Housecalls

Underwriting Case Studies & Insights

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Our Casebook

By Richard Braun, MD

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SCOR Global Life increasingly is recognized as a key participant in the life reinsurance market worldwide. We were pleased to see that SCOR's geographic scope was implicit in Standard & Poor's upgrade of the company to AA- this past September. The ratings agency specifically acknowledged SCOR Global Life's presence in the Americas as a key component of the company overall. The benefits of a financially strong risk partner cannot be understated, but we also should consider the value that this global position contributes to our clients beyond the balance sheet.

For purposes of this newsletter I wish to focus specifically on the value that our global community of medical directors and underwriters add to the success of SCOR Global Life and to our clients. Our Americas staff relied on our colleagues in Europe for important updates to our disability insurance manual. We looked to our peers in Asia to improve our critical illness capabilities. In turn, our Americas teams shares critical insight in mortality assessment, particularly from the perspective of a market with multiple risk classes.

We also have seen this collaboration in this newsletter. Earlier this year we were pleased to have Dr. Evans, a cardiologist in our Paris office, contribute his specialized knowledge about patent foramen ovale. In this issue we welcome Dr. Gabriela Buffet, an Associate Medical Director and specialist in infectious disease on our Paris-based Research & Development team. Dr. Buffet was vital in following the recent Ebola outbreak and keeping the company and clients apprised of the risks. With a medical degree from South America, Dr. Buffet represents the growing global nature of the insurance medicine practice and SCOR's commitment to medical R&D.

In this final issue for 2015 we present two more uncommon medical conditions for your consideration. HTLV 1 infection is endemic to some areas but usually goes unrecognized until a complication develops. Cardiac papillary fibroelastoma is simply rare. And our newsletter would not be complete without Dr. Rooney's Underwriting Puzzler.

On behalf of Dr. Rooney and SCOR's medical staff worldwide, I'd like to wish you and your company a prosperous New Year. We appreciate the trust you have placed with us and we look forward to serving you in 2016 and beyond. ∞

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SCOR Global Life

Case #1
Human T-lymphotropic Virus – Type 1

By Gabriela Buffet, MD
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Dr. Buffet joined SCOR Global Life in 2006 as Associate Medical Director, Research & Development. She earned her medical degree with a specialization in internal medicine from the Federal University of Rio Grande in Brazil, where she later served as a professor of Infectious Diseases. Gabriela has also received the certificate in Epidemiology, Statistics and Clinical Research (University "Paris-Sud") and a master's degree in Microbiology and Infectious Diseases (ESSSCAN, Spain). She is a Member of the Infectious Diseases Society of America.

A 43-year-old male applied for life insurance. He donated blood in 2001 and was found to be seropositive for Human T-cell Leukemia/Lymphoma Type 1 (HTLV-1) virus. He was last tested in 2008 and was ELISA and Western blot positive for HTLV-1. No proviral load was done. His parents were from Jamaica, but he was born in New York. He is being followed yearly with Complete Blood Counts which have been normal.

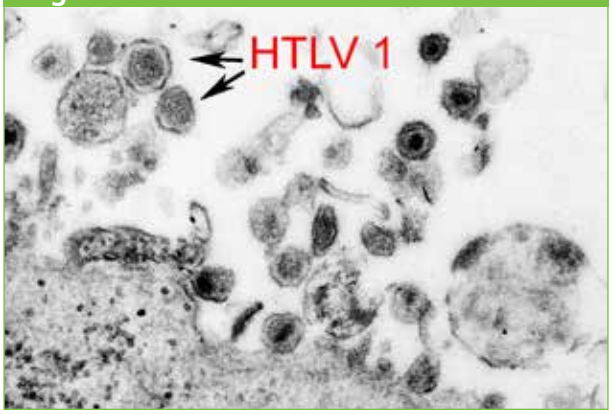
Question

What is HTLV-1, and what are its mortality implications for testing positive?

Answer

HTLV-1 was the first human retrovirus discovered (1979). HTLV-1 predominantly affects T lymphocytes. HTLV retroviruses are RNA viruses that use an enzyme called reverse transcriptase to produce DNA from RNA. HTLV-1 infection has been associated mainly with neurological, hematological and inflammatory diseases, especially HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP) and adult T-cell leukemia/lymphoma (ATL/ATLL).

Figure 1 – HTLV-1 Virus



Epidemiology

HTLV-1 is present worldwide with highly endemic areas in Japan, Melanesia, Australia, West Africa, the Caribbean, the United States (Central Florida), Central and South America and the region of Mashhad Iran (Figure 2). It is estimated that at least 10-25 million people worldwide are infected with HTLV-1. In North America (outside of Florida), the prevalence of HTLV-1 seropositivity among blood donors is very low, on the order of 1 case per 10,000 blood donors.

HTLV-1 has three modes of transmission:

- Perinatal: 10%-25% of breastfed children born to mothers infected with HTLV-1 will be infected. The mother-child transmission is mainly associated with breastfeeding for over six months
- Sexual, occurring mainly from male to female
- Blood transfusion or transplantation of organs or tissues

HTLV-1 prevalence is strongly dependent on age and sex, with higher rates associated with older age and with female sex.

Pathophysiology

In the life cycle of HTLV-1, the viral RNA is transcripted (reverse transcription) into a DNA provirus that integrates into the host genome. New virions are produced via the viral integrated DNA.

HTLV-1 can infect different cell types; however, its spread is supported mainly by CD4+ cells. HTLV-1 infection induces the clonal proliferation of T-lymphocytes.

The majority of people infected by HTLV-1 remain asymptomatic. People who exhibit signs or symptoms usually are exposed to the infection for long periods before it becomes manifest.

Some factors contribute to the virus/host interaction and in progression from the asymptomatic state to the disease:

- Elevated proviral load is the most evident risk factor for transition from the asymptomatic carrier status to myelopathy and hematological disease
- Genetic host characteristics (Human Leukocytes Antigen) participate in the modulation of immune response and influence the development of symptomatic disease.

HTLV-I associated diseases are generally slow to progress, and the majority of persons infected remain asymptomatic for life:

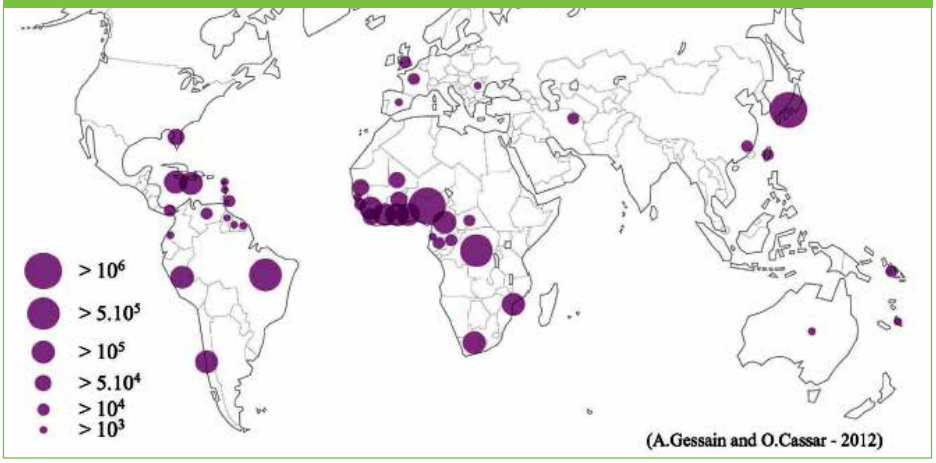
- Adult T-cell leukemia/lymphoma is associated with the malignant proliferation of transformed leukocytes carrying HTLV-I provirus
- HLTV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP) is a chronic progressive myelopathy characterized by spastic paraparesis, sphincter dysfunction and mild sensory disturbance in the lower extremities directly related to HLTV-1 infection
- HTLV-1-infected individuals also are at increased risk of developing inflammatory diseases, such as alveolitis, Sjögren's syndrome, uveitis, arthropathy and polymyositis.

Diagnosis & Treatment

The most common diagnostic test of HTLV-1 infection is antibody detection. The enzyme immunoassay (EIA) is commonly used, followed by a confirmatory Western Blot.

PCR assays have been developed to quantify viral presence (proviral DNA load). Some studies have established a link between high proviral load and disease evolution.

Figure 2 – Prevalence of HTLV-1 Worldwide



While geographically diverse, the primary concentrations of HTLV-1 cases occur in West Africa and Central and South America. (Source: http://www.frontiersin.org/)

Asymptomatic seropositive patients should be followed with annual follow-up visits. Laboratory evaluation may be limited to a complete blood and WBC differential count. Some prospective studies of HTLV-1 carriers identified increases in the absolute lymphocyte and platelet counts in active disease. Atypical lymphocytes (Flower Cells) may be observed in peripheral blood. In addition hypergammaglobulinemia and false-positive syphilis test results can be seen.

Treatment of asymptomatic HTLV-1 carriers is not currently indicated. No treatment has demonstrated a real efficacy for symptomatic patients. Current clinical trials including monoclonal antibody therapy are ongoing for ATL/ATLL and HAM/TSP treatment.

Prognosis

The lifetime risk of developing adult T-cell leukemia/lymphoma (ATLL) has been estimated at 2%-6% among HTLV-1 carriers. The latency period is approximately 20 to 40 years after infection, with a slightly higher risk among HTLV-1 infected males. The risk of disease development increases among transfusion and transplant recipients, who may develop the disease with a much shorter incubation time.

Among the associated malignancies, only smoldering ATL has a relatively good prognosis, with a 5-year survival rate of 70%. For the other forms (chronic, acute or lymphoma) the prognosis at 5 years is poor.

Human T-lymphotropic Virus – Type 1 (cont.)

The risk of developing HAM/TSP has been estimated at 0.25%–3.8% of infected persons. The prognosis of HAM/TSP is poor, with progression of neurologic deterioration and disability.

HTLV-1 infected persons are at risk of developing hematological or neurological diseases, but a majority of them are only carriers. However 2%-6% of them will develop a hematological malignancy with high mortality risk.

Returning to the Case

Approximately 95% of a cohort infected by HTLV 1 will not develop viral related diseases and can be expected to have population mortality. Approximately 5% are anticipated to have a reduced life expectancy due to viral related illness. Applying this ratio to varying reduced life expectancies in a 43-year-old male results in a mild to moderate extra mortality risk for the group as a whole. ∞

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Case #2
Cardiac Papillary Fibroelastoma

Richard Braun, MD
Vice President & Chief Medical Officer

A 42-year-old female applied for life insurance. Nine years prior to the application she was diagnosed with a fibroelastoma of the aortic valve by transesophageal echocardiogram. Detailed records from that time were not included. Within the year prior to application she complained of palpitations and had a 24- hour ambulatory heart monitor. This revealed 2027 isolated Ventricular Ectopic Beats, 1317 episodes of bigeminy, and 5 runs of ventricular tachycardia lasting 3-6 beats. She was started on Metoprolol. She also had an exercise test during which she exercised to 12 minutes. It showed decreasing ectopy with exercise, and the tracing was negative for ST changes. A repeat transthoracic echo again showed the presumed ~ 6 mm fibroelastoma of the aortic valve and an ejection fraction of 51%.

Question

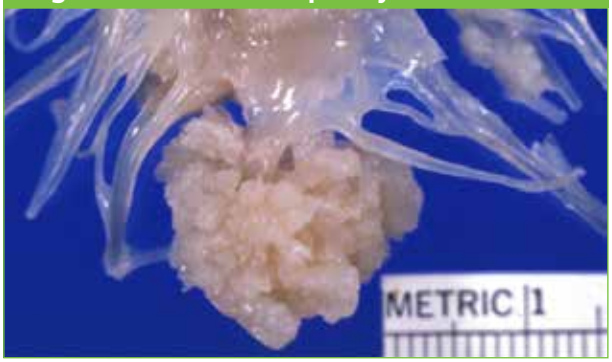
What is a fibroelastoma, and what are the prognostic implications?

Answer

Primary cardiac tumors are very rare, with an estimated incidence of less than 0.1 percent in the population. Much more common (20 times) are metastatic cancers to the heart from primaries occurring elsewhere in the body. When tumors do arise primarily in the heart, they are benign more than 75% of the time. Primary malignant tumors of the heart are exceptionally rare and beyond the scope of this case review.

The most common benign heart tumor in adults is a myxoma. Myxomas typically arise in the left atrium (80%) with fewer (20%) arising in the right atrium. The second most common type of cardiac tumor in adults is the fibroelastoma (Figure 1), also known as cardiac papillary fibroelastoma (CPF). A review article encompassing 725 cases of CPF revealed that 55% of cases occurred in males. Most cases were discovered between the ages of 70-79, although that may be related to increased use of cardiac imaging, as the mean age was 60 years. The age range was newborn to age 92. The average size of the tumors was 9 mm with a range of 2 to 70 mm. The location of the CPF tumors in the series are listed in Figure 2, along with the percentages found at each location.

Figure 1 – Cardiac Papillary Fibroelastoma



While heart tumors are rare overall, fibroelastoma ranks as the second most common primary cardiac growth. Cardiac papillary fibroelastoma typically has multiple fronds attached by a small pedicle. Some have described them as looking like a sea-anemone.

The cause of CPF is not known, and no familial predisposition has been reported.

30%–50% or more of CPF tumors are asymptomatic and discovered incidentally via a transthoracic echocardiogram (TTE), magnetic resonance imaging (MRI), computed tomography (CT) or at autopsy. Symptoms, when present, are related to complications of the tumor. Embolic complications in the form of cerebrovascular accident or transient ischemic attack are the most common symptomatic presentation, although emboli to peripheral arteries and coronary arteries have also been described.

Tumors on the right side of the heart may cause pulmonary emboli. Large mobile tumors can obstruct blood flow across a valve or coronary artery ostia. These complications may result in symptoms like angina, myocardial infarction or sudden death. Chronic obstruction may cause heart failure. Syncope or presyncope are not uncommon as symptoms associated with large tumors.

The diagnosis of CPF is initially suspected from seeing a small valvular or endocardial mass which may be mobile or sessile. The mass often appears to be

Cardiac Papillary Fibroelastoma (cont.)

Figure 2 – Locations of Papillary Fibroelastoma

Location	% Present
Aortic valve	44%
Mitral valve	35%
Tricuspid valve	15%
Pulmonary valve	8%
Left ventricle	9%
Left atrium	<2%
Atrial septum	
Right Ventricle	

Figures represent 611 cases reviewed. The total is > 100% because 6.2% had tumors in multiple sites (one patient had 8 tumors at various locations).

speckled with echolucencies near the edges caused by the "fronds" or papillary projections on the surface of the tumor. Transesophageal echocardiography (TEE) is often required to confirm the diagnosis and best characterize the tumor. In one study of CPF > 2mm in size, the sensitivity and specificity of TTE was 88.9% and 87.8% respectively. CT or MRI can also be used to additionally define the tumor or to image coronary arteries for signs of ischemia or embolization (magnetic resonance or computed tomographic angiography). Cardiac catheterization is usually not required and carries a risk of dislodging tumor fragments or thrombi resulting in damaging emboli.

Treatment of CPF is surgical excision. Prognosis is excellent after successful excision, with several sources reporting no known recurrences. Some authors have suggested that some tumors can be monitored, with or without antiplatelet treatment. Proposed indications for surgery include a tumor that is mobile or > 1 cm in size, a young patient, low surgical risk, associated cardiac conditions that require surgery, a history of embolic complications and/or the presence of symptoms. At least one study has identified tumor location on the aortic valve as having an adjusted odds ratio of ~ 4.1 for future risk of tumor embolism.

Since surgical excision is common with CPF, we were unable to find much data on untreated tumors. One small series of 45 patients with presumed CPF by TTE followed for 552+706 days showed 3 embolic events (2 TIA, 1 CVA) for an incidence of 6.6%. Another study followed a small group of 25 patients who did not have surgery but had reported adverse outcomes. 12 had CPF-related death due to valve obstruction or coronary artery embolization. Four others had non-fatal embolization (2 coronary, 1 cerebral, 1 pulmonary).

Returning to the Case

While some case series mentioned atrial fibrillation in association with CPF, especially when arising from the mitral valve, none mentioned ventricular ectopy as a prominent feature. Sudden cardiac death did occur, and CPF was later identified on autopsy. One mechanism of sudden death was thought due to the tumor seeding emboli to the coronary arteries. These emboli may be due to thrombus forming on the surface of the tumor or tumor material detaching. Given the recent symptoms and findings in this case, it appears prudent to postpone coverage until definitive treatment has stabilized the clinical situation. ∞

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Up to Date – Cardiac tumors, last accessed 12/1/2015.

Underwriting Puzzler...

By William Rooney, MD, FAAFP, EMBA
Vice President, Medical Director

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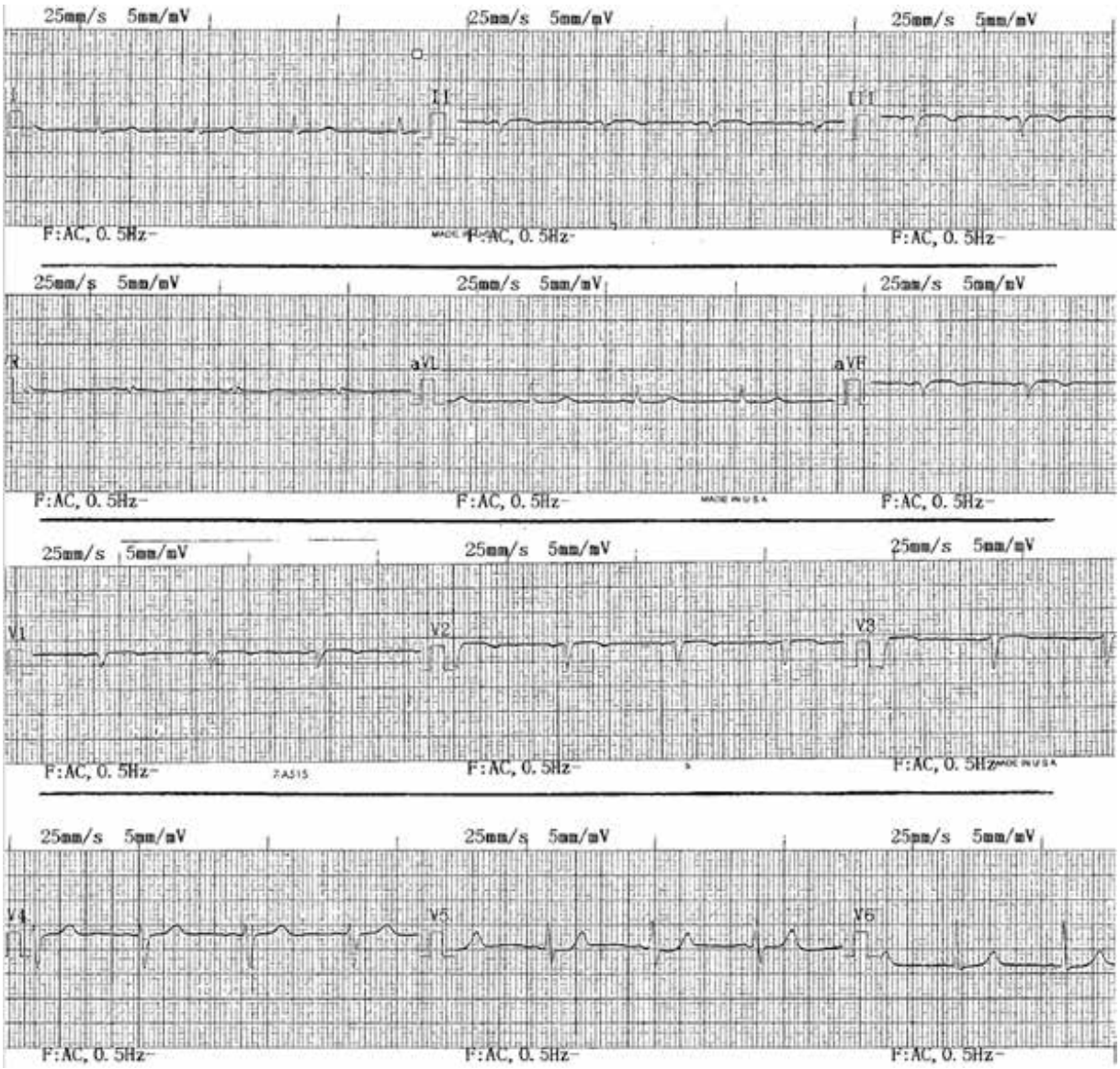
In this issue of the Puzzler Dr. Rooney presents another EKG. What is the major abnormality presented in this EKG?

To find the answer, be sure to visit the *Housecalls* page on www.scorgloballifeamericas.com.
Click on the "December Puzzler" Powerpoint presentation to confirm your findings. ∞



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The upgrade of our rating to AA- by S&P and Fitch* demonstrates the relevance of SCOR's business strategy, which continues to withstand the current macroeconomic and market environment. It confirms SCOR as a Tier 1 global reinsurer. The Group's strength is a clear benefit for our clients."

Denis Kessler
Chairman & Chief Executive Officer

* Fitch on July 21, Standard & Poor's on September 7, 2015.

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