Chemotherapy Induced Acute Pericarditis in a Child
Muhammad Arif Khan, Abdul Rahman, S. Almoukirish, Shehla Jadoon and Tarek S. Momenah

ABSTRACT
A 9 years boy diagnosed with nasopharyngeal carcinoma was started on chemotherapy protocol including 5-fluorouracil. After 90 hours of 5-fluorouracil infusion, he developed severe retrosternal chest pain. Electrocardiography showed signs of acute pericarditis and was managed with ibuprofen and 5-fluorouracil was discontinued. The 5-fluorouracil rarely causes cardiac complications such as angina pectoris and pericarditis in adult patients. We report acute myopericarditis in a child caused by 5-fluorouracil, which is a very rare complication of 5-fluorouracil in pediatric age group.

Key Words: Pericarditis. 5-Fluorouracil. Chemotherapy. Retrosternal chest pain.

INTRODUCTION
The 5-fluorouracil associated cardiotoxicity is more apparent when used in combination with other drugs like docetaxel and cisplatin. The 5-fluorouracil may cause cardiotoxicity very rarely. The incidence of cardiotoxicity associated with 5-FU ranges between 1.5% to 18%. It may cause coronary artery spasm presenting as angina or myocardial infarction. It may lead to coronary artery spasm presenting as angina or myocardial infarction. Majority of patients (48%) have anginal symptoms and 2% have cardiogenic shock. Rarely, it is reported to cause acute pericarditis with chest pain and elevated ST segment in adults.

CASE REPORT
A 9 years boy was diagnosed as nasopharyngeal carcinoma stage III. He had epistaxis of 6 months duration. He had no lymphadenopathy or organomegaly. Computed tomogram of sinuses showed large nasopharyngeal mass with skull base invasion but no metastasis to brain. Magnetic resonance imaging and Technitium 99m bone scintigraphy confirmed the above findings. The biopsy of mass was taken which showed non-keratinizing, undifferentiated nasopharyngeal carcinoma (WHO type III). It was decided to treat with chemotherapy prior to irradiation. The chemotherapy protocol was to give six cycles of cisplatinum 80 mg/m²/day single dose and then 5-fluorouracil 1000 mg/m²/dose continuous infusion for 4 days. During the first cycle while receiving 5-fluorouracil continuous infusion approximately for 90 hours developed severe retrosternal chest pain aggravated by lying supine and relieved on leaning forward. Clinical examination revealed tachycardia and normal blood pressure, respiratory rate and temperature. There was no friction rub. Electrocardiogram showed evidence of sinus tachycardia, ST segment elevation which was concave upwards and J point notching in leads I, II, V1-V6 while ST segment depression in leads V1 and avR (Figure 1). The Troponin T 112 IU/dl and creatinine phosphokinase MB (CPK MB) was normal. The trans thoracic echocardiogram showed normal ventricular function and no evidence of valvular regurgitation or pericardial effusion. The patient was started on ibuprofen 10 m/kg/dose three times a day and 5-fluorouracil was discontinued. The serial electrocardiograms were taken and cardiac enzymes repeated daily. On third day, the electrocardiogram showed ST segment returned to baseline while T-waves were inverted in V5 and V6. The troponin T level returned gradually to normal on 4th day, ST segment returned to nearly normal baseline and T-wave inversion reverted in leads II, III and V1-V6 (Figure 2).

Figure 1: ECG at time of diagnosis shows normal sinus rhythm, ST segment elevation, concave upwards(STE) seen in lead I, II, V3-V6 with J point notching and ST segment depression in lead avR and V1. PR segment depression seen in leads I, II and V3.
The patient remained symptom free for one week and had normal cardiac enzymes. The repeat electrocardiogram and echocardiogram were normal (Figure 3). He was discharged home on oral ibuprofen. He is asymptomatic till last clinic visit 15 months after above complication. After discontinuation of above regimen the nasopharyngeal carcinoma was treated with interferon prior to radiotherapy.

**DISCUSSION**

The pericardium is a fibroelastic covering of heart and has two layers: visceral and parietal pericardium separated by pericardial space.\(^1,2\) The pericardial space contains 15 - 50 ml of clear fluid (ultrafiltrate of plasma) in adults while 10 - 15 ml in children. The inflammation of pericardium is called pericarditis. The term myopericarditis is used to denote inflammation of pericardium predominantly associated with some myocardial inflammation. The pericarditis may be an isolated disease or a manifestation of underlying systemic disease. The etiology of pericarditis is diverse.

It may be idiopathic, or secondary to infectious (bacterial, viral, tuberculous), rheumatologic diseases, gastrointestinal diseases, tumor, radiation, trauma, post-cardiac surgery and anticancer medicines.\(^3,4\)

The most common sign of acute pericarditis is chest pain, usually worsened in supine position. At least two of the following four criteria are generally present in a patient with acute pericarditis: chest pain, pericardial friction rub (abnormal heart sound), ECG changes of pericardial effusion.\(^5,6\)

Very rarely 5-fluorouracil may cause cardiotoxicity. The incidence of cardiotoxicity associated with 5-FU ranges between 1.5% - 18%. It may cause coronary artery spasm presenting as angina or myocardial infarction.\(^3,4\) It may lead to coronary artery spasm presenting as angina or myocardial infarction.\(^3-5\) The majority of patients (48%) have anginal symptoms and 2% have cardiogenic shock. Rarely, it is reported to cause acute pericarditis with chest pain, elevated ST segment in electrocardiogram and raised cardiac enzymes.\(^3-5\) The anticancer drugs like doxetaxel, cisplatin and 5-fluorouracil are known cardiotoxic agents in adult patients.\(^5\) The toxic effects of these drugs increase when used in combinations.\(^5\) The above mentioned agents are reported to cause severe retrosternal chest pain possibly due to pericarditis in adult population which resolved on discontinuation of this regimen. Such patients need alternative chemotherapy protocols.\(^5\) Rarely, it is reported to cause acute pericarditis with chest pain, elevated ST segment in electrocardiogram and raised cardiac enzymes. The reported clinical manifestations are angina in 48%, myocardial infarction in 23%, arrhythmias in 16%, acute pulmonary edema in 7% and cardiac arrest and pericarditis in 2% of the cases. Such patients need alternative chemotherapy protocols and possibly radiation therapy.\(^5,6\) The risk factors for cardiotoxicity with 5-fluorouracil are not known. Possible risk factors for toxicity are previous cardiovascular disease, radiation treatment and concurrent use of other cardiotoxic agents.\(^5\) The treatment of acute pericarditis should be directed to underlying etiology after acute management. The treatment of cardiotoxicity of 5-fluorouracil depends upon the presentation. It may be treated with calcium channel blockers, beta blockers, nitrates and nitroglycerine.\(^5,6\) The pericarditis associated with 5-fluorouracil is treated with non-steroidal anti-inflammatory agents like aspirin and ibuprofen.

The pathogenesis of this induced cardiotoxicity is not well understood. Coronary vasospasm has been suggested to be involved in the pathophysiology of this syndrome. Interference with myocyte metabolism is another proposed mechanism. This was demonstrated on echocardiography by reduced ejection fraction and significant akinesis of the left myocardium during the attacks. This did not correspond to a major coronary
artery distribution, suggesting a direct chemotherapeutic or drug metabolite-mediated toxic action on myocytes. This patient had severe chest pain, deranged troponin-T and elevated ST segment which suggested pericarditis. The coronary angiogram was not considered as the presentation was typical of acute pericarditis and patient responded to non-steroidal anti-inflammatory agent so, the enzyme and electrocardiogram changes reverted to normal without the need for vasodilators. Moreover, the ventricular function was normal without any segmental wall motion abnormalities.

REFERENCES