Case Reports

Intrapericardial chemotherapy for the management of neoplastic cardiac tamponade

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ABSTRACT

A young patient with disseminated osteogenic sarcoma presented with cardiac tamponade. She was successfully managed with pericardiocentesis and intrapericardial instillation of cisplatin. There was no reaccumulation of pericardial fluid or recurrence of tamponade until the patient's death 12 months later. Intrapericardial chemotherapy may be effective in the management of cardiac tamponade secondary to malignancy.

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Pericardial involvement in patients with malignancy is not uncommon. Studies have shown that the incidence of cardiac metastases at autopsy is 3.4% overall and 10.7% in cases with a neoplasm.[1] Development of cardiac tamponade in patients with malignant pericardial effusion is a potentially life threatening condition and can cause sudden death. For this reason, early diagnosis and treatment are warranted. This could result in good palliation of symptoms and prolongation of survival. Several therapeutic approaches including surgical intervention, radiotherapy and intrapericardial chemotherapy have been employed in patients with symptomatic malignant pericardial effusion. However, there are no clear cut guidelines regarding the optimum management of these patients. Here we present our experience in the management of a young patient with neoplastic cardiac tamponade, who was treated with pericardiocentesis and intrapericardial chemotherapy.

Case Report. A 17-year old, Sudanese girl was referred to King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia (KSA), with a 9 months history of swelling at the distal end of the left thigh. She was diagnosed to have osteosarcoma with vascular invasion extending to the surrounding soft tissues. She underwent left above knee amputation a week later and received 6 cycles of chemotherapy using cisplatin and doxorubicin. Subsequent clinic visits were insignificant until 2-years later when she was found to have a cavity lesion and nodule in the lower lobe of the right lung by chest x-ray. This was confirmed as a metastasis from osteosarcoma by histopathology. Lung metastases progressed in size within the next year involving the middle and lower lobes of the left lung. Within these times, she underwent resection of pulmonary metastases thrice and received several cycles of systemic chemotherapy. Three and a half years from her initial diagnosis, she was admitted with complaints of left shoulder pain, shortness of breath and cough. On examination the blood pressure was 135/80 mm Hg, respiratory rate 18/min and pulse rate was 90/min. Jugular venous pressure was not raised. On chest

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examination, there was total absence of breath sounds and dullness to percussion on the left hemithorax. Chest x-ray revealed an almost opaque left hemithorax with obliteration of the left cardiac border. Computed tomography scan of the chest showed a huge left upper lobe mass extending to the left main pulmonary vessels. Small metastatic nodules were seen in both lungs. There was a large pericardial effusion probably due to direct invasion as the large mass continued with the pericardial sac. **(Figure 1)** Over the next few days, her dyspnea progressed and physical findings including pulsus paradoxus and elevated jugular venous pressure suggested cardiac tamponade. An urgent echocardiogram revealed a large pericardial effusion with evidence of tamponade and diastolic collapse of the right atrial wall. A large mass was seen inside the pericardium adjacent to the lateral wall of the left ventricle measuring 8 x 4 cm. At this stage cardio-thoracic surgeons were consulted, however, it was decided that due to several previous metastatectomies causing adhesions, surgical intervention would be difficult and hazardous. On the 14th hospital day, the patient's symptoms further deteriorated and she was in critical condition with impending death. Her blood pressure had dropped to 90/60 mm Hg and pulse rate was 140/min. She was severely dyspneic with a respiratory rate of 48/min. Subsequently, the patient was transferred to the coronary care unit where a pericardiocentesis was performed under fluoroscopic and echocardiographic guidance, with continuous electrocardiographic, blood pressure and peripheral oxygen saturation monitoring. An indwelling catheter was inserted through the subxiphoid access. More than 1500 ml of hemorrhagic pericardial fluid was drained. Immediately after the pericardiocentesis a dramatic improvement in patient's symptoms and signs were noted. After complete drainage of fluid, cisplatin 10 mg in 20 ml normal saline was instilled directly into the pericardial space, over a period of 5 minutes. After cisplatin instillation, the catheter was clamped for 4 hours and then reopened. She was given intrapericardial cisplatin for 5 consecutive days in the same manner. Following the completion of chemotherapy the catheter was removed. There was no complication related to the instillation of chemotherapy. In particular there was no evidence of arrhythmia, nausea, hypotension or retrosternal pain. Her hematological and renal profile was not changed after the chemotherapy. A follow up echocardiogram carried out 2 weeks after the treatment revealed minimal pericardial effusion and a considerable decrease in the size of intrapericardial tumor was also noted. A week later, she was started on systemic chemotherapy using methotrexate. She received a total of 8 cycles. Although the patient subsequently experienced problems, including progression of pulmonary and bone metastases, there was no clinical or radiological evidence of recurrence of the pericardial effusion until she died 12 months later, secondary to widespread pulmonary metastases. **(Figure 2)**

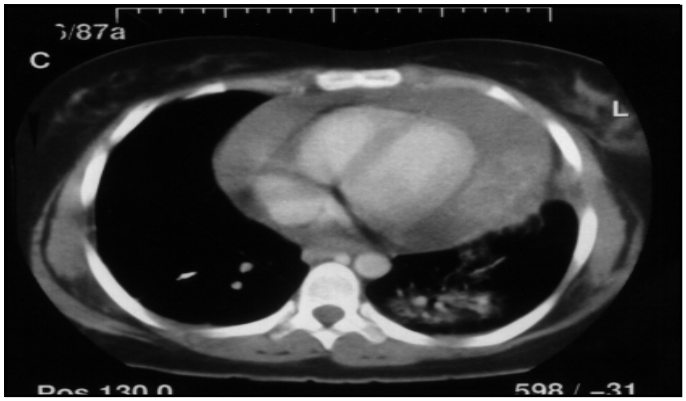

Figure 1 - Computerized tomography of the chest showing massive pericardial effusion and tumor invading the pericardial sac.

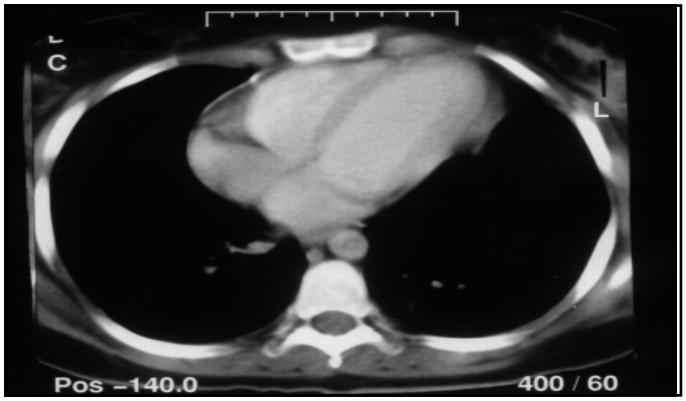

Figure 2 - Computed tomography. There was no significant pericardial effusion 6 months after intrapericardial instillation of cisplatin.

Discussion. Development of cardiac tamponade in a patient with malignant pericardial effusion is an emergency in oncology practice. This condition warrants urgent intervention to relieve immediate symptoms and to decrease the hemodynamic effects of cardiac tamponade. Unfortunately in many patients with cancer this emergency is not diagnosed early leading to considerable morbidity and life threatening cardiovascular collapse.[2] Echocardiography is the diagnostic modality of choice in patients suspected to have malignant pericardial effusion; not only does it help to confirm the diagnosis of pericardial effusion, it is also useful in determining the extent and location of the effusion and presence or absence of loculations or pericardial deposits. In addition, some information may be gained regarding the presence or absence of cardiac tamponade.[3] Once the diagnosis of significant pericardial effusion or cardiac tamponade has been confirmed, the next step should be prompt withdrawal of fluid by pericardiocentesis. The pericardial puncture should be carried out under electrocardiographic and blood pressure monitoring in association with fluoroscopy or echocardiographic guidance. It is

recommended that a maximum quantity of fluid is removed. Pericardiocentesis alone is effective in the emergency management of neoplastic tamponade. However, the fluid may reaccumulate rapidly unless additional therapeutic approaches are initiated. Pericardiocentesis, therefore, should be followed by a definitive medical or surgical procedure. The direct intrapericardial instillation of chemotherapeutic agents, radioactive compounds and sclerosing agents have all been reported to successfully decrease the rate of reaccumulation of pericardial fluid in patients with malignant effusion.[4-6] Cisplatin is a chemotherapy drug which has demonstrated considerable activity in a variety of tumors when it is administered intravenously. Intrapericardial instillation of Cisplatin was first employed by Markman and Howell[7] for a patient with advanced adenocarcinoma with massive malignant pericardial effusion. The authors reported a dramatic decrease in reaccumulation of pericardial fluid which persisted until the patient's death 4 months later. After this experience intrapericardial cisplatin was utilized further by other centers.[8] Tomkowski et al[9] reported a series of 9 patients with malignant pericardial effusion, who were treated with a direct intrapericardial administration of cisplatin. All the patients achieved a complete response to treatment; for example no more fluid reaccumulation was observed. Eight patients died of primary disease progression without evidence of cardiac tamponade or stricture.[9] We chose cisplatin for our patient as it has shown good efficacy in previous studies, as well as being one of the most effective chemotherapeutic agent in the treatment of osteogenic sarcoma. It is possible that a direct cytotoxic effect of high platin concentration helped achieve an excellent result, not only regarding the reaccumulation of fluid but also the disappearance of intrapericardial tumor extension.

Our case report illustrates a very important issue in the management of patients with malignant pericardial effusion. Once a patient has been diagnosed to have malignant neoplasm, most physicians have a fatalistic approach to these patients. Although the presence of pericardial effusion in a patient with malignancy is usually indicative of advanced disease and the prognosis is poor, it should not always be considered a terminal event. We strongly believe that symptomatic neoplastic pericardial effusion and cardiac tamponade should be diagnosed and treated vigorously. Many of these patients are severely ill at presentation, however, if treated promptly, besides offering immediate relief, significant improvement in the quality of life is possible, as evident in our patient.

In conclusion, intrapericardial chemotherapy is an effective, well tolerated and safe treatment modality for neoplastic pericardial effusion. We suggest that physicians should consider this approach, among other approaches, used to prevent malignant pericardial fluid accumulation after pericardiocentesis.

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