 30–40% of the cases this condition is inherited as an autosomal dominant trait (8,14,15). The classic presentation of this syndrome is with symptomatic sustained ventricular tachycardia, with electrocardiographic evidence of a left bundle branch block pattern. This arrhythmia may lead to fatigue and syncope on minimal exertion. Unfortunately, a proportion of the patients will present with sudden cardiac death (4,17). Thus, ARVD has the potential to cause sudden incapacitation, which is a major concern in modern aerospace medicine. We present the case of an aviator in which a diagnosis of ARVD was established after an episode of sustained ventricular tachycardia that occurred with no relation to flight activity. Occurrence of this event during flight may have led to sudden incapacitation, thus emphasizing the importance of establishing an early diagnosis of ARVD, particularly in aviators.

CASE REPORT

A 46-yr-old Apache AH pilot was hospitalized in July 2003 with a complaint of palpitations without loss of consciousness. Family history was non-revealing and he was taking no medications. An electrocardiogram revealed a monomorphic ventricular tachycardia. Echocardiographic examination revealed signs suggestive of arrhythmogenic right ventricular dysplasia. He underwent right and left coronary catheterization, which was found to be normal. A biopsy was taken from the interventricular septum, but was found to be non-diagnostic. Electrophysiologic study (EPS) was conducted with no demonstrable focus of an arrhythmia. The diagnosis was substantiated by an MRI, which demonstrated areas of subepicardial fat infiltration, highly suggestive of ARVD. Following establishment of the diagnosis, an automatic implantable cardioverter defibrillator (AICD) was implanted and treatment with sotalol was begun. The pilot is now 3 mo following the procedure with no occurrence of palpitations. The Israeli Air Force Medical Board decided to ground the aviator permanently.

Retrospective examination of the patient’s medical records revealed an abnormal electrocardiographic pattern since his enlistment in 1975. This pattern included right axis deviation and inverted T waves in the inferior limb leads and in V3–V5. Epsilon waves, typical of ARVD, were not evident. Based on these findings, he underwent an echocardiographic examination and exercise testing prior to his enlistment in the Israeli Air Force; both were found to be normal. In 1988, at the age of 31, he was temporarily grounded because of the occurrence of multiple ventricular premature beats (VPBs) on a resting electrocardiogram. Stress testing (Bruce protocol) demonstrated a single VPB at the beginning of the test and Holter examination revealed multifocal VPBs. He was waivered to flying duties based on this workup. In 1992, he was hospitalized because of a transient ischemic attack (TIA) which manifested as right hemiparesis. CT revealed a hypodense infarct in the right basal ganglia and an MRI examination revealed similar findings. An echocardiographic examination was found to be normal and he underwent...
a transesophageal echocardiogram which demonstrated an atrial aneurysm without a right-left shunt and with no evidence of a thrombus. Thickened chordae tendinea were demonstrated in the right ventricle. Non-invasive carotid evaluation revealed irregularities of the carotid arteries and, therefore, a carotid angiography was performed and found to be normal. Workup for a hypercoagulable state, including protein S, protein C, anti-thrombin 3, Lupus anticoagulant, ANF, VDRL, protein electrophoresis, and homocysteine was found to be normal. Treatment with aspirin was begun and he was returned to flying duty with a co-pilot in 1996 after neurologic examination and neuropsychological evaluation were found to be normal. A routine stress test performed in August 2002 demonstrated the ECG pattern described above with a few VPBs. No additional tests were performed and he remained in active flying duty until the occurrence of the above-mentioned arrhythmia.

**DISCUSSION**

Arrhythmogenic right ventricular dysplasia (ARVD) is a common cause of sudden death in young people. It was first described in Dalla Volta in 1961 (4), but the term was coined by Frank Fontaine in 1978 (1). ARVD has a male predilection of 3:1, and 80% of patients are detected before their 40th birthday. Thiene et al. discovered that post-mortem examination showed evidence of ARVD in 20% of sudden deaths in people under the age of 35 (17). The prevalence of this condition is 1:5000 and in 30–40% of the cases, it is inherited as an autosomal dominant trait, with incomplete penetrance and variable expression. The clinical manifestations of ARVD vary from the asymptomatic state to a severely symptomatic patient due to cardiac arrhythmias. Occasionally, sudden death may be the first manifestation. The diagnosis should be entertained in any patient who presents with frequent palpitations, lightheadedness, near syncope or syncope in the absence of a clear precipitating factor, and has either multifocal VPBs or nonsustained or sustained ventricular tachycardia (VT), particularly of the left bundle branch block morphology. Other warning signs include a positive family history and an abnormal electrocardiogram. The electrocardiogram serves as one of the key screening diagnostic tests and is abnormal in 70% of cases (1). Precordial T wave inversion in V1–V3 and sometimes through V6 is the most common finding. A unique finding, present in only a third of the patients, is a distinct notch in the secondary upstroke near the ST transition, termed the Epsilon wave. It results from slow conduction in the diseased right ventricular free wall.

Echocardiographic features of ARVD include right ventricular dilatation, bulging of the right ventricle during diastole, dyskinesia of the inferobasal free wall during systole, exaggerated trabecular pattern within the right ventricle, and structural abnormalities of the moderator band (2,9,15). The presence of these findings is associated with serious ventricular arrhythmias and progressive right ventricular infiltration, even in asymptomatic individuals. MRI is the best technique for outlining the subepicardial fat infiltration characteristic of ARVD. This method has the ability not only to describe right ventricular morphology but also to highlight areas of myocardial involvement (3,6). These areas of adipose tissue distribution correspond with the focus of the arrhythmia (13).

Endomyocardial biopsy is another diagnostic modality that may help to confirm the diagnosis, provided it is directed to the affected areas. The major limitation is that, although the disease usually involves the right ventricular free wall, the biopsy is often obtained from the ventricular septum in order to avoid perforation. Thus, negative results are often obtained in the presence of ARVD and a negative biopsy does not rule out the diagnosis. Electrophysiologic studies are used to define the morphologic characteristics of the arrhythmia and guide radio-frequency ablation of the arrhythmogenic focus.

McKenna et al. published diagnostic criteria for the diagnosis of ARVD in 1994. These clinical criteria were divided into minor and major criteria in six categories: family history; ECG depolarization/conduction abnormalities; ECG repolarization abnormalities; arrhythmias; global or regional dysfunction; and structural alterations and tissue characteristics of walls. The diagnosis of ARVD is fulfilled in the presence of two major criteria, one major and two minor criteria, or four minor criteria from different categories (12). These criteria are useful, but the diagnosis of ARVD is still difficult in the preliminary stages of the disease.

Treatment options for ARVD include drug therapy, radio-frequency catheter ablation, and surgical therapy. Drug therapy is based on three main agents: sotalol; class 1C agents; or amiodarone. In a study performed in 88 subjects with ARVD, single anti-arrhythmic therapy was judged satisfactory in 21 cases and combined therapy in 19 additional cases (11). Radio-frequency is appropriate as a first approach for ventricular tachycardia ablation in ARVD, but its effectiveness is less than 40% at the first session. Fulguration is effective for VT ablation and should be used in the same session after ineffective radio-frequency ablation. However, fulguration requires expertise, general anesthesia, and more than one session in more than 50% of subjects. Radio-frequency and fulguration plus other forms of therapy, including pacemakers and automatic implantable cardioverter defibrillators, provide a clinical success rate of 81% to 93% (5). Drug therapy is frequently used in combination with placement of a defibrillator in order to control the arrhythmia (1). Surgical therapy is reserved for the most resistant cases and may result in right heart failure (1).

**Aeromedical Concerns**

Since the early days of aviation, the potential for in-flight incapacitation has been a matter of concern for the flight surgeon. In recent years, the importance of screening for potential causes of incapacitation has increased, due to the fact that a greater proportion of flight hours are flown in single-seat aircraft. Cardiovascular conditions were found to be the leading cause for sudden incapacitation in civil aviation (10), whereas McCormick et al. found that the leading medical causes
for incapacitation in the USAF were neurologic conditions. In McCormick’s report, cardiovascular causes ranked second as a cause for in-flight incapacitation and gastrointestinal causes ranked third (10). This was attributed to the fact that military aviators represent a younger age group and are thus less susceptible to ischemic heart disease. Although the older age group is, in fact, more susceptible to sudden incapacitation from cardiovascular causes, some cardiovascular conditions are more frequent in the young age group. These causes should be thoroughly screened for due their lethal potential. ARVD is a condition potentially capable of causing in-flight incapacitation and thus every effort must be made to diagnose it. The screening tools for cardiovascular conditions used in aviation medicine include the history, the physical examination, and the resting electrocardiography. Flight surgeons should, therefore, be familiar with the typical findings of ARVD and should conduct an aggressive search for the diagnosis in suspicious cases. This search should also be conducted in those with a positive family history of sudden death and in those with a history of unexplained syncope, even in the presence of a normal ECG. This workup should include an echocardiographic examination with particular attention to the right ventricle and in problematic cases, additional tests, such as MRL, should be conducted.

We believe that an echocardiographic examination should be performed in all cases of sudden death in a young family member, since a large proportion of the cases of ARVD are inherited. In this pilot, the resting electrocardiogram was pathologic since his enlistment, demonstrating inverted T waves in the inferior limb leads and in V3–V5 with multiple VPBs. He, therefore, underwent an extensive evaluation in order to establish a diagnosis using the methods available at the time. The findings on the exercise testing and the echocardiogram were considered normal and he was consequently approved for continued aviation service. The echocardiographic finding of a thickened chordae tendinea in the right ventricle may have been an early sign of this pilot’s disease, but was not regarded as such. The combination of the electrocardiographic and echocardiographic findings should have raised suspicion regarding the possible diagnosis of ARVD. The pilot was first evaluated in 1977, whereas the entity of ARVD was first described in 1978. We believe that awareness of the entity of ARVD when the pilot was initially examined may have led to an earlier diagnosis. Earlier diagnosis may have allowed screening of this pilot’s family members. The arrhythmia was not related to flight, but it certainly had the potential to cause in-flight incapacitation. Since the pilot flew a two-seat aircraft, the arrhythmia would probably not have resulted in a mishap, yet it had the ability to cause injury to the pilot and may have resulted in premature mission termination. There are no reports of an association between ARVD and TIAs in the absence of a right to left shunt, which was not demonstrated in our patient, yet the young age of the pilot and the association between two such rare entities makes it possible that the two are related. Needless to say, the presence of ARVD is incompatible with active flight. This is due to the potential for ventricular tachycardia, but even those who are well controlled under treatment are prone to treatment side effects and recurrence of the arrhythmia under stressful conditions.

**CONCLUSIONS**

ARVD, though a rare entity, is a relatively common cause of cardiac disease in the young. Its potential for causing in-flight incapacitation makes it particularly important in aviators. Flight surgeons should be aware of this condition and should conduct an aggressive pursuit of the diagnosis in suspicious cases. The diagnosis should also be suspected in those with a family history of sudden death in the young or unexplained syncope. Greater awareness of this entity would probably prevent cases of sudden death and in-flight incapacitation.

**REFERENCES**