Acquired Heart Failure in Children

Developed by Umairah Boodoo, BSc., and Dr. Tapas Mondal, MD FRCPC for PedsCases.com

Introduction

Hi everyone and welcome to another PedsCases.com podcast! Today's podcast will be addressing acquired heart failure in children. My name is Umairah Boodoo and I am a medical student at McMaster's Michael G. DeGroote School of Medicine in Ontario, Canada. This podcast was developed for pedscases.com with guidance from Dr. Tapas Mondal, Associate Professor and Pediatric Cardiologist at McMaster University.

Objectives

By the end of this podcast, listeners will be able to:

1. Define heart failure and the etiologies of acquired heart failure.
2. Describe the clinical manifestations of heart failure, noting distinctions among different age groups.
3. Explain the diagnostic evaluation for pediatric patients with heart failure.

Please note that this podcast will not address the management of pediatric heart failure.

Introduction to Heart Failure[3]

We will use a case to anchor this podcast. I will be uncovering the case bit by bit as we progress and there will be some prompting questions. It would be a good idea to pause the podcast periodically to think of your answers. I will then provide answers to the prompting questions once we have covered that objective. Let's kick things off by painting a clinical vignette!

A previously healthy, 3-year-old child is brought to the ED by her parents with a chief concern of vomiting. She has had three episodes of non-bilious, non-bloody emesis over the past day and now appears fatigued. She has no fever, diarrhea, abdominal pain, rashes, or upper respiratory symptoms. Her past medical and family history are unremarkable.

This is your first prompting question: what is your differential diagnosis?

Does heart failure come to mind at all? As a listener, I want you to think about why or why not. We will circle back to this idea shortly once we have learned more about pediatric heart failure.

Heart failure (HF) results from structural or functional cardiac abnormalities that impair the ventricles' ability to either fill with and/or eject blood. As a result, the heart cannot maintain adequate cardiac output to effectively perfuse vital organs and tissues. HF can occur in children who either have a structurally normal heart or who have congenital heart disease. This podcast will specifically focus on HF in children with anatomically normal hearts, i.e., acquired HF.

An understanding of pediatric heart failure is important for all physicians as 87% of cases of new-onset HF only reach a diagnosis when the patient is in a state of severe decompensation. In addition, less than 50% of children who present with symptomatic HF survive for 5 years without cardiac transplantation. Thus, early diagnosis and effective treatment remain significant challenges. Being able to recognize heart failure begins with an understanding of the various etiologies, which brings us to our next section.

Etiologies of Acquired Heart Failure[2,3,4,5]

Most cases of acquired heart failure occur due to ventricular dysfunction, which leads to impaired ejection of blood from the ventricle. Ventricular dysfunction can result from myocarditis, cardiomyopathy, myocardial ischemia or infarction, arrhythmias, drugs, and non-cardiac causes. Let's go through each one.

Myocarditis

Myocarditis is characterized by inflammation of the myocardium with necrosis of the myocytes. It is usually due to a viral pathogen, with the most common ones being adenovirus, coxsackievirus, parvovirus, and influenza virus. Recently, acute myocarditis has also been seen as a complication of SARS CoV-2 or COVID-19 infection. The main characteristic of COVID-19 myocarditis has been its association with major multisystem inflammatory syndrome, or MIS-C. Cases of myocarditis have also been reported post-mRNA vaccines.

Less commonly, myocarditis can occur secondary to a bacterial, drug, or toxic exposure. Although the inciting agent causes the initial damage, molecular mimicry between the

agent and myocytes leads to an autoimmune response that results in inflammation of the myocardium and disease progression. Acute myocarditis may be followed by a complete recovery of left ventricular function or may result in a secondary dilated cardiomyopathy with chronic HF. Since the most common etiology of pediatric myocarditis is viral, a common finding in the history is a recent respiratory or, less commonly, gastrointestinal illness in the past two weeks. Patients will typically have prodromal symptoms such as myalgia, malaise, and fever prior to the onset of HF. Another common symptom is chest pain.

Cardiomyopathy

Next, we will talk about cardiomyopathy (CM), which is the most common cause of acquired heart failure in children. CM is a disease of the heart muscle. The estimated incidence is approximately 1 case per 100,000 children per year. There are several types of cardiomyopathies: dilated, hypertrophic, and restrictive.

Of the CMs, dilated cardiomyopathy (DCM) is the most common phenotype and accounts for 50-60% of cases. DCM is characterized by dilation and impaired contraction of one or both ventricles, resulting in systolic dysfunction. Commonly implicated viruses include parvovirus B19, HHV-6, coxsackievirus, influenza virus, CMV, and HIV. These viruses can cause myocarditis and subsequent development of DCM. There is also a genetic basis to DCM. Genetic DCM usually follows an autosomal dominant inheritance pattern, although other modes of inheritance have been described.

Hypertrophic cardiomyopathy (HCM) is the second most common phenotype, accounting for 25-40% of all cases. In HCM, hypertrophy of the left ventricle leads to a normal or reduced left ventricular volume and diastolic dysfunction. There are many causes of HCM including syndromal abnormalities, myocardial glycogen or lysosomal enzymopathies, and sarcomeric mutations. Left ventricular systolic function is usually preserved in children with HCM and thus HF is rare. However, syncope or presyncope related to left ventricular outflow tract (LVOT) obstruction or ventricular arrhythmias is well described in school-aged children and adolescents. In LVOT obstruction, there is systolic anterior motion (SAM) of the mitral valve. When high velocity blood is ejected from the left ventricle during systole, the mitral valve is pushed towards the septum, narrowing the outflow tract and creating impedance to blood flow.

Left ventricular noncompaction accounts for 9% of pediatric CM cases. In this phenotype, there is a hyper-trabeculated or “spongy” left ventricular endomyocardial layer, within an outer thin-walled compacted layer of muscle. During normal cardiac

development, the myocardium is initially trabeculated with finger-like projections. As the coronary vasculature develops to provide blood flow to the myocardium, the left ventricular trabeculations regress and the myocardium undergoes the process of compaction. This occurs between gestational weeks 5 - 8. When this process does not occur, the result is left ventricular noncompaction. This phenotype is also frequently encountered in the setting of decompensated heart failure, similar to DCM.

Lastly, restrictive cardiomyopathy (RCM) and other CM types account for 3% of cases. RCM is characterized by nondilated, non-hypertrophied ventricles with impaired ventricular filling. RCM is much less common than either DCM or HCM outside the tropics, but is a frequent cause of death in Africa, India, South and Central America, and Asia, due to the high incidence of endomyocardial fibrosis in those regions. The cause of endomyocardial fibrosis is unknown, but contributing factors may include infection, environmental exposure, immunologic processes, and genetics.

Myocardial Ischemia/Infarction

Next, we will touch on myocardial ischemia, which is uncommon in the pediatric population. Rarely, coronary vasculitis due to Kawasaki disease may present with myocardial ischemia and left ventricular dysfunction. In addition, patients with an anomalous left coronary artery arising from the pulmonary artery (ALCAPA) usually present with symptoms of infarction and are often in heart failure. Lastly, infarction due to premature atherosclerotic disease is quite rare in childhood but can occur in homozygous familial hypercholesterolemia.

Arrhythmias

A complete heart block, which occurs when atrial impulses fail to reach the ventricle, may lead to HF if the junctional escape rhythm is not fast enough to maintain adequate cardiac output. In addition, supraventricular and ventricular arrhythmias, such as supraventricular tachycardia, atrial flutter, or ectopic atrial tachycardia, can lead to HF.

Drugs

There are also several drugs that have been implicated in pediatric HF, the most common of which is anthracycline. This cardiotoxic drug is a chemotherapy agent and pediatric cancer patients who have been treated with anthracycline carry a lifelong risk of developing ventricular dysfunction and HF. Thus, oncology patients with current or previous treatment with anthracycline will benefit from HF screening through periodic echocardiographic evaluation, regardless of the presence or absence of symptoms.

Developed by Umairah Boodoo and Dr. Mondal for Pedscases.com
December 2022

Non-Cardiac Causes

Non-cardiac causes of HF include those that increase oxygen demand (sepsis, HIV infection), reduce oxygen carrying capacity (severe anemia), increase afterload (obstructive sleep apnea and bronchopulmonary dysplasia leading to pulmonary hypertension), or increase preload (chronic kidney disease).

We just covered a lot of information, so let's do a quick recap! HF results from structural or functional cardiac abnormalities that impair the ventricles' ability to either fill with and/or eject blood, leading to poor cardiac output. Important etiologies include myocarditis, cardiomyopathy, myocardial ischemia or infarction, arrhythmias, drugs, and non-cardiac causes. Our next section will focus on signs and symptoms.

Signs and Symptoms

The clinical picture of heart failure results from decreased cardiac output or from compensatory mechanisms to correct a state of low cardiac output. It is a syndrome that involves multiple organ systems. In pediatrics, the symptoms will vary with the age of the patient - thus, we will break it down by age group.

Infants and young children presenting with HF may display the following signs: tachypnea, diaphoresis during feeds, feeding difficulties (prolonged feeding time, decreased feed volumes, vomiting, feeding refusal), pallor, easy fatigability, irritability, and poor weight gain. Less commonly, patients may have cyanosis, facial edema, dependent edema, and ascites. This is in stark contrast to adult heart failure, where the more common symptoms do include edema and ascites.

In older children and adolescents, common symptoms include GI symptoms such as abdominal pain, nausea, vomiting, poor appetite, and poor weight gain. Respiratory symptoms may include easy fatigability, recurrent or chronic cough with wheezing, orthopnea, dyspnea, and effort intolerance. The uncommon symptoms include palpitations, chest pain, dependent edema, and ascites.

Remember our 3-year-old child with 3 episodes of vomiting and fatigue? Differential diagnoses could include severe dehydration secondary to gastroenteritis or other viral illness, conduction block, or toxic ingestion - perhaps an acetylcholinesterase inhibitor. However, now that we know that young children can present with non-specific symptoms such as vomiting and easy fatigability, we should include heart failure in our differential!

Developed by Umairah Boodoo and Dr. Mondal for Pedscases.com
December 2022

Physical Exam[3]

Let's continue the story with a physical exam…

On exam, the patient is somnolent but responsive to tactile stimulation. Her extremities are cool and mottled, with a delayed capillary refill. Auscultation reveals clear lungs and normal heart sounds with no murmurs, gallops, or rubs. Her heart rate is 40 beats per minute.

What are the most concerning findings on this patient's physical exam? What do they indicate?

The findings on the physical exam in a heart failure patient will be related to the degree of decreased CO and pulmonary or systemic congestion. In this section, we will talk about the physical exam findings in the context of its pathophysiology.

1. Decreased Cardiac Output
    a. Tachycardia: cardiac output depends on heart rate and stroke volume. Thus, by increasing HR, CO can be improved
    b. Signs of poor perfusion: cool and mottled extremities, delayed capillary refill, diminished peripheral pulses, low systolic blood pressure
    c. Extra heart sound: S3 may be heard in patients with diminished CO or volume overload (gallop rhythm)
2. Pulmonary congestion
    - Pulmonary edema prevents air from reaching pulmonary capillaries, resulting in a V/Q mismatch → perfusion without ventilation
    - Tachypnea
    - Increased work of breathing: retractions, use of accessory respiratory muscles, grunting, nasal flaring
    - Auscultatory findings: wheezing and rales, which is more common in older children as compared to infants
3. Systemic Congestion
    a. Ascites
    b. Hepatomegaly
    c. Bilateral pitting edema

One way to organize a patient's physical exam findings is to think about their temperature and how "wet" they are.

- A patient who is warm and dry has neither poor perfusion nor congestion
- A patient who is warm and wet has adequate perfusion and congestion

- A patient who is cold and dry has poor perfusion and no congestion
- A patient who is cold and wet has poor perfusion and is congested

Looping back to the case, there are several aspects of this patient's presentation that are concerning. She is bradycardic as a normal heart rate for a 3-year-old child is between 80 - 130 beats per minute.

We should note that tachycardia is more commonly seen in an acutely ill patient as it relates to fever, fear, dehydration, or pulmonary pathology. If a child with tachycardia and poor perfusion worsens with fluid administration (i.e., they become more tachycardic or show signs of worsened perfusion/BP readings), this is highly concerning for heart failure. This is because their cardiac output is so poor that they cannot tolerate the extra volume. **Thus, it is important to note that tachycardia can be seen in a failing heart due to decreased ventricular contractility or arrhythmias.** This is in contrast to a child with dehydration, for example, whose heart rate should stabilize and perfusion improve with fluid resuscitation. Bradycardia is more rarely seen and warrants concern for cardiac dysfunction.

Furthermore, this patient's extremities are cool and mottled with delayed capillary refill, suggesting diminished peripheral perfusion. She also presents with altered mental status. Thus, this child is hemodynamically unstable and we would need to stabilize her before we proceed with diagnostics.

The patient is given a normal saline bolus, started on an isoproterenol drip, and given 6L of oxygen by face mask. Her heart rate increases to 140 beats per minute and she maintains an oxygen saturation of 100%.

Diagnostics[3]

Now that we have stabilized the patient, we are ready to think about ordering diagnostic tests. The diagnosis of HF is based on a combination of clinical, echocardiographic, and laboratory findings. The unstable patient who presents with cardiogenic shock must first and foremost receive prompt treatment to restore adequate perfusion before investigating the underlying cause of HF. We have managed to do that with our patient!

A **chest radiograph** is the first-line investigation in children with suspected HF. Signs of HF that may show up on the radiograph include cardiomegaly and pulmonary congestion (pulmonary interstitial edema and pleural effusion).

The next investigation to order is an **ECG**. The most common finding on ECG will be sinus tachycardia. However, ST segment and T wave abnormalities are common in all forms of cardiomyopathy and myocarditis. Inferolateral Q waves are also commonly seen in patients with ALCAPA. In ventricular hypertrophy, such as in cases of HCM or DCM, there may be increased QRS voltage. Conversely, in cases of myocardial edema or pericardial effusion, which may be seen in myocarditis, there may be decreased QRS voltage.

Moving on to laboratory tests, **brain-natriuretic peptide (BNP)** levels are helpful in determining the severity of HF. BNP levels correlate negatively with ejection fraction and are therefore a good marker of ventricular dysfunction. It is also useful in distinguishing HF from respiratory or other non-cardiac disease and should be used as a confirmatory test in the acute evaluation of pediatric HF.

Troponin is a sensitive biomarker for myocyte injury and is elevated in myocarditis and myocardial ischemia. We also need a **complete blood count** as anemia can exacerbate the severity of HF symptoms and, if present, should be worked up to determine the underlying cause.

Serum **chemistries** will help us establish baseline electrolytes prior to initiating therapy which may include diuretics or ACE inhibitors. In severe HF, there may be hyponatremia. **Liver function studies** may be elevated due to hepatic congestion and right heart failure. Additionally, **glucose, acid-base status, urea, creatinine, and thyroid hormone** should be assessed at initial presentation and as needed to monitor the patient's ongoing clinical status.

Once the patient is medically stabilized, further investigations will help us determine the underlying etiology. An **echocardiogram** will establish whether the patient has a structurally normal heart or underlying congenital heart disease. It will also assess ventricular size and function, with ventricular dysfunction defined as an ejection fraction of <56% or fractional shortening <29%. Cardiomegaly is highly predictive of ventricular dilation on echocardiography, with a high specificity and negative predictive value. Cardiomegaly may be seen in DCM of the left ventricle. In RCM, biatrial enlargement may be seen.

Now, when would we consider doing a **cardiac MRI**? Cardiac MRI is showing increasing diagnostic potential in the primary CMs and myocarditis. It can be used as a less invasive option versus endomyocardial biopsy to identify inflammation in myocarditis. However, important limitations include the need for sedation and inaccessibility at certain centers.

Developed by Umairah Boodoo and Dr. Mondal for Pedscases.com
December 2022

Ambulatory ECG or **Holter monitoring** might be indicated in children with symptoms suggesting arrhythmia, such as palpitations or syncope. It may also be indicated in higher arrhythmia risk groups, such as patients with primary RCM or HCM, with tachycardia-induced CM, or those on antiarrhythmic therapy.

Exercise testing can also be useful in known or suspected CM to assess functional class and help with risk stratification. **Genetic testing**, particularly for HCM, can help us determine if there is a genetic component.

In myocarditis, **blood cultures** and **viral PCR** can help identify an underlying infectious etiology.

Now that we are equipped with this knowledge, we can order tests for our patient.

ECG monitoring reveals intermittent third-degree heart block with bradycardic episodes, resulting in decreased responsiveness.

A chest radiograph shows no cardiomegaly, effusion, pulmonary infiltrate, or edema.

A VBG reveals a metabolic acidosis, with a pH of 7.09 and a base deficit of 16. Laboratory values show a BNP of 1150 , troponin I 50.54 (N: <9 ng/L), and CK-MB of 65 (N: 0.79 - 4.13 ug/L), indicating myocardial damage.

Ultimately, the patient is transferred to the pediatric ICU for ongoing monitoring and treatment. Blood cultures and viral PCR come back negative.

An echocardiogram reveals normal ventricular contractility with left ventricular wall edema and an abnormal shortening fraction of 29%.

Rheumatologic studies are significant for low complement levels.

A cardiac catheterization and biopsy showed lymphocytic infiltration with myocyte necrosis, myocardial edema, and early interstitial collagen deposition (however, we should note that biopsy is not commonly done for diagnostic purposes).

Developed by Umairah Boodoo and Dr. Mondal for Pedscases.com
December 2022

Case Take-Aways[1]

This would be a good time to summarize the case! A previously healthy, 3-year-old child comes in with 3 episodes of non-bloody, non-bilious emesis and fatigue. She has no other symptoms. On exam, she is initially bradycardic, with cool extremities and mottled skin, suggesting poor perfusion. After fluid resuscitation, IV administration of a beta-agonist, and supplemental oxygen, her heart rate stabilizes and she maintains her oxygen saturation well. Diagnostic tests reveal intermittent third-degree heart block with bradycardic episodes, a metabolic acidosis, and elevated BNP/troponin/CK-MB, indicating myocardial damage. A biopsy shows lymphocytic infiltration with myocyte necrosis and myocardial edema. Chest radiograph, blood cultures, and viral PCR are negative.

Now that we have a comprehensive picture, what is your diagnosis?

Ultimately, this patient was treated with IVIG and methylprednisolone for suspected myocarditis with improvement of her symptoms and lab values. She is discharged on day 12 with captopril and a prednisone taper. In her follow-up appointments at the cardiology clinic, she has a normal exam, echocardiogram, and exhibits a return to normal behaviour.

An important take-away for this case is that myocarditis should always be considered in the differential diagnosis of children who present with a viral prodrome and/or nonspecific respiratory or abdominal symptoms associated with hemodynamic instability or cardiac rhythm abnormalities.

Diminished peripheral pulses or cool, mottled extremities suggest poor peripheral perfusion, which may be due to poor ventricular function or decreased cardiac output, even in the setting of vomiting and decreased oral intake.

Initial testing should include a 12-lead ECG, chest radiograph, and cardiac enzymes if heart failure is suspected. An ECG may show features of congenital or ischemic heart disease, arrhythmia, and pre-excitation, although the most common finding is sinus tachycardia. A chest radiograph may show cardiomegaly or pulmonary edema but can also be completely normal. Elevations in cardiac enzymes can help delineate the severity of disease and prognosis.

Developed by Umairah Boodoo and Dr. Mondal for Pedscases.com
December 2022

Conclusion

We will wrap up this podcast by looping back to our learning objectives.

First, we set out to define HF and understand the etiologies of acquired heart failure. HF results from structural or functional cardiac abnormalities that impair the ventricles' ability to either fill with and/or eject blood, resulting in inadequate cardiac output. Heart failure in children with structurally normal hearts has various etiologies including myocarditis, cardiomyopathy, myocardial infarction or ischemia, arrhythmias, drugs, and non-cardiac causes. Myocarditis is usually caused by a preceding viral infection, such as adenovirus and coxsackievirus. Myocarditis can lead to DCM, which, along with HCM, are the most common cardiomyopathies. Myocardial ischemia is rare in the pediatric population. The most commonly implicated drug in pediatric HF is anthracycline, a cardiotoxic chemotherapeutic agent.

Secondly, we wanted to describe the clinical manifestations of heart failure, noting distinctions among different age groups. Early diagnosis of heart failure in the pediatric population begins with maintaining a high index of suspicion as it may present with a wide range of nonspecific signs and symptoms. Unlike in adults, where the most common findings on physical exam are those directly related to fluid overload, such as elevated JVP and bilateral pitting edema, these are less commonly presenting signs in the pediatric population. Thus, the clinician should start with a thorough history and physical examination while paying special attention to the presenting vital signs.

Lastly, we wanted to explain the diagnostic evaluation for pediatric patients with heart failure. Initial testing should include an ECG, chest radiograph, and cardiac enzymes. Further testing is indicated depending on the etiology of the disease. All patients with heart failure should undergo periodic follow-up echocardiography to reassess ventricular function with respect to medical therapy.

And that brings us to the end of this podcast! I hope this podcast has equipped you with the knowledge to recognize pediatric heart failure and have a robust framework for thinking through the different etiologies. Thank you to Dr. Mondal for all of his help throughout the making of this podcast and Dr. Karen Forbes for all the edits. Thanks for listening, everyone!

Developed by Umairah Boodoo and Dr. Mondal for Pedscases.com
December 2022

References

1. Caglar, D., Brown, J. C., & Klein, E. J. (2009). Illustrative presentations of the failing heart in the acutely ill child: Two case reports. *Cases Journal*, *2*(1). https://doi.org/10.1186/1757-1626-2-9326
2. Cooper, L. T. (2019, May 19). *Definition and classification of the cardiomyopathies*. UpToDate. Retrieved April 14, 2022, from https://www.uptodate.com/contents/definition-and-classification-of-the-cardiomyopathies?search=dilated+cardiomyopathy&source=search_result&selectedTitle=4~150&usage_type=default&display_rank=4#H6
3. Kantor, P. F., Lougheed, J., Dancea, A., McGillion, M., Barbosa, N., Chan, C., Dillenburg, R., Atallah, J., Buchholz, H., Chant-Gambacort, C., Conway, J., Gardin, L., George, K., Greenway, S., Human, D. G., Jeewa, A., Price, J. F., Ross, R. D., Roche, S. L., … Wong, K. (2013). Presentation, diagnosis, and medical management of heart failure in children: Canadian Cardiovascular Society Guidelines. *Canadian Journal of Cardiology*, *29*(12), 1535–1552. https://doi.org/10.1016/j.cjca.2013.08.008
4. Tissières, P., & Teboul, J.-L. (2020). SARS-COV-2 post-infective myocarditis: The tip of covid-19 immune complications? *Annals of Intensive Care*, *10*(1). https://doi.org/10.1186/s13613-020-00717-0
5. Waigner, M., & Morgan, J. P. (2022.). *Causes of dilated cardiomyopathy*. UpToDate. Retrieved April 14, 2022, from https://www.uptodate.com/contents/causes-of-dilated-cardiomyopathy?search=dilated+cardiomyopathy&topicRef=4943&source=see_link#H17