

Chest pain in a 12-year-old boy: when is it a harbinger of poor outcome?

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Abstract Chest pain is usually a benign presentation in children who present to emergency departments (ED) or primary care centers. Unlike adults, where chest pain is commonly due to cardiac causes, in children the cause is more likely secondary to non-cardiac causes. Here we present a case of a child known to have hyper-eosinophilic syndrome (HES) who presented with sudden onset of chest pain and had a rapidly progressive and fatal outcome in the ED. We discuss the ED approach to the child with chest pain and review acute myocardial infarction (AMI) in children.

Case history and course

A 12-year-old boy known to have idiopathic HES presented to our ED with a complaint of cough, shortness of breath (SOB), and severe chest tightness for the previous 1 h. He had been diagnosed with refractory HES 4 years back, with a course complicated by multiple organ involvement. Previous medications included cyclosporine, prednisolone, hydroxyurea, and imatinib. At the time of his current presentation he was on prednisolone 10 mg t.i.d., cyclosporin A 50 mg b.i.d., hydroxyurea 750 mg o.d., and ciprofloxacin 250 mg o.d.

The chest tightness was acute and later became more consistently associated with the chest pain. The pain was localized to the central right side and although not quantified was severe enough to make him cry. It was non-radiating in character and aggravated by breathing. The cough was described as productive of yellowish phlegm without blood. He denied fever or sweating.

His vital signs were as follows: heart rate 124 bpm, blood pressure 108/92 mmHg, respiratory rate 32 breaths/min, temperature 36.3°C. In general he appeared anxious and in significant pain, grasping his chest. Pulses were regular and prominent. He had good and equal air entry, with bilateral crackles. There was no wheezing. The heart sounds were regular S1 and S2 without any additional sounds. The chest wall was non-tender. The abdomen was non-tender and without any organomegaly. The patient was oriented and coherent; no focal deficits on cranial nerve exam. He was noted to have a chronic extensive eczematous rash involving the trunk and abdomen.

Our patient received two doses of albuterol nebulizer treatments. As the severity of the chest pain progressed, treatment with O₂ via nasal cannula was initiated and intravenous access was established.

The first ECG, done 20 min after his presentation, is shown in Fig. 1. At that time the presumptive diagnosis of AMI was entertained. Morphine 2 mg intravenously was initiated as well as aspirin 100 mg po. Nitroglycerin and heparin were also ordered but were not administered. His labs showed: WBC $22.5 \times 10^9/l$ and neutrophils 59%, hemoglobin 77 g/l (normal: 110–149 g/l), pH 7.21 (normal: 7.35–7.45), HCO₃⁻ 5.9 mmol/l, urea 4.4 μmol/l (normal: < 8 μmol/l), creatinine 59 μmol/l (normal: 53–88 μmol/l), creatinine kinase 230 units/l (normal: 40–170 units/l), troponin 2 μg/l (normal range: <0.35 μg/l). Other investigations were within normal limits.

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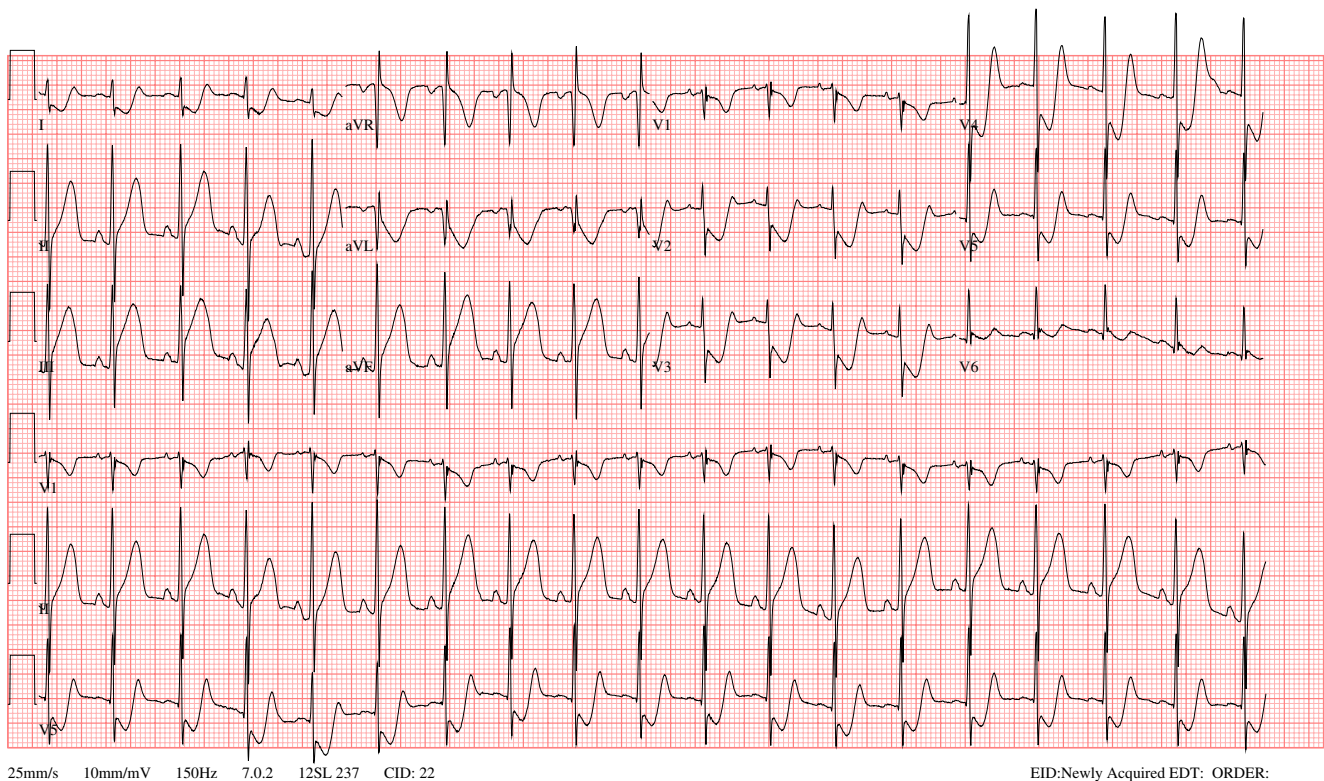


Fig. 1 First ECG done 20 min after the patient's presentation

Approximately 20 min later, the child's ECG showed the patterns in Figs. 2 and 3. The patient's condition deteriorated with the development of hypotension, weak pulses, and a decrease in level of consciousness.

Resuscitation included intubation and the activation of the advanced cardiac resuscitation protocol. He received three doses of atropine 0.5 mg, ketamine 2 mg and rocuronium 25 mg and four doses of epinephrine (0.3 mg each). His condition continued to progress without response to therapy and the patient died after developing a terminal ventricular rhythm.

Discussion

Despite the rarity of serious pathological conditions in children presenting with chest pain, the rapidity of progression of our patient's condition illustrates the need to develop a systematic approach to the child who presents with a complaint of chest pain in the ED.

ED incidence of chest pain in children is much less common (0.06%) as compared to adults (2.21%) [1–3] and occurs equally in boys and girls with a mean age of 12 years. Studies have shown that, unlike adults, the cause of chest pain in children is rarely due to cardiac causes [4], but as illustrated by our case the complaint is not always benign, and serious cardiac and noncardiac causes must be identified.

Causes of chest pain in children are diverse and the role of the ED physician is to differentiate between the minor causes and those that pose a threat to life, and to act in a timely manner to stabilize the patient [5]. A suggested way to classify this symptom is to consider cardiac and noncardiac causes of chest pain (Tables 1 and 2). These tables show the diverse causes of chest pain in children, and as such only a thorough history and physical examination with an understanding of the various etiologies will lead to the correct diagnosis of the cause of the chest pain. In a small percentage of children, laboratory or radiologic or other invasive interventions will be required to better define the cause of the symptoms.

It is important to note at this time that the history and physical examination of a child with chest pain can be particularly problematic. Firstly, parental anxiety commonly is associated with the child with chest pain. This may be due to parental concern that the child is developing an ischemic event similar to that associated with atherosclerosis in adults. Secondly, children may not be able to describe the effectively (eg. quality of pain, associated symptoms). Also, the physical examination, as always in children, can be hampered by an anxious or crying child. Therefore, the examining physician needs to make a special effort to comfort both the child and the parents to maximize the chances of a thorough history and physical examination.

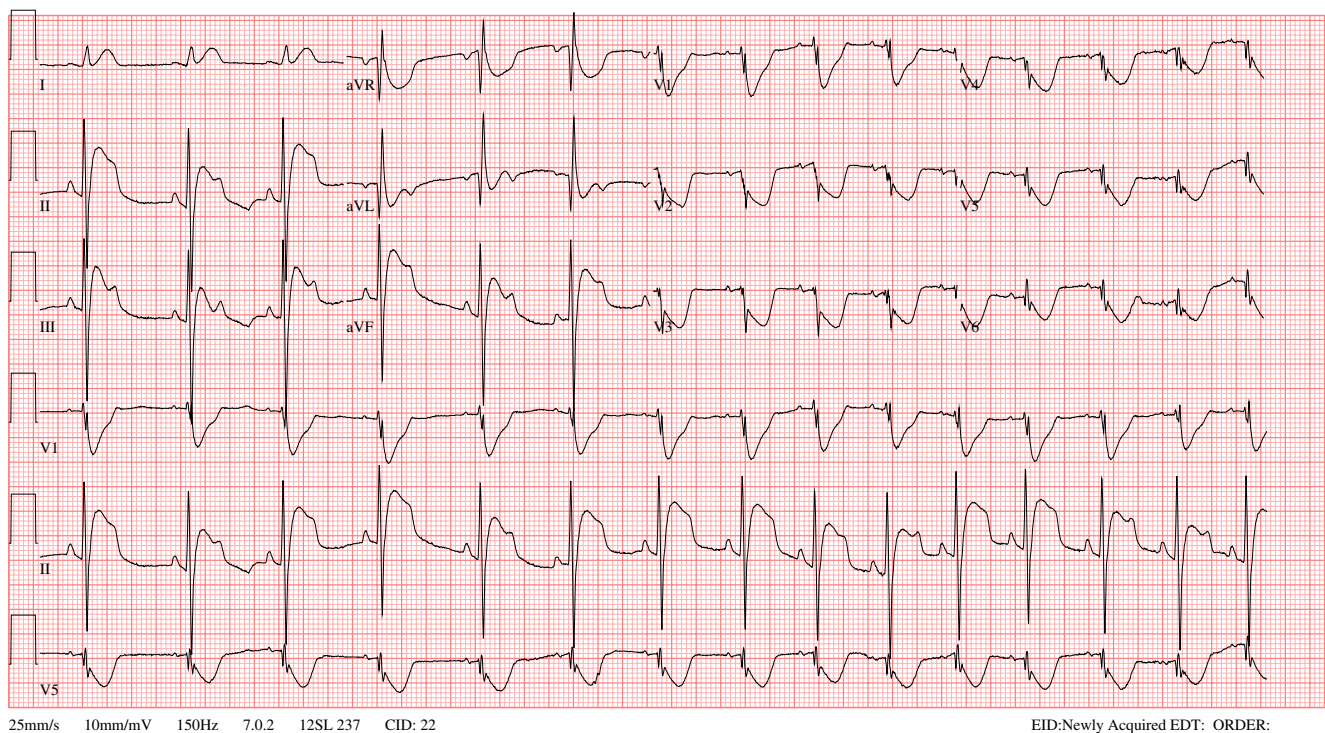


Fig. 2 ECG approximately 10 minutes after initial ECG

A detailed history of the chest pain should include the character of the pain, location, radiation, duration, and frequency as well as activities that exacerbate or alleviate the pain.

Generally, musculoskeletal chest pain is sharp and well localized and is commonly exacerbated by positional changes or by inspiration. In the adult literature, the reproducibility of the pain by palpation of the chest wall has been found to not be specific enough to rule out coronary artery disease [6–8], although in children such data have not been validated. We find that chest pain in children is commonly related to vague or distant chest trauma or carrying of heavy objects such as school bags.

Cardiac chest pain is generally described as crushing, squeezing, or pressure-like and is usually exacerbated by exertion. It may radiate to the shoulder, arm, neck, or jaw.

Relief of pain when sitting up may indicate pericardial causes of chest pain while worsening of pain with movement or deep inspiration is more indicative of non-cardiac causes. The presence of cough, fever, or dyspnea may suggest pulmonary causes of the pain while worsening of the pain post meals, or when lying down, may suggest gastroesophageal reflux disease.

Additional historical factors useful in evaluating a child with chest pain include symptoms such as shortness of breath, diaphoresis, and nausea. These symptoms are commonly associated with cardiac causes of chest pain, but are not specific or sensitive independently.

Syncope and palpitations are additional symptoms which may be difficult to elicit in children but if present may be indicative of cardiac causes such as dysrhythmia, ischemia, or outflow tract obstruction.

Other historical facts of importance include the presence of hypertension, diabetes, obesity, asthma, previous thromboembolic phenomena, hypercholesterolemia, gastroesophageal reflux, Marfan syndrome, and Kawasaki disease.

Patients with recent cardiac surgery and those with congenital cardiac disease should be assessed carefully for cardiac causes of chest pain which may include pericardial effusion, dysrhythmias, and ischemia. Patients with metabolic syndromes or family history of syndromes such as lipoprotein deficiencies and homocystinuria are also predisposed to have ischemia and therefore should be assessed thoroughly with further investigations.

A complete list of current and past medications has to be obtained, and in particular the use of corticosteroids or other immunosuppressants which have been associated with the development of ischemic heart disease, as well as the previous or current use of oral contraceptives which may predispose the child to atherosclerosis. A family history of hypercoagulable states such as proteins S and C deficiency or antiphospholipid syndromes are important pieces of the history which predispose to thromboembolic phenomena such as pulmonary embolism and ischemic heart disease.

Finally, in adolescents with chest pain, it is vital to ask about substance abuse (crack, cocaine, or amphetamines) as well as the sniffing of solvents which have all been

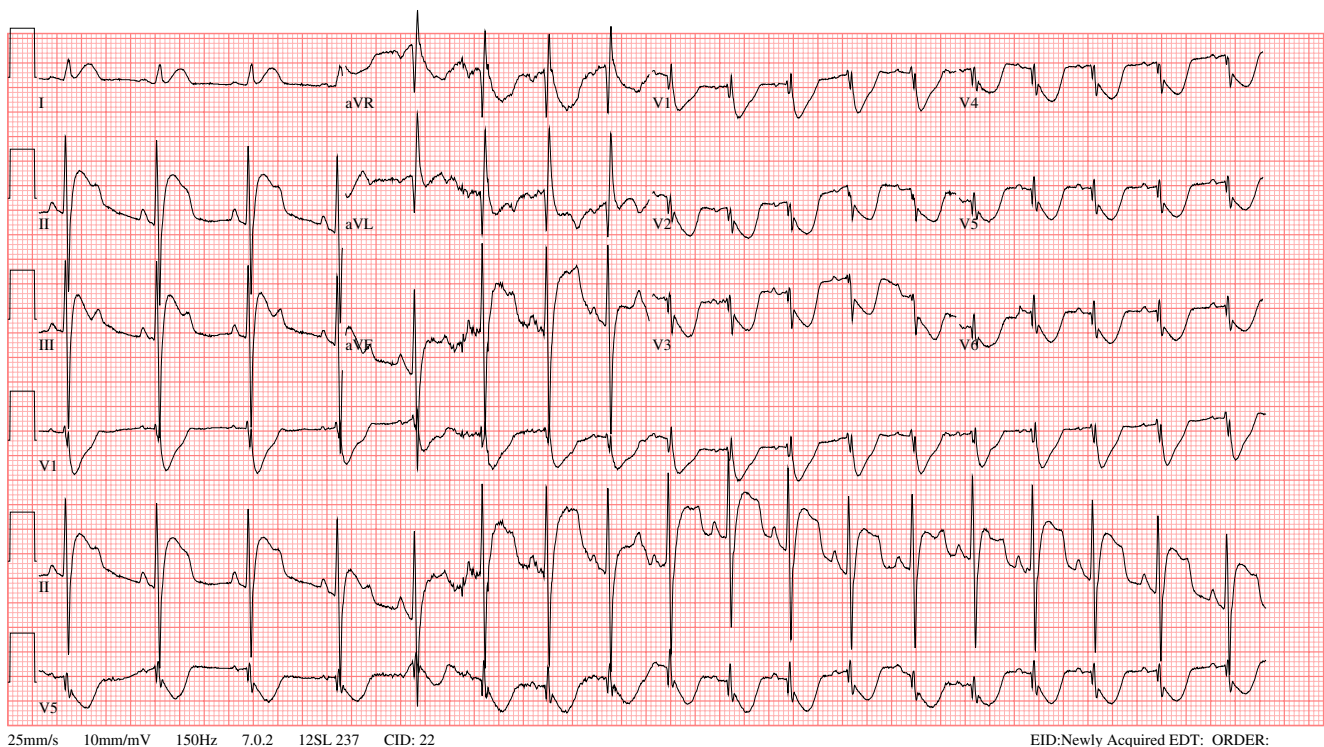


Fig. 3 ECG approximately 20 min after the initial ECG

associated with development of ischemic heart disease and chest pain.

The general examination should identify the child in severe distress who needs immediate treatment for life-threatening conditions. This starts with evaluation of the airway, breathing, and circulation (ABCs) as well as the presenting vital signs. For example, a gasping or cyanotic patient needs immediate intervention prior to completion of the physical examination, which may consist of simply giving oxygen or establishing an airway to relieve obstruction. Once this is stabilized, the patient's vital signs need to be reviewed carefully. The importance of the vital signs cannot be overstated and a good rule is any abnormality of the vital signs should be investigated or the cause clarified prior to discharge of a patient.

Although the respiratory rate is a very sensitive tool for identifying patients with pneumonia, an increased respiratory rate (in accordance to the norms for age) was found to have a sensitivity of 71–83% in different age groups and a negative predictive value of 96–99% in pneumonia [9, 10], but was not specific enough to rule out other etiologies.

The temperature may be useful in identifying children with infectious or autoimmune causes of chest pain, such as pneumonia, pleural effusions, pericarditis, or myocarditis.

The presence of tachycardia may be due to a variety of causes and does not serve to differentiate between cardiac and noncardiac causes of chest pain. Although a signifi-

cantly high heart rate for age (generally above 200 bpm in children) should raise the concern for dysrhythmias.

Pulse oximetry commonly known as the fifth vital sign is a particularly helpful tool and abnormalities have to be taken seriously. Although not specific, serious causes include pneumonia, pneumonitis, and pulmonary embolism as well as nonspecific cardiac dysfunction

A complete chest and cardiovascular examination is essential. The chest wall should be evaluated for signs of trauma, tenderness (suggesting musculoskeletal pain), or subcutaneous air (suggesting a pneumothorax or pneumomediastinum). There may be rales, wheezes, or decreased breath sounds if there is a pulmonary pathological condition or murmurs, rubs or muffled heart sounds if there is a cardiac pathological condition.

Based on the findings on the history and physical examination, the physician should decide whether the patient requires further investigation. These could include a chest X-ray (anteroposterior and lateral), laboratory investigations, and/or an ECG. The chest X-ray will help confirm the presence of rib fractures, pneumonia, pneumothorax, pleural and pericardial effusions, while the laboratory investigations may suggest infectious processes. Patients with a higher suspicion of cardiac etiology of chest pain may require measurement of creatine kinase isoenzyme muscle-brain (CK-MB) fraction and/or troponins. Troponin is a particularly sensitive and specific marker of myocardial ischemia as it is only released from

Table 1 Noncardiac causes of pediatric chest pain

Musculoskeletal disorders
• Chest wall strain
• Direct trauma/contusion
• Rib fracture
• Costochondritis
• Slipping rib syndrome
Respiratory disorders
• Severe cough
• Asthma
• Pneumonia
• Pneumothorax/pneumomediastinum
• Pulmonary embolism
Psychologic disorders
• Stress-related pain
Gastrointestinal disorders
• Reflux esophagitis
• Esophageal foreign body
Miscellaneous disorders
• Sickle cell crises
• Abdominal aortic aneurysm (Marfan syndrome)
• Pleural effusion (collagen vascular disease)
• Shingles
• Pleurodynia (coxsackievirus)
• Breast tenderness (pregnancy, physiologic)
Idiopathic

damaged myocardium unlike CK and lactic dehydrogenase (LDH). In our patient, the troponin level was 2 µg/l. The normal range is <0.35 µg/l.

The ECG is a sensitive tool to identify many cardiac causes such as dysrhythmia and ischemia as well as pulmonary causes such as pulmonary embolism which can present with S1 Q3 and inverted T3. These findings are specific but not sensitive and it is important to note that the normal ECG does not rule out a cardiac pathological condition.

Our patient's ECG showed ST depression, in the anterolateral leads V2–V6 (Fig. 1). These findings are classically consistent with anterolateral AMI. This pattern progressed in Fig. 2 with further evidence of expansion of the myocardial ischemia.

In contrast to the ECG in adults, where electrocardiographic criteria for the diagnosis of cardiac ischemia is well defined, analogous criteria in infants and children are ambiguous. The difficulty relates to age-dependent differences in the pediatric electrocardiogram, the presence or absence of congenital heart disease, and multiple and

diverse etiologies of myocardial injury that lead to an ischemic pattern on the ECG [11].

Other invasive diagnostic studies such as cardiac catheterization or cardiac biopsy will be dictated by the condition of the patient and the decision of the cardiologist. These procedures may be useful in confirming causes of AMI, whether it is due to coronary ischemia or myocarditis [12], and in addition, catheterization provides the opportunity of opportunity of revascularization therapy.

AMI in children is rare and the causes vary depending on the age at presentation (Table 3). Overall, the most common cause of AMI in children is anomalous origin of the left coronary artery, which may present in the neonatal period with unexplained sudden death, or later with persistent irritability, or evidence of heart failure. Myocarditis, the most likely cause of our patient's presentation, is a frequently missed cause of myocardial ischemia with an incidence of only 0.012% of patients seen in the ED but with a postmortem examination prevalence of 17% in children with sudden or unexpected deaths. [13, 14].

Although thrombotic diseases present similarly with AMI and/or heart failure, the age at incidence of thrombotic coronary disease depends on the primary disease. For example, thrombotic disease due to Kawasaki disease will occur earlier than thrombosis due to hypercoagulable states which usually peak at puberty. Other rarer causes are related to postoperative complications of congenital heart disease such as following repair of D-transposition of the great arteries (TGA).

Although the causes of myocardial ischemia may be different than in adults, the management is similar. This

Table 2 Cardiac causes of pediatric chest pain

Coronary artery disease—ischemia/infarction
• Anomalous coronary arteries
• Coronary arteritis (Kawasaki disease)
• Ischemic heart disease
Arrhythmia
• Supraventricular tachycardia
• Ventricular tachycardia
Structural abnormalities
• Hypertrophic cardiomyopathy
• Severe pulmonic stenosis
• Aortic valve stenosis
• Mitral valve prolapse
Infection
• Pericarditis
• Myocarditis

includes starting oxygen therapy, establishing intravenous access, and close monitoring. Specific therapy includes relief of pain and anxiety and decreasing catecholamine response. Aspirin or other antiplatelet agents should be given on arrival. Morphine sulfate and nitroglycerin (sublingual, spray, or intravenous) are the first-line anti-anginal medications. These should be titrated until the symptoms subside or side effects develop [15].

Depending on the patient's condition, heart failure or antiarrhythmic agents may need to be added. We found no data supporting the use of beta blockers in children with AMI.

A mainstay of therapy in adults with evidence of acute myocardial ischemia is reperfusion therapy (medical) or definitive percutaneous cardiac interventions (PCI), depending on the patient's condition, access to cardiac catheter labs, other support services, and expertise of the treating cardiologists. The performance of cardiac catheterization may have provided the opportunity for revascularization therapy, but this was not pursued because of the limited expertise in performing this diagnostic and therapeutic procedure in the unstable patient at our institute. Although our patient died rapidly, the question of whether an adult with a similar presentation would have been managed similarly is an important one. Importantly, the cause for such a presentation in an adult is almost always coronary in origin. Therefore, the opportunity for diagnosis and therapy with PCI or thrombolysis is much more clear as compared to the child who may have evidence of myocardial injury but with presumably healthy coronary arteries.

Our case is interesting because of the rarity of such a rapid tragic outcome in a child with a seemingly benign complaint of chest pain. This illustrates the importance of always considering the broad range of causes of chest pain in children even when the majority of the patients are likely to have less dramatic sequelae. In addition, the presence of underlying disease should always increase awareness of the potential of multisystem involvement.

Patient was known to have a long-standing HES, which refers to a group of leukoproliferative disorders characterized by an overproduction of eosinophils that results in organ damage of virtually any organ [16, 17]. Our patient had previous involvement of his pulmonary and integumentary system but never the cardiovascular system. The development of cardiac disease in children with HES is not predictable, and the severity of cardiac injury does not clearly correlate with the degree of peripheral eosinophilia [18]. Patients with cardiac involvement due to HES may present with symptoms of dyspnea, chest pain, signs of heart failure, mitral or tricuspid regurgitation, or cardiomegaly. Although all layers of the heart can be affected in HES, it is believed the myocardial involvement is the most common.

On rare occasions, as in our patient, patients present with evidence of acute AMI. It is this infarction, as evidenced by the ECG changes and the rise in troponin, which was the suspected cause of the chest pain and the devastating outcome. In AMI, the ECG findings could be subtle such as T-wave inversion or with more classic evidence of ischemia. Echocardiography may demonstrate intracardiac thrombi and evidence of fibrosis and increase in endomyocardial echo density in areas of fibrosis in addition to evidence of acute ischemia. Although the exact cause of the myocardial ischemia could not be confirmed without either cardiac catheterization or obtaining a tissue biopsy, it is suspected this AMI pattern was due to acute myocarditis.

In HES, the underlying cardiac pathological condition is thought to be a myocarditis secondary to eosinophilic infiltration of the myocardium (eosinophilic myocarditis, EM). EM evolves through three stages: an acute necrotic stage, an intermediate phase characterized by thrombus formation along the damaged endocardium, and the final fibrotic stage. Due to the acuity of our patient's presentation, we suspect our patient was in the acute necrotic stage, but no tissue diagnosis was obtained. The possibility of toxin-related myocarditis (due to previous and current use of immunosuppressants) or coronary artery obstruction cannot be ruled out.

Table 3 Causes of acute myocardial infarction in children

Causes	
Anomalous left coronary artery	Takayasu's disease
Coronary artery stenosis or spasm	Cardiomyopathy
Myocarditis	Marfan syndrome
Cardiac trauma	Kawasaki disease
Sickle cell disease	Illicit drugs, cocaine, amphetamine
Nephritic syndrome	Homocystinuria
Repair of D-TGA	Tetralogy of Fallot
Toxin	Autoimmune

In general, immunosuppressants have a wide range of cardiac-related complications such as myocarditis, and corticosteroids in particular, which are the most commonly used immunosuppressants, have been associated with a wide range of cardiac complications such as cardiomyopathy or coronary thrombosis due to hypercoagulable states.

Conclusion

From this case, we conclude that physicians dealing with the pediatric population will commonly deal with patients who present with chest pain, the cause of which may be life threatening. The approach to such a scenario requires a thorough history and physical exam and a risk assessment of the patient. If the risk is deemed to be significant, then more investigations and consultations may be warranted.

Although not done in our patient, when presented with biochemical evidence of myocardial injury and an ECG consistent with myocardial infarction in a child, more invasive procedures such as cardiac catheterization, endomyocardial biopsy, or autopsy should be performed to differentiate between the various causes of myocardial tissue damage. The timing and location of such interventions will be dictated by the medical condition of the patient and the expertise of the supporting staff. Treatment should be started as early as possible and may require consultation with those with more experience managing myocardial injury.

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