CASE REPORT

Airway compromise due to adenoid cystic carcinoma obstructing the distal trachea: a review of current management and clinical trials

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SUMMARY

An 84-year-old man presented with a 2-month history of intermittent stridor and worsening difficulty in breathing. Chest X-ray and flexible nasendoscopy were unremarkable but following further deterioration a CT scan revealed an obstructing lesion in the distal trachea. Bronchoscopy revealed an infiltrative tumour arising 3 cm above the carina causing 90% obstruction. The mass was biopsied and surgically debrided to leave a patent airway. Histological analysis revealed a diagnosis of adenoid cystic carcinoma. Transthoracic surgical resection was unsuccessful and the patient continues to be effectively managed with periodic bronchoscopic debulking and radiotherapy. This case highlights the diagnostic and therapeutic dilemmas posed by distal tracheal lesions and the need for specialist input for effective management.

BACKGROUND

Adenoid cystic carcinoma (ACC) is a rare malignancy reported to account for less than 1% of tumours of the head and neck.[1] ACC arise from mucous secreting cells, usually of the salivary glands and upper respiratory tract. The most commonly affected sites are the salivary glands but ACC is known to occur in the oesophagus, nasopharynx and trachea, other sites outside the head and neck have also been reported.[2]

Tracheal tumours account for less than 2% of respiratory tract tumours with ACC being the second commonest cause after squamous cell carcinoma.[3 4] When ACC arise within the trachea their presentation is usually related to intraluminal effects such as wheeze, stridor, dyspnoea and haemoptysis.[5]

Although slow growing in nature ACC are known to run a progressive clinical course and are prone to both late local recurrence and distant metastases.[6]

The mainstay of current treatment involves surgical resection +/− radiotherapy depending on factors such as site, stage and biological behaviour of the tumour.[7]

A recent review of the literature suggests that optimal treatment is wide-margin surgical resection and tracheal reconstruction where possible.[8]

Currently there is almost no role for chemotherapy in the treatment of ACC although early clinical trials are underway with promising initial results.[9]

CASE PRESENTATION

An 84-year-old man was referred to otolaryngology clinic with a 2-month history of progressively worsening difficulty in breathing and intermittent stridor, initially attributed to a concurrent upper respiratory tract infection. He experienced marked worsening of symptoms when lying flat, with no cough, bronchial wheeze or other respiratory symptoms. On further questioning the patient had experienced a gradual reduction in exercise tolerance and shortness of breath on exertion over the previous 6 months which he had attributed to an intermittent upper respiratory tract infection. The patient had no relevant medical history other than hypertension, hypercholesterolaemia and type 2 diabetes, was a non-smoker and had no exposure to causes of occupational lung disease. He was completely independent and enjoyed a good quality of life.

On initial examination he was comfortable at rest with no signs of cyanosis with occasional inspiratory and expiratory stridor/monophonic wheeze with an otherwise clear chest. Initial investigation with flexible nasendoscopy revealed an essentially normal larynx and chest X-ray was unremarkable. The patient was discharged and a CT thorax was ordered to be performed on an outpatient basis.

The patient re-presented before the CT was performed as an emergency to his local accident and emergency department 1 week later with worsening stridor acutely dyspnoeic, hypoxic and cyanosed. The patient was initially managed with high-flow oxygen and an urgent CT performed. The patient was then transferred to a specialist otolaryngology centre.

INVESTIGATIONS

CT scanning of the thorax revealed an intraluminal lesion obstructing the distal trachea, causing greater than 90% obstruction of the airway (figure 1). The lesion is confluent with the tracheal wall and localised with no other lesions in the thorax (figure 2).

DIFFERENTIAL DIAGNOSIS

- Malignant: squamous cell carcinoma, ACC, adenocarcinoma, bronchial carcinoid
- Benign: squamous papilloma, chondroma, hamartoma

TREATMENT

The patient was managed with epinephrine nebulisers, steroids and Heliox before being taken to

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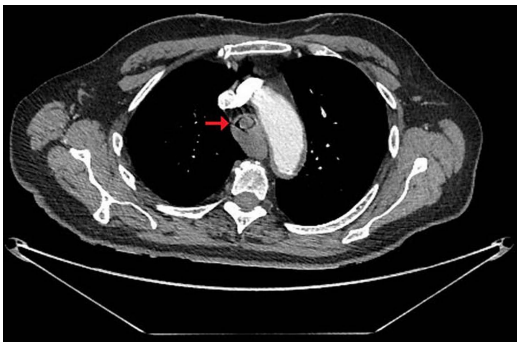

Figure 1 CT scan of the thorax demonstrating tumour obstructing trachea in transverse plane.

theatre. Heliox is a medical gas comprising oxygen 21% and helium 79%, with a lower density than air, which reduces turbulence and increases laminar flow, reducing work of breathing and improving gaseous exchange.[10]

Anaesthesia was accomplished using propofol and an airway was maintained with a rigid subglottic jet ventilation catheter passed distally to the tumour. Rigid bronchoscopy was performed and an infiltrative tumour arising from the posterior tracheal wall visualised, approximately 3 cm from the carina. The tumour was biopsied and surgically debrided until maximal airway patency was achieved.

OUTCOME AND FOLLOW-UP

The debulking procedure was free from complications, the patient recovered well and was discharged home the following day.

Histology of the biopsied tumour confirmed the diagnosis to be ACC. H&E staining of the sample demonstrated features typical of ACC well-circumscribed mucoid 'cysts' and highly nuclear cells (figure 3).

The patient later underwent elective cardiothoracic surgery for definitive resection. The standard procedure for ACC of the trachea is sleeve resection with primary anastomosis usually undertaken via sternotomy or right thoracotomy.[11 12]

This was attempted via right thoracotomy but the procedure was abandoned due to intraoperative complications as the trachea was adherent to the oesophagus and the tumour deemed to be surgically unresectable. As definitive surgical resection was not possible several other options were available and discussed with the patient. The options available included repeat rigid-bronchoscopic debulking, radiotherapy or palliative measures such as stent insertion.

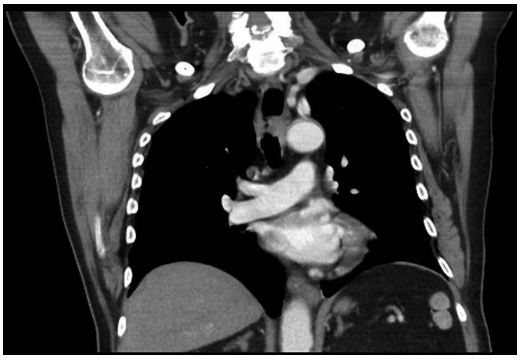

Figure 2 CT scan of the thorax demonstrating tumour obstructing trachea in coronal plane.

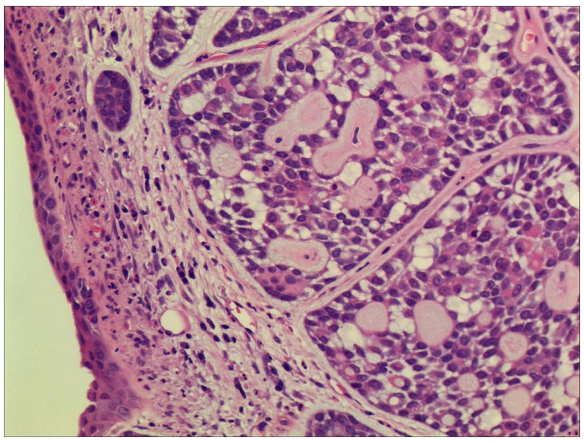

Figure 3 Histology from biopsied tissue demonstrating typical features of adenoid cystic carcinoma, well-circumscribed mucoid 'cysts' and small cells with hyperchromatic angular nuclei (H&E stain, magnification ×400).

The options were discussed and based on several factors including the patient's good quality of life, he was managed with further surgical debridements and radiotherapy.

Over the subsequent 18 months the patient has had two further debridements under rigid bronchoscopy. The patient also received radiotherapy for distal disease progression to a total of 55 Gy in 25 fractions. Lung metastases have also been identified but are progressing slowly and the patient remains asymptomatic.

The combination of surgical debridement and radiotherapy continue to maintain airway patency and the patient remains clinically well and continues to enjoy a good quality of life.

DISCUSSION

This case clearly demonstrates the complications of airway compromise in late presentation of tracheal ACC. There are similar cases in the literature of ACC affecting the trachea.[13] One report highlights the diagnostic difficulty tracheal ACC presents having been mistaken for asthma for several years before diagnosis and treatment.[14]

ACC have also been recorded in the literature in the buccal mucosa, hard palate and tongue base and have been reported as skull base tumours from salivary glands.[15–17]

Rarely ACC have been reported along the more distal respiratory tract and has been recorded in a teenager as a bronchial mass.[18]

Treatment of ACC

In a large case series at the University of Toronto, Maziak *et al* report 38 cases of ACC over 32 years. They reported mean survival of 9.8 years following complete surgical resection, 7.5 years following incomplete resection and 6.2 years following radiotherapy alone. An operative mortality rate of 9% was recorded.[19]

A review of 135 patients with ACC treated at Massachusetts General Hospital and Harvard Medical School between 1962 and 2002 was conducted by Gaissert *et al*. They report 5 year survival rates of 52% in surgically resected ACC and only 33% in surgically unresectable cases with 10 year survival rates of 29% and 10%. Significant improvements in mortality were found to be associated with surgically resected tumours with complete resection and negative histological margins. However they also reported an overall operative mortality of 7%.[20]

Radiotherapy has been demonstrated to provide definitive treatment for unresectable tracheal tumours.[21] In one report patients with ACC were treated to a total of 80 Gy with conventional photon radiotherapy, with one patient remaining free from recurrence at 5 years.[22]

Neutron beam radiotherapy has also been shown to achieve good results with a study of 19 patients with surgically unresectable ACC who were treated with neutron radiotherapy reporting an actuarial 5 year survival rate of 89%.[23] The role of radiotherapy for patients who have had surgical resection with microscopic residual tumour has also been demonstrated.[24]

Recent advances in radiotherapy such as intensity-modulated radiotherapy have also been demonstrated in the adjuvant treatment of ACC.[25]

Airway stenting is further option which is usually reserved for palliative patients once it has been decided that surgery or radiotherapy are not possible. Stents come in a number of varieties the main choice being between self-expanding metal stents and silicon stents such as the Dumon stent. The advantages of self-expanding metal stents in the treatment of airway stenosis are that they offer a wider lumen and can be placed with flexible bronchoscopy. The disadvantages are that they induce granulation tissue, that they can fracture and that they can be very difficult to remove. Silicone stents such as the Dumon stent have the advantage of being easy to remove but their placement is more complex requiring rigid bronchoscopy and general anaesthesia.[26]

Current chemotherapy trials

ACC has not been shown to be successfully treatable with traditional systemic chemotherapy.[27] ACC are known to express particular biomarkers such as VEGF (vascular endothelial growth factor) and c-kit mutations which are known factors for metastatic spread and are potential targets for treatment with targeted molecular therapies such as tyrosine kinase inhibitors.[28] Multiple clinical trials have been conducted for several existing targeted therapies which have already been shown to be effective in other forms of cancer to attempt to demonstrate efficacy in ACC.

Imatinib is a tyrosine kinase inhibitor used in the treatment of chronic myeloid leukaemia which had been demonstrated to be ineffective as monotherapy for ACC but has been shown to produce a partial response when used in combination with cisplatin in phase II clinical trials.[29]

Learning points

- Distal tracheal masses should be remembered as a rare but serious cause of progressively worsening difficulty in breathing.
- Management of distal tracheal airway occlusion should occur at centres with access to specialist surgical and anaesthetic expertise.
- Adenoid cystic carcinomas (ACC) are uncommon, arise from glandular cells and are slow growing but prone to local recurrence and distant metastases.
- Management of ACC may require repeat treatments due to local and distant recurrence.
- ACC are amenable to definitive treatment by surgical resection or radiotherapy, palliative measures such as stent insertion, with the potential for future chemotherapy.

Cetuximab is an epidermal growth factor receptor inhibitor which is usually used in the treatment of bowel or head and neck cancer which has also been shown to be favourable when used in combination with cisplatin in chemotherapy or chemoradiotherapy.[9]

Sunitinib is a multi-kinase inhibitor used in the treatment of renal cell cancer, in a recent phase II trial it did not produce a response in ACC but was shown to prolong tumour stabilisation.[30] The authors of this trial identified several factors that limit effectiveness of clinical trials in ACC such as the small numbers of patients, the prevalence of single centre trials and the slow growing nature of the disease. They therefore suggest strategies to improve phase II clinical trials such as development of multicentre trials, the use of imaging analysis and the further development of biomarkers.

In conclusion ongoing clinical trials and the development of new molecular-targeted therapies may provide new chemotherapeutic treatment options for ACC.

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Patient consent Obtained.

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