CASE REPORT

Rare cause of atrial fibrillation: a thymic mass

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SUMMARY

A 62-year-old African-American man admitted to the emergency room with chest pain and exertional dyspnoea. He was found to be in rapid atrial fibrillation with pulmonary oedema. A transoesophageal echocardiogram performed prior to cardioversion showed a depressed left ventricular function (ejection fraction 30%) and an extracardiac heterogeneous echodensity compressing the right atrium and the superior vena cava. CT of the chest confirmed an anterior mediastinal mass measuring 13.5×6.6×10.1 cm, exerting a mass effect on the right atrium with mediastinal and right hilar adenopathy. CT-guided biopsy of the mediastinal mass revealed thymic carcinoma (squamous cell subtype). The metastatic workup was negative. The mass was deemed surgically unresectable due to its proximity to the heart. Chemotherapy was initiated with carboplatin/paclitaxel every 3 weeks with plans for intensity modulated radiotherapy after one to two cycles of chemotherapy. The patient recently had a repeat CT scan of the chest showing regression of the tumour.

BACKGROUND

The case portrays the importance of looking for unusual pathological entities leading to atrial fibrillation (AF). It also presents an opportunity to study a rare malignancy like thymic carcinoma.

CASE PRESENTATION

A 62-year-old African-American man with a medical history of hypothyroidism and diabetes mellitus, presented to the emergency room with a 1-week history of chest pain, palpitations and exertional dyspnoea. He was found to be in rapid AF with flash pulmonary oedema. The physical examination was significant for elevated jugular venous pulse; bilateral crackles on lung examination, irregular heart rate and 2+ pedal oedema. The patient was started on diltiazem drip for rate control, heparin for anticoagulation and was diuresed with furosemide. A transoesophageal echocardiogram performed prior to cardioversion showed depressed LV function and an extracardiac heterogeneous echodensity compressing the right atrium and superior vena cava (SVC). A CT scan of the chest with contrast was performed which showed an anterior mediastinal mass measuring 13.5×6.6×10.1 cm (figure 1) with mediastinal and right hilar lymphadenopathy exerting mass effect on the right atrium.

INVESTIGATIONS

CT-guided biopsy of the mediastinal mass revealed thymic carcinoma (squamous cell subtype) (figure 2). Immunohistochemical stains were positive for cytokeratin AE1/3, CK7, P63 (figure 3), CD5 and

Figure 1 CT scan of the chest with contrast showing mediastinal mass measuring 13.5×6.6×10.1 cm exerting mass effect on the right atrium.

Figure 2 Histological examination of thymus biopsy (H&E stain) shows hypercellular specimen with large atypical epithelioid cells, pleomorphic nuclei and eosinophilic cytoplasm.

Figure 3 Stains positive for P63 which is marker for squamous differentiation.

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PAX8. Cells were negative for CK20, CD45 (figure 4), CD20, CD3, TTF-1 (figure 5) and Napsin-A. The metastatic workup (bone scan, MRI brain and CT abdomen/pelvis) was negative.

DIFFERENTIAL DIAGNOSIS

Differentials included germ cell tumour, lymphoma, thymoma and bronchogenic neoplasm. A normal testicular examination with normal serum alpha fetoprotein (AFP) and levels made germ cell tumour less likely. Germ cell tumours and high-grade lymphomas are generally aggressive cancers and have rapid onset of symptoms compared to thymic neoplasms which are usually more indolent. Histopathological staining for TTF-1 and CD5 is used to differentiate bronchogenic neoplasm from thymic carcinoma. In our case, negative TTF-1 staining ruled out a lung primary and positive staining for CD5 was more consistent with a thymic neoplasm.^{1 2}

Radiographic features help to differentiate between thymoma and thymic cancer. The presence of irregular contour, necrotic or cystic component, heterogeneous enhancement, lymphadenopathy and great vessel invasion are strongly suggestive of thymic carcinoma.³ In the case of our patient, the mass was described as heterogeneous with multiple areas of hypodensities within the mass which were suggestive of necrosis. Also seen were multiple enlarged conglomerate lymph nodes in the mediastinum and right hilum.

Figure 4 Stains negative for CD 45 which is a marker for haematopoietic cells, thus making lymphoma less likely.

Figure 5 Stains negative for TTF-1 which is a marker for lung and thyroid carcinomas.

TREATMENT

The National Comprehensive Cancer Network guidelines suggest carboplatin/paclitaxel as first-line chemotherapy due to the risk of cardiomyopathy with anthracycline-based regimens.⁴ This patient already had a depressed ejection fraction, thus treatment was initiated with carboplatin/paclitaxel. He was scheduled to receive three cycles, every 3 weeks along with intensity modulated radiotherapy. Though surgical resection is the best initial treatment, in our patient, the mass was deemed unresectable due to its proximity to the heart.

OUTCOME AND FOLLOW-UP

The patient received two cycles of carboplatin/paclitaxel and repeat imaging showed regression of the mass. He has had no recurrence of his AF.

DISCUSSION

Recent studies have shown an increased frequency of AF in patients with cancer. The reasons are multifactorial including mass effect, atrial remodelling due to the inflammatory milieu of cancer, paraneoplastic conditions triggering autoimmunity against atrial structures and the side effects of chemotherapeutic agents.⁵ AF can be an independent prognostic factor for patients with malignancy.⁵ Mediastinal tumours can rarely present with arrhythmias. Few case reports exist of bronchogenic cysts and mediastinal teratoma causing AF.⁶ However, no specific cases of thymic carcinoma presenting as AF were found. Thymoma and thymic carcinomas are rare with an annual incidence of 1.5 per million persons. Their 5-year survival rate is 30–50%.¹ Thymic carcinomas can have variable presentations such as chest pain, cough, SVC syndrome and phrenic nerve palsy. CXR/CT/MRI/PET scan can aid in diagnosis. Radiologically, a mass is seen in the anterior mediastinum and ~80% of the time there is invasion of contiguous mediastinal structures.⁷ In a study involving 60 patients with thymic carcinoma, with mean age of 45 years, it was found that there was no statistical association between survival and demographic features of patients including age, sex and form of presentation.⁷ Morphological features that correlated with poor response included poorly circumscribed lesions, absence of lobular growth pattern, mitotic counts exceeding 10/10 HPF and high-grade histology.⁷ In our patient the mass was found to be poorly circumscribed, with areas of necrosis and MIB-1 stain was positive for 50% cells, pointing towards a rapidly proliferating tumour. The Masoka classification system is used to determine stage and prognosis of thymic carcinoma.⁸ As per this classification, the tumour in our patient was stage 3, signifying a 5-year survival rate of 68%. The treatment for thymic malignancy remains controversial; most studies have suggested benefit from a multimodal approach involving surgical resection, platinum-based combination chemotherapy and radiotherapy.⁹ Forty patients with histologically confirmed thymic carcinoma were retrospectively studied (1984–1998) by Ogawa *et al*¹⁰ and it was found that complete resection, histology and Karnofsky performance status were the factors which were found to impact survival. Seventy-five per cent (12 of 16) of the patients who underwent complete resection were alive and free of disease at the first follow-up.¹⁰ This supports the consensus that early surgical excision is the best way to approach this disease. However, in cases like our patient where the tumour is unresectable, chemotherapy becomes the primary treatment.

Anthracycline and platinum regimens

There are limited studies that have been carried out to determine the efficacy of combination chemotherapy in thymic

carcinoma. ADOC (cisplatin, doxorubicin, vincristine and cyclophosphamide) chemotherapy was found to have a response rate of 91.8%, however, the study group was small including only eight patients.¹¹ In a phase II study of carboplatin/paclitaxel¹² in tumours of the thymus, 46 patients were enrolled out of which 23 had thymic carcinoma. The response rate seen was 21.7%, with median survival time of 20 months, compared to 91.8% response rate with ADOC regimen. Thus anthracycline-based regimens remain the standard of care. In patients like the one presented here with compromised cardiac function, carboplatin/paclitaxel is an acceptable alternative. Owing to the rarity of these tumours it is difficult to perform randomised controlled clinical trials and make precise treatment recommendations. Studies are ongoing which involve molecular profiling of thymic tumours to delineate a genetic mutation (EGFR, KRAS, PIK3CA, KIT, PDGFRA) which can be susceptible to a targeted therapy.¹³

Learning points

- ▶ Consider extracardiac causes of atrial fibrillation.
- ▶ Learn the differential diagnosis of mediastinal mass and tests to differentiate them.
- ▶ Multimodal treatment of thymic carcinoma.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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