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Imaging and intervention for Coronary Artery Disease following irradiation of malignant thymoma

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Abstract

Thymomas are rare malignant epithelial growths, constituting 20% of mediastinal tumours. Resection followed by irradiation may be employed in all thymomas except for stage 1 thymomas. Mediastinal irradiation is associated with coronary artery disease. The mean duration of presentation of post-irradiation coronary artery disease is 16 years (range 3-29 years). In our patient coronary artery disease was found only a year post irradiation. A 55 year old male who presented with complaints of dyspnoea, retrosternal chest pain and heaviness since one year underwent resection for malignant thymoma followed by radiotherapy. He presented with coronary artery disease a year after undergoing mediastinal irradiation. On follow-up, patient was treated successfully by coronary artery bypass graft. This case is an unusual occurrence and suggests that mediastinal irradiation may result in significant coronary artery disease as early as within one year.

Keywords: Thymoma, Coronary artery disease, Coronary artery bypass graft, Mediastinal irradiation.

Introduction

Thymoma is a neoplasm of the thymus originating in the gland's epithelial tissue. It is a slow-growing tumour that spreads by local extension. Metastases are usually confined to the pleura, pericardium, or diaphragm, whereas extrathoracic metastases are uncommon. Resection followed by irradiation may be employed in all thymomas except for stage I thymomas.[1] Degree of encapsulation and invasion of adjacent structures in thymomas are significant in defining malignancy.[2] Mediastinal irradiation is associated with coronary artery disease (CAD) as well as damage to various cardiac structures such as the pericardium, myocardium, heart valves and the aorta.[3-7] The mean duration of presentation of post-irradiation CAD is 16 years (range: 3-29 years).[6] We present a case of a male patient who presented with CAD only a year after undergoing resection of thymoma and mediastinal irradiation.

Case Presentation

A 55 year old male presented with complaints of dyspnoea, retrosternal chest pain and heaviness since one year. He was a known hypertensive and ex-smoker. His cardiac work up was unremarkable and revealed a normal thallium scan. He then underwent a chest roentgenogram which showed widening of the mediastinum. This finding was suggestive of either a mediastinal mass or lymphadenopathy. Computed tomography (CT) scan was carried out which gave indications of a large soft tissue mass located in the mediastinum, spanning from just above the aortic arch to the level of the heart, with dimensions of 8 x 9 x 9.5 cm. This was followed by a trans-esophageal echocardiogram that revealed an echogenic mobile density at aortic root which appeared to be secured with the left coronary cusp of the aortic valve. On further analysis it was concluded to be a vegetative mass. The left ventricle was found to be of normal size and reported to have a normal ejection fraction. Electrocardiography (ECG) recordings

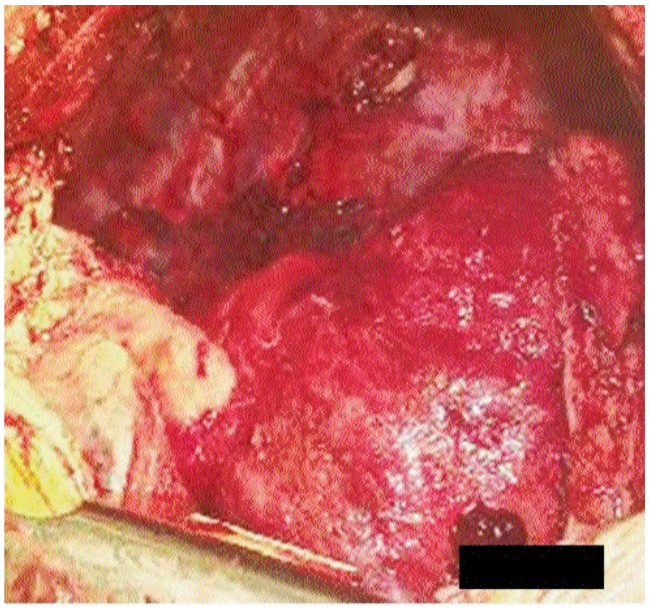

Figure-1: The figure displays the tumour, sparing the vagus nerve.

were unremarkable. The laboratory results were within normal ranges with, serum alpha fetoprotein level of 3.55ng/mL, Beta- HCG of <2mU/ml and serum HDL of 1.96mmol/L.

Further exploration of the nature of mass was done by means of three procedures; bronchoscopy, video-assisted thoracoscopy (VATS) and biopsy. While bronchoscopy confirmed normal airways, VATS and biopsy established the presence of a thymoma.

On account of the above information, resection of the mass was planned. After induction of general anaesthesia, median sternotomy was performed. A large mass encasing the innominate vein was identified in the anterior and superior aspect of the mediastinum.The mass was found to be in close approximation of the pericardium, left phrenic nerve and the vagus nerve with the fibrous pericardium adherent to serous pericardium.

The tumour was found to be extending medially towards the left upper lobe of the lung, sparing the hilum, ribs and sternum. The tumour along with the anterior aspect of the pericardium, fastened closely with the innominate artery and vein, left carotid artery and the arch of aorta was removed. The left phrenic nerve which was masked by the tumour had to be sacrificed. The vagus nerve was unharmed (Figure-1). The dimensions of the tumour was 10x12cm (Figure-2).

Histopathological analysis of the specimen revealed a mixed type B2 invasive thymoma.

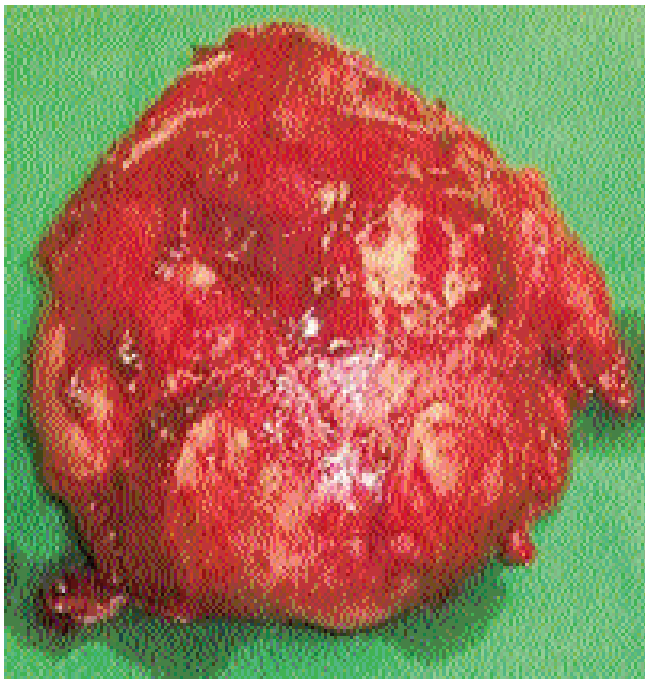

Figure 2: This figure displays the thymoma with dimensions of 10cm X 12 cm.

Tumour resection was followed by radiation therapy of a dose of 5400 centigray (cGY) over a length of one and a half month. The patient remained free of symptoms for one year after which he presented with complaints of chest pain exacerbating on exertion. Exercise tolerance test was performed which revealed alterations in ECG. Angiography was carried out which unveiled three-vessel CAD. The mid and distal segments of the right coronary artery were 100%, left circumflex artery was 70-80% and left anterior decending artery was 70-90% occluded.

A Coronary Artery Bypass Graft (CABG) was planned and performed. Four saphenous vein grafts were employed (first on obtuse marginal one, second on posterior descending and two sequential grafts on the left anterior descending artery). The patient made good recovery and was discharged 7 days post-surgery. Four years follow up and CT angiography findings have indicated patent grafts. Currently, the patient is healthy and has not had recurrence of a thymic tumour.

Discussion

Thymic tumours form a class under common anterior mediastinal tumours.[2] Thymoma refers to a malignancy originating from epithelial cells of thymus. It constitutes 20% of the tumours of mediastinum accounting for about 50% of the tumours in adults. It has an incidence of 0.15 cases per 100,000.[8] Often, thymoma is considered to have a docile growth pattern but it does have the ability to give rise to local invasion and intrathoracic recurrences.[8] The treatment of choice for thymomas is complete resection whenever possible. Resection is associated with low mortality and morbidity.Simple enucleation of a thymoma is not highly recommended because it may result in recurrence. This is elucidated by the possibility that non-resected thymic tissue can act as a potential site for future development of an additional thymoma or it can result in the presence of multiple small lobules of tumours not detectable on gross examination at the start of operation.[2]

In non-invasive thymoma (stage I), post-operative radiation therapy is not essentially required. This has been reaffirmed because of evidence put forward by studies which explain that incidence of recurrence has been low even without radiation therapy.[8,9] On the contrary, recurrence rates for completely resected invasive thymomas are higher and hence warrant irradiation along with resection to prevent local relapse.[9,10] The recommended dose of radiation therapy ranges from 30 to 60 Gy in 1.8 to 2.0 cGy fractions over a span of three to six weeks. Treatment fields and dose fractions should be arranged and monitored to minimize complications. Treatment portals may include single anterior field, unequally weighted (2:1 or 3:2) opposed anterior-posterior fields, wedge-pair, and

multifield arrangements.[9]

The incidence of radiation induced injury is 5% to 30%. Mediastinal irradiation toxicity depends on the amount of normal tissues included within the radiation portal and can result in a wide variety of injuries ranging from minor fibrosis to heavy scarring and fusion of the mediastinal structures. Extensive pericardial, myocardial, vascular, and valvular damage can also occur along with the aortic arch and great vessels.[5] Amongst possibility of incurring the injury, the most commonly involved structure is pericardium while the structure least likely to be damaged is the conduction system. Many patients treated with radiation therapy for thoracic malignancies survive the malignancies but become susceptible to early development of ischaemic heart disease with the majority not having classic risk factors for the development of CAD.[4]

In case of CAD, the distribution of lesions correlate with the radiation dosimetry. Irradiation may cause pathological intimal denudation leading to intimal damage and thrombus formation. Radiations may lead to fibrosis and cell proliferation, after damage to media. These mechanisms may contribute to coronary atherosclerosis and cause early failure of venous grafts in case of CABG. Accelerated atherosclerosis occurs in irradiated arteries and this leads to impaired patency of grafts.[7]

Performance of CABG in a patient with history of irradiation is challenging because of severe mediastinal and pericardial fibrosis. Surgeons may be reluctant and cautious about using internal thoracic artery as a site of intervention for myocardial revascularization in patients with a history of thoracic radiotherapy. The reason being that irradiation may result in sclerosis of connective tissue surrounding the internal thoracic artery.[7] While performing CABG in our patient internal thoracic artery was not used, instead two sequential reverse saphenous vein grafts were placed on the left anterior descending artery.

One limitation needs to be addressed. Since the initial cardiac workup included thallium scan only and coronary angiography was not performed, pre-existing non-significant CAD could not be completely ruled out. Hence, had that been the case, radiation might have accelerated the progression of pre-existing CAD rather than causing it.

Conclusion

In conclusion, our patient presented with CAD in only a year post radiation, while the mean time period from mediastinal irradiation to development of CAD is 16 years (range 3-29 years).[6] Hence, this case is an unusual occurrence and suggests that mediastinal irradiation may result in significant coronary artery disease as early as within one year.

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