Welcome to SCOR’s Housecalls
By Richard Braun, M.D.
Vice President & Chief Medical Officer

This issue marks the first issue of Housecalls under the SCOR banner. Incorporating the Housecalls newsletter into SCOR’s existing newsletter offering reinforces our commitment to our clients, with a periodical focused on real-world issues that confront underwriters and medical directors.

Similar to our production of The Messenger we intend to provide clients both print copy and electronic versions of Housecalls. If you have received this issue you already are on the mailing list to receive future issues. We will also use our NewsBreak email alert to provide links to case studies featured in the current issue.

We are excited about continuing and expanding on this newsletter. In future issues you will see new contributing authors in addition to our regular writers. We also will explore non-medical cases, such as financial underwriting. Still, our readers should recognize the same approach to content that has made Housecalls a valued newsletter.

In this issue we examine the case a 38 year-old male applicant who we discover suffers from dilated cardiomyopathy, and how we should approach this candidate from a medical and risk perspective. We also address autoimmune chronic urticaria as evidenced in a 39 year-old female life insurance applicant.

Dr. Rooney presents another “Underwriting Puzzler,” related to an ECG of an applicant with an admitted history of a “Mustard Procedure.” Feel free to try your hand at our puzzler – we’ll provide the answer in the next issue.

On behalf of the entire SCOR Medical and Underwriting teams, we welcome you to the new, yet familiar Housecalls. Please feel free to contact me or anyone on our medical and underwriting team with questions or comments.

This Issue

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By William Rooney, MD, FAAFP, EMBA
Medical Director, Vice President.
A 38 year-old man applies for life insurance. He states that he was in good health until approximately 6 months prior to application. Medical records reveal that at that time he presented to his doctor complaining of being very tired. On exertion he noticed chest pain and shortness of breath accompanied by cold sweats. Family history was significant for “heart disease” in his father, who died in his late fifties.

The proposed insured was admitted to the hospital and serial cardiac enzymes were normal. An ECG was normal. A Lexiscan stress was performed and was interpreted as a 43% left ventricular ejection fraction (LVEF), diffuse hypokinesis compatible with cardiomyopathy, a prominent apical cleft, and a diaphragmatic artifact. Continued evaluation included an echocardiogram that showed a generalized hypokinesis of the left ventricle and an LVEF of 45-50%. The echo also showed normal thickness of the left ventricular septum and posterior wall, normal valve structure and function, and a pulmonary artery systolic pressure (PASP) estimated at 33 mmHg.

On admission, the only blood abnormality was Alanine transaminase (ALT) of 59 U/L. Admission B-type Natriuretic peptide (BNP) was normal at 7 pg/ml. He was diagnosed with cardiomyopathy and treated with Ibuprofen and Enalapril. A cardiac catheterization report dated about one week after the initial hospital discharge was also in the records. It showed “normal” coronaries and mild inferior left ventricular hypokinesis with an estimated LVEF of 50-55%. No follow up medical records were included. Abnormalities on the insurance labs included aspartamine transaminase (AST) of 63 U/L, ALT of 137 U/L, Gamma-glutamyltransferase (GGT) of 70 U/L.

Q: What are the considerations and mortality implications of cardiomyopathy?

Answer: For classification purposes cardiomyopathies can be divided into Hypertrophic (those that exhibit thickened heart walls), or Dilated (those having normal or thin heart walls that are not contracting adequately, resulting in a reduced LVEF). The current case is one of dilated cardiomyopathy (DCM). The most common cause of DCM in the US is coronary artery disease (CAD) and ischemia. If you remove systemic and mechanical causes of dilated cardiomyopathy, like hypertension, CAD, valvular abnormalities, and pericardial diseases, then estimations of the prevalence of cardiomyopathy vary from 14 to 36 adults per 100,000 in the U.S. The yearly incidence in adults is estimated at 7 per 100,000, but may be underdiagnosed. In adults, dilated cardiomyopathy arises more often in men.

In the majority of cases of non-ischemic,
dilated cardiomyopathy, the cause is never determined. Some estimates suggest that the familial type is a cause in 20-48% of all cases. One study looked at initial cases of non-ischemic, dilated cardiomyopathy, and subsequently screened first degree relatives for left ventricular dysfunction. Twenty percent of the probands had family members with evidence of cardiomyopathy. The predominant mode of inheritance is autosomal dominant, but can be X-linked, autosomal recessive, or mitochondrial. A number of genetic abnormalities have been identified in dilated cardiomyopathy. Most affected genes are encoding for either cytoskeletal or sarcomeric proteins, which are basic structural proteins in the heart muscle. The yield for genetic testing in dilated cardiomyopathy in adults is low, 20% or less, when screening for a large number of genes. The younger the patient with DCM, the more likely that a genetic cause will be investigated, but hereditary DCM can manifest up through age 60. Lower LVEF and the presence of ventricular arrhythmia predict a higher risk of sudden cardiac death.

Another common cause for non-ischemic dilated cardiomyopathy of adults in Western Society is alcoholism. Alcohol has been estimated to cause 21-36% of cases. More than 80% of these cases occur in men. Individuals consuming > 90 grams of alcohol (7+ drinks) per day for more than 5 years are at risk of developing alcoholic cardiomyopathy (40%-50% less is required in women). And while less than 5%-10% of alcoholics ever develop DCM related congestive heart failure, 90-95% of alcoholics will have “mild” abnormalities of myocardial contractile function. With abstinence from alcohol, the cardiac function can return to normal over a period of 1-2 years. But, with a return to drinking, the DCM is likely to recur. The mortality with continued alcohol abuse has been reported at ~50% in four years.

It is most likely that infectious pathogens cause the majority of the remaining cases of non-ischemic adult DCM. Worldwide, Chagas’ disease is the most common infective endocarditis. It is a parasitic disease primarily seen in endemic, rural areas. Viral infections are the most likely cause of infectious myocarditis in the Western countries. Viruses causing myocarditis, identified through endomyocardial biopsy, include parvovirus B19, adenovirus, coxsackievirus B, influenza A, human herpes virus 6, cytomegalovirus, Epstein-Barr virus, herpes simplex virus type I, HIV, and Hepatitis C virus (HCV). Symptoms may be mild and mimic other illnesses. In autopsy studies of sudden death in young people up to 12% will have evidence of myocarditis. In myocarditis the ECG often shows nonspecific changes of ST segments and T waves. On echocardiography there is evidence of reduced LVEF with or without dilatation, and regional wall motion abnormalities are common. Cardiac troponins are often elevated, while Creatine Kinase-MB (CK-MB) is less sensitive. Endomyocardial biopsy is generally reserved for those with refractory heart failure. Giant cell myocarditis should be considered when ventricular tachycardia is a prominent feature of the presentation. It only occurs in 10-20% of biopsied cases, but is usually fatal without heart transplantation. In general with myocarditis, mild cases with minimally reduced LVEF often improve within a few weeks. If the LVEF is more severely affected (<35%), it can lead to a chronic DCM with a poor prognosis.

The remainder of non-ischemic DCM

DCM Causes
- Genetic abnormalities
- Alcohol
- Infectious pathogens
- Other less common causes include chemotheraphy, radiotherapy, toxins, autoimmune disorders, endocrinopathies, nutritional deficiencies, pregnancy, and tachycardia-mediated cardiomyopathy.
may be attributed to less common causes such as: chemotherapy; radiotherapy; toxins (cocaine, cobalt, etc.); autoimmune disorders; endocrinopathies (pheochromocytoma, hypothyroidism, etc.); nutritional deficiencies; pregnancy; and tachycardia-mediated cardiomyopathy.

Going forward, cardiovascular magnetic resonance (CMR) imaging may be a useful way to identify myocardial fibrosis, which predicts mortality and sudden death in non-ischemic DCM. A study of 472 patients found that fibrosis by CMR conferred a hazard ratio of 2.43 for all-cause mortality when compared to DCM with no fibrosis (after adjustment for LVEF and other risk factors). LVEF at presentation and the presence of fibrosis were the most powerful predictors of all-cause mortality in this study with a median follow-up of 5.3 years.

Returning to the Case

As in many cases of cardiomyopathy, we do not have a clear cause. Looking at the top 3 causes of non-ischemic DCM in Western countries – hereditary; alcoholic; and infectious – any could apply. The family history of early death from “heart disease” is without sufficient detail, so hereditary cardiomyopathy is a possibility. Initial response to treatment does not rule out the possibility that an underlying familial cardiomyopathy might exist. There was no detailed record of alcohol use, and the elevated liver function test on admission and the insurance labs warrant further inquiry. A transient viral myocarditis is also a possibility, although the normal troponins on the original admission could be counted against that diagnosis.

It would appear prudent to await further follow-up to include repeat echocardiography and investigation of the liver test elevations before considering the diagnosis and ultimate prognosis in this case.

References


Case Two: Autoimmune Chronic Urticaria

A 39 year-old woman applies for life insurance. Her medical records reveal 2 normal deliveries in the past 5 years with the last about 1 year prior to application. She also had a history of thyroitis followed by hypothyroidism at age 35. Six months prior to application she began experiencing itchy red wheals appearing on her chest and shoulders and disappearing within 24 hours. The wheals recurred several times per week. Her primary care provider diagnosed hives, and started non-drowsy, 2nd generation antihistamines. He also suggested new hypoallergenic soaps, detergents, and careful monitoring of “trigger” foods.

Despite these efforts, the symptoms continued and she was referred to an Allergist. He diagnosed Chronic Autoimmune Urticaria. He prescribed a different 2nd generation antihistamine and added Cyclosporine to her regimen. Her last visit, one month prior to application, revealed good control of the symptoms, and her doctor advised stopping the Cyclosporine and increased the dosage of the antihistamine.

Q: What is Autoimmune Chronic Urticaria, and what are the mortality implications?

A: Urticaria (hives) is a common skin condition that will be experienced by ~ 20% of the population during their lifetime. Atopic (allergic) individuals are more prone to develop urticaria. A hive is a circumscribed, edematous, usually itchy, red or white plaque that changes in size over the few hours or day that the lesion exists. Usually new hives appear as older ones resolve. Hives occur because of the release of histamine by Mast cells. The histamine causes skin capillaries to dilate and leak protein-rich plasma into the surrounding tissue. If this process is superficial, the result is hives. If the deeper dermis and subcutaneous tissue is affected, it is called angioedema. The swelling resolves as the plasma is gradually resorbed.

Most episodes of urticaria are acute and caused by drug reactions, foods & food additives, contact with triggering antigens, infections, insects, etc. Only in ~ 0.5% of the population does the disorder become chronic, defined as lasting > 6 weeks. In ~ 45% of these chronic cases the cause is diagnosed as autoimmune, although in a majority the exact cause is never determined.

In individuals with chronic urticaria (CU) the extent of the work up should be guided by the history and physical. Complete Blood Count (CBC), Erythrocyte Sedimentation Rate (ESR), Hepatitis B & C titers, and Antinuclear Antibody (ANA) are often performed. Depending on the results, more specialized testing for ova & parasites, serum complement levels, rheumatoid factor, thyroid antibodies, autoantibodies to IgE, or skin biopsies might be needed. Occasionally testing for physical causes of urticaria, such as pressure, ultraviolet light, or cold is performed. And allergy testing for reactions to foods and common antigens may also be performed.

Treatment, beyond the avoidance of suspected drugs and allergens, begins with non-drowsy, 2nd generation antihistamines (Zyrtec, Claritin, Allegra, Clarinex, Palgic, Xyzal) often in higher than recommended doses. A short course of systemic corticosteroids can be considered for symptom relief, but is not recommended for long periods. Addition of H2 antihistamines (Tagamet, Pepcid, Axid, Zantac) may have some limited benefit. Cyclosporine has been effective in chronic urticara that was unresponsive to antihistamines. More recently, Omalizumab (an anti-IgE monoclonal antibody) was reported to be effective in diminishing clinical signs and symptoms in patients resistant to antihistamines.

Urticaria can interfere with the quality of life, causing stress in areas of work and family, but are not considered life-

Autoimmune Chronic Urticaria

- Chronic is defined as lasting >6 weeks
- ~ 45% of chronic cases the cause is diagnosed as autoimmune
- Majority the exact cause is never determined
threatening. Angioedema, however, can cause swelling of the lips, tongue, and airway and may be life threatening in some cases. A detailed discussion of angioedema will have to wait until a future publication.

Two instances where urticaria may be life threatening would be: exercise induced urticaria - which can be associated with symptom progression to laryngeal edema, hypotension and shock; and Schnitzler syndrome – a disorder characterized by urticaria, fever, bone pain, arthralgias, arthritis and monoclonal IgM gammopathy. Up to 15% or more with Schnitzler syndrome will eventually develop a lymphoproliferative disorder.

Returning to the Case
The history of thyroiditis is interesting since one large study found that females with CU were 23 times as likely to have hypothyroidism as were females in the general population. Some authors suggest close monitoring of thyroid hormone levels and possibly adding to the dose as a way to reduce the urticaria. That same study found an increased risk of the development of several autoimmune diseases (rheumatoid arthritis, Type I diabetes, Sjogren syndrome, Celiac disease, Systemic Lupus) within the 10 years following the diagnosis of CU, when compared to the general population. However, these diagnoses still remain relatively rare. In the case presented, we would not anticipate any additional mortality risk.

References


Kaplan A. What the first 10,000 patients with chronic urticaria have taught me: A personal journey. *J Allergy Clin Immunol* 2009;123:713-7.
Underwriting Puzzler...

By William Rooney, MD, FAAFP, EMBA

Dr. William (Bill) Rooney is Medical Director, Vice President. Dr. Rooney's responsibilities include facultative case review work, researching and updating The Guide, researching and writing articles for a variety of SCOR publications and more. He earned a Medical Degree from the University of Missouri – KC (1981) & an Executive Master's in Business Administration from Benedictine College in Atchison, Kansas (2009). He is Board Certified in Family Medicine with the American Board of Family Medicine.

This issue’s Underwriting Puzzler involves interpreting an ECG performed on a 31 y/o male who is applying for life insurance. To try your hand at the Puzzler, download the Powerpoint show from our website at www.scorgloballifeamericas.com.

In the policy application the applicant mentions having a “Mustard Procedure” as a child. How would you interpret this ECG? After inspecting it for technical issues, you will be able to examine the ECG using our usual routine:

1. Rhythm
2. Axis
3. Intervals
4. Q waves
5. Hypertrophy
6. ST/T waves

If you have any questions, ideas, or if you would like to talk with Dr. Rooney, email him at: brooney@scor.com

To download this edition of the Puzzler, log on to the SCOR Global Life Americas website (www.scorgloballifeamericas.com). Move your cursor to the Publications tab and choose Housecalls from the drop down menu. You will see the latest Puzzler on the 2014 tab, which is displayed when you open the Housecalls page.
Expert Content on Medical & Underwriting Topics

If you would like to review or print case studies published in previous issues of Housecalls, you can access them at www.scorgloballifeamericas.com. Click the “Publications” tab and then select “View all issues of Housecalls.” All back issues are archived here. Figure 1 on the right lists Case Studies by publication date.

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