Novel treatment (new drug/intervention; established drug/procedure in new situation)

Neuroendocrine carcinoma presenting as cardiac tamponade and dramatic response to steroids

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Summary

A healthy young man presented with cardiac tamponade. He underwent pericardial window and biopsy revealed chronic inflammation. Two years later, he presented with respiratory failure. CT of the thorax revealed prominent anterior mediastinal mass abutting the brachiocephalic vein consistent with thymic tumour. Open lung biopsy revealed metastatic intermediate-grade neuroendocrine carcinoma with lymphangitic spread. Corticosteroids were started for palliation. He made a remarkable improvement clinically and radiologically in 2 days of starting steroids. Thymic neuroendocrine carcinomas are very aggressive and the clinical presentation is varied and atypical. Our patient presented with cardiac tamponade. Malignancy should be considered in the differential diagnosis of unexplained cardiac tamponade. The other important point illustrated by our case is the dramatic response to the steroids. Treatment of metastases of any tumour of thymic origin with steroids could be an option when more conventional therapeutic methods fail.

BACKGROUND

This is a rare case with a unique presentation and this patient had an unusual course of illness. The learning point in this case is that 'malignancy should be high on the differential diagnoses'. The other important point brought out by this case is the dramatic response to the steroids warranting research.

CASE PRESENTATION

A healthy male in his early thirties presented to his local hospital with a 3-day history of chest discomfort and

an unwell feeling. His medical history was notable for orchidectomy for undescended testis and premature coronary artery disease in his mother. He was a smoker. Physical examination revealed faint heart sounds and pulsus paradoxus. Chest x-ray revealed cardiomegaly. Electrocardiogram revealed low-voltage complexes and poor R wave progression. CT of the chest revealed bilateral pleural effusions and massive pericardial effusion. Echocardiogram revealed tamponade physiology (figure 1). The patient was transferred to our tertiary care hospital

Figure 1 Two-dimensional apical four-chamber view showing a large pericardial effusion, right ventricular and right atrial wall collapse that is consistent with tamponade.

Figure 2 Chest x-ray on May 26, 2007 showing extensive bilateral infiltrates.

Figure 3 CT chest showing thymoma with bilateral lung infiltrates.

Figure 4 Tumour staining positive for synaptophysin suggesting neuroendocrine origin.

Figure 5 Lung biopsy showing tumour cells in the alveolar septa representing lymphatic spread.

where he underwent pericardial window with drainage of bloody fluid. Fluid analysis revealed an exudative pericardial effusion. Gram stain, fungal and bacterial cultures were negative and patient tested negative for purified protein derivative. Thyroid-stimulating hormone was within normal limits. Antinuclear antibody, double-stranded DNA

antibody, anti-smooth muscle antibody, HIV and β -human chorionic gonadotropin were also negative. Sedimentation rate was 5. Pericardial biopsy revealed chronic inflammation. He was discharged a week after recovery.

The patient's course in the next 2 years was notable for recurrent emergency room visits and hospitalizations for

Figure 6 Solid nodular focus of neuroendocrine tumour involving the subpleural lung.

recurrent dyspnoea, chest pain and flu-like symptoms. During his evaluation, he had repeat echocardiogram that showed no evidence of pericardial effusion and was treated for possible pericarditis. Chest CAT scan revealed bilateral pleural effusions and residual thymic tissue. He was treated empirically for pneumonia.

Two years later, the patient returned to his local emergency room for progressive shortness of breath, fever, and back and chest pain.

INVESTIGATIONS

Chest x-ray revealed upper and lower lobe opacities (figure 2). Echocardiogram revealed large pleural effusions and pericardial effusions. Thoracentesis revealed hemorrhagic fluid. The patient's respiratory status rapidly deteriorated requiring mechanical ventilation. Chest CAT scan revealed rapid worsening of bilateral consolidations with evidence of a prominent anterior mediastinal mass abutting the brachiocephalic vein consistent with thymic tumour (figure 3). An abdominal CAT scan revealed multiple sclerotic lesions involving the sacrum, iliac bones and liver consistent with metastasis; his abdominal CAT scan in December of 2006 was reported as unremarkable. Pleural fluid cytology revealed atypical cells with positive staining for BER-EP4, chromogranin and synaptophysin consistent with neuroendocrine carcinoma (figure 4). Open lung biopsy revealed metastatic intermediate grade neuroendocrine carcinoma with lymphangitic spread (figures 5 and 6).

DIFFERENTIAL DIAGNOSIS

- ▶ Small-cell lung carcinoma
- ▶ Metastatic carcinoma
- ▶ Infectious process.

OUTCOME AND FOLLOW-UP

Based on the patient's clinical picture, pathology findings and the presence of thymic tumour on the chest CAT scan, it was concluded that the patient's neuroendocrine carcinoma was of thymic origin. Corticosteroids were not started intentionally as anti-tumour therapy but for palliation. He was started on a moderate dose of solumedrol. He made a remarkable improvement clinically and radiologically in 2 days of starting steroids (figures 2 and 7). His oxygen requirements decreased and chest x-ray showed a dramatic improvement in bilateral airspace disease. He became well enough to be extubated. He continued to do well and was sent home on tapering steroids. Surgery was not an option for him due to the extensive nature of the disease. He was given chemotherapy with cisplatin and etoposide. He did not respond to chemotherapy and died within a year.

DISCUSSION

Thymic neuroendocrine carcinomas are usually very aggressive and early diagnosis is crucial for management of the condition. The clinical presentation is varied and atypical. Clinical signs of thymic carcinoids are not distinct and are present in only about 30% of the patients.¹ There have been approximately 10 documented cases of thymic tumours presenting with cardiac tamponade.²⁻⁵ All of them were thymic epithelial tumours. A review of the literature indicates that pulmonary adenocarcinoma is the most common cause of cardiac tamponade presenting as the first presentation of malignancy.²

Delay in diagnosis of cardiac tamponade, even in the face of typical features, has been a consistent feature in reported cases. Malignancy should be considered in the differential diagnosis of unexplained cardiac tamponade.

Figure 7 Chest x-ray showing resolving infiltrates 4 days later on May 30, 2007.

In the case series by Campbell *et al*,^{6 7} pericardial biopsy yielded diagnosis in 93% of the patients but the pericardial fluid yielded a diagnosis in only 15 (26%) patients, 11 of whom had malignant effusions.

Neuroendocrine tumours are usually gastroenteric or thymic in origin. Thymic origin is usually confirmed by the presence of Hassal's corpuscles. Prognosis is mainly dependent on the degree of differentiation. Thymic neuroendocrine carcinomas may be designated as well-differentiated, moderately differentiated or poorly differentiated tumours. Tumours occurring in the thymus with well-differentiated features are associated with survival rates of 50% at 5 years. The survival rates of moderately differentiated and poorly differentiated tumours at 5 years are 20% and 0%, respectively.⁸

Our patient presented with cardiac tamponade. On presentation, pericardial fluid analysis did not reveal the aetiology for cardiac tamponade. Malignancy did not become high on the differential diagnosis until the patient's clinical course deteriorated. The other important point illustrated by our case is the dramatic response to the steroids. He remained free of respiratory symptoms for at least 6 months.

Sofer *et al* for the first time in 1952 reported the regression of thymoma to adrenocorticotrophic hormone. Since then, few others have described regression of thymoma to steroids. The most recent study was the one by Ardizzone *et al* in 2005 about the complete remission of an octreotide-resistant thymoma to corticosteroids.^{9–13} The mechanisms of action of corticosteroids in thymomas remain speculative. Glucocorticoid-induced apoptosis was also reported in immature thymocytes¹⁴ and peripheral mature

lymphocytes.¹⁵ However, such receptors have not been found in human thymomas.

Treatment of metastases of any tumour of thymic origin with steroids could be an option when more conventional therapeutic methods fail. More research in this area is needed before making any final conclusions regarding the use of steroids in thymic neuroendocrine carcinomas.

Learning points

- ▶ Malignancy should be considered in the differential diagnosis of unexplained hemorrhagic cardiac tamponade. Patients need to be closely monitored and extensively evaluated for occult carcinoma.
- ▶ Thymic neuroendocrine carcinomas are aggressive and early diagnosis is crucial as they may be amenable to surgery in the early stages.
- ▶ Thymic origin is confirmed by the presence of Hassal's corpuscles.
- ▶ Steroids can be considered as a treatment option in the management of thymic tumours.

Competing interests None.

Patient consent Not obtained.

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