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CLINICAL RECORD

Rhabdomyosarcoma of the trachea: first reported case treated with proton beam therapy

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Abstract

Objective: We report a case of rhabdomyosarcoma of the trachea in a 14-month-old child, and we present the first reported use of proton beam therapy for this tumour.

Case report: A 14-month-old girl presented acutely with a seven-day history of biphasic stridor. Emergency endoscopic debulking of a posterior tracheal mass was undertaken. Histological examination revealed an embryonal rhabdomyosarcoma with anaplasia. Multimodality therapy with surgery and chemotherapy was administered in the UK, and proton beam therapy in the USA.

Conclusion: Only three cases of rhabdomyosarcoma of the trachea have previously been reported in the world literature. This is the first reported case of treatment of this tumour with proton beam therapy. Compared with conventional radiotherapy, proton beam therapy may confer improved long-term outcome in children, with benefits including reduced irradiation of the spinal cord.

Key words: Rhabdomyosarcoma; Trachea; Proton Beam Therapy; Paediatric

Introduction

Rhabdomyosarcoma is an aggressive, malignant neoplasm originating from the embryonal mesenchyme. It is the most common paediatric sarcoma but is uncommon in adults.[1–3] Rhabdomyosarcoma may occur at any site. About 30 per cent of reported cases have occurred in the head and neck. Rhabdomyosarcoma of the trachea is extremely rare.

Over the last four decades, a multimodality approach to therapy has been adopted, including surgery, multidrug chemotherapy and radiotherapy.[4] Patients with non-metastatic rhabdomyosarcoma have an overall survival rate of greater than 70 per cent with multimodality therapy.[5] Complete extirpation improves overall five-year survival to approximately 86 per cent, compared with only 30–50 per cent after incomplete resection.[6]

Methods

A literature search of the Medline, EMBASE, CINAHL and AMED databases and the Cochrane Database of Systematic Reviews, using the Ovid Collection, was conducted to identify scientific publications relevant to paediatric rhabdomyosarcoma.

Case report

A 14-month-old girl presented to Royal Manchester Children's Hospital, UK, with a seven-day history of progressive, biphasic stridor exacerbated by exercise and crying. There was no clinical improvement in the airway following intravenous dexamethasone and nebulised adrenaline administered in the emergency department.

Emergency direct laryngo-tracheo-bronchoscopy revealed a tumour arising from the postero-lateral tracheal wall and reducing the lumen diameter by 70 per cent. This tumour was debulked, using paediatric microlaryngoscopy instruments, and specimens sent for histological analysis. The child was intubated and managed on the paediatric intensive care unit.

Computed tomography confirmed the presence of a tumour located between the trachea and the oesophagus, with no visible cervical metastases (Figure 1).

Five days later, extubation was successful at the first attempt, and the patient was weaned off steroids after two weeks. The biphasic stridor was noted to have resolved following debulking of the tumour.

The initial differential diagnosis included tracheal pseudotumour. However, histopathological examination revealed an embryonal rhabdomyosarcoma, with desmin and muscle-specific actin staining smooth and striated muscle in several stages of skeletal muscle morphogenesis, from stellate undifferentiated mesenchymal cells to fully differentiated myofibres (Figure 2).

The paediatric multidisciplinary team (MDT) at Royal Manchester Children's Hospital, UK, advised nine cycles of chemotherapy with ifosfamide, vincristine and actinomycin, with review after three cycles to assess the response and to agree a definitive plan for local control. After the third cycle, tumour volume reduction was demonstrated on direct laryngo-tracheo-bronchoscopy and magnetic resonance imaging (MRI). Residual tumour was then resected macroscopically via an external approach, with preservation of the

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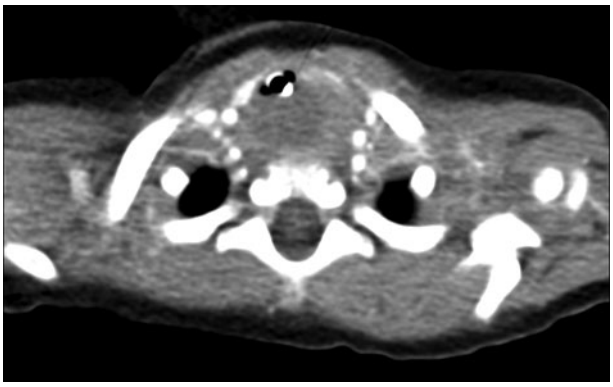

FIG. 1

Axial computed tomography of the upper thorax with endotracheal tube *in situ*, demonstrating a large soft tissue mass posterior to the trachea.

recurrent laryngeal nerves. Histological examination of the resection specimen demonstrated anaplastic features in the residual embryonal rhabdomyosarcoma.

The paediatric MDT next advised proton beam therapy with continuing concurrent chemotherapy. Proton beam radiotherapy was administered at the University of Florida Proton Therapy Institute, Jacksonville, Florida, USA (50.4 Gray in 28 fractions).

A second MRI scan demonstrated complete response to multimodality therapy (Figure 3).

At the time of writing, the child was 30 months old and continued to be followed up by the paediatric otolaryngology and paediatric oncology services. She had completed treatment eight months previously, and currently showed no evidence of recurrent tumour.

Discussion

Paediatric airway obstruction is almost exclusively caused by benign conditions. During the initial presentation of our case, the differential diagnosis included a foreign body and subglottic haemangioma. Our case highlights the fact that, rarely, the cause of paediatric airway obstruction can be a malignant tumour. Malignant tumours that may affect the trachea in children include lymphoma, thyroid carcinoma and neuroblastoma.[7] Our patient represents only the fourth case of rhabdomyosarcoma of the trachea to be reported in the world literature, and the first UK case.

Rhabdomyosarcoma was first described in 1854 by Weber, who reported a malignant tumour in which cells exhibited features of striated muscle.[8] The head, neck and genitourinary tract are the most common sites, and the airways are very rarely involved.[9] Within the head and neck, rhabdomyosarcoma most commonly presents in the face, followed by the orbit, the nasal cavity and paranasal sinuses, and the nasopharynx. Less common sites include the parotid gland, neck,

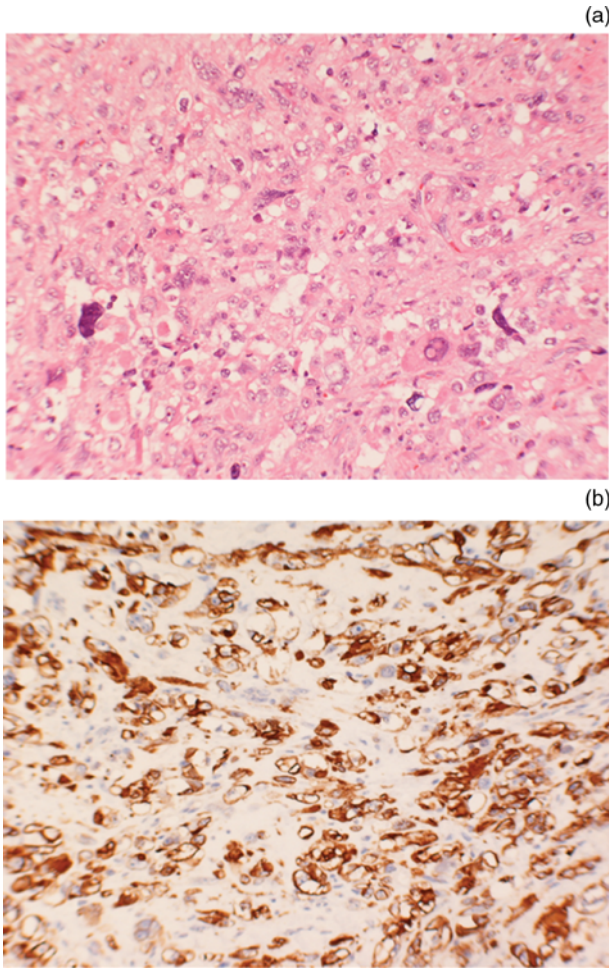

FIG. 2

Photomicrographs of the resection specimen demonstrating: (a) anaplasia (H&E; 400×); and (b) immunohistochemical desmin staining (400×).

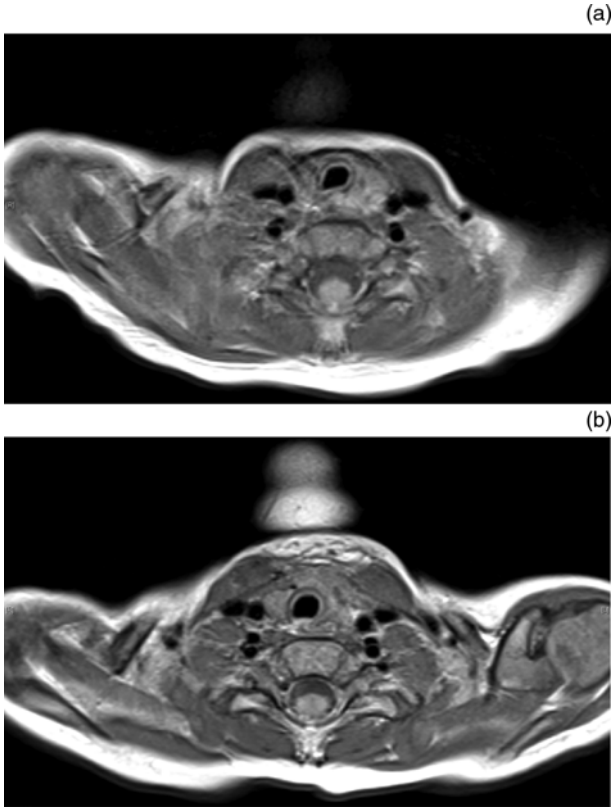

FIG. 3

Serial axial magnetic resonance imaging of the upper chest, demonstrating tumour size reduction (a) after three cycles of chemotherapy with ifosfamide, vincristine and actinomycin; and (b) after nine cycles of this same chemotherapy together with surgery and proton beam therapy plus concurrent chemotherapy.

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infratemporal fossa, oral cavity and larynx.[10] Rhabdomyosarcoma predominantly affects children and young adults, with approximately 87 per cent of patients aged under 15 years; it rarely occurs in patients over 25 years old.[6] There is a male predominance, with a ratio of approximately 1.4 males to 1.0 female.[6]

Tracheal rhabdomyosarcoma has been reported in three cases: a 12-year-old girl from Israel presenting with a polypoid, intratracheal mass; a 15-year-old girl from Sweden with a tumour of the anterior wall of the upper trachea; and a 7-year-old boy from Poland with a tumour of the lower trachea and left main bronchus.[11–13]

The Israeli girl was admitted with severe dyspnoea, and emergency tracheostomy was performed following failed intubation. A globular tumour arising from the trachea and occluding the lumen was endoscopically removed, and a diagnosis of tracheal embryonal rhabdomyosarcoma was made. The patient received radiotherapy (4500 Gy) to both hila, plus multidrug chemotherapy with vincristine, actinomycin, cyclophosphamide and adriamycin over a two-year period, resulting in complete remission.[11]

The 15-year-old, Swedish girl presented with progressive dyspnoea requiring tracheostomy. Intra-operatively, a tumour was found on the anterior wall of the upper trachea, which was partially resected along with complete resection of the thyroid gland. Multidrug chemotherapy with vincristine, actinomycin D, cyclophosphamide and adriamycin produced little response. Concurrent chemoradiotherapy (50 Gray) with etoposide and cisplatin resulted in minimal tumour volume reduction. Radical surgery was undertaken. Post-operatively, the patient developed a left-sided, malignant pleural effusion and subsequently died.[12]

The seven-year-old, Polish boy presented with severe, biphasic stridor, and a foreign body was suspected. However, at bronchoscopy a tumour of the trachea and left main bronchus was identified and debulked, and a tracheostomy was inserted. The tumour was shown to be an embryonal rhabdomyosarcoma. Multidrug chemotherapy with vincristine, adriamycin, cisplatin and cyclophosphamide, plus cobalt-60 radiotherapy, was administered over one month; the tracheostomy tube was then removed. However, the tracheostomy was reinserted and further combination chemotherapy (with the same regimen) was administered at two years after the initial presentation, due to recurrent tumour; a tracheal stricture was also dilated. A further recurrence, four years after the first diagnosis, was debulked with endotracheal laser on two occasions, in Munich; a malignant tracheal stricture was then resected, via thoracotomy, with end-to-end anastomosis. Six years after diagnosis, the tracheostomy was removed. No further details were given, no radiological images were presented, and there was no other description of the tumour extent.[13]

Of the subtypes of rhabdomyosarcoma, embryonal is the commonest, particularly in children under 15 years of age, as in our case.[1] The most recent classification system, from the Intergroup Rhabdomyosarcoma Study Group, correlates histological subtype with prognosis. The embryonal subtype has an intermediate prognosis, undifferentiated and alveolar subtypes have a poorer prognosis, and the rarer botryoid and spindle cell subtypes have a better prognosis.[14]

In our case, anaplastic aggregates were seen within the tumour; these are known to adversely affect survival. Diffuse sheets of anaplasia are a worse prognostic sign than scattered anaplastic cells; in our case, the extent of anaplasia was intermediate.[15]

Prognosis also varies by site. The most favourable locations are the orbit and genitourinary tract, while retroperitoneal rhabdomyosarcoma has the worst prognosis.[6]

Lower age confers a better prognosis, although patients aged less than one year have a worse prognosis.[16]

Isolated cervical nodal metastasis confers a five-year survival rate of only 30 per cent.[17]

- **Acute paediatric airway obstruction is very rarely due to malignancy**
- **Tracheal rhabdomyosarcoma is an extremely rare cause**
- **Treatment is by surgery, multidrug chemotherapy and radiotherapy**
- **Proton beam therapy is a new, effective treatment for rhabdomyosarcoma**
- **It reduces distal tissue irradiation and may help prevent secondary malignancy**

The most important prognostic factor seems to be complete surgical extirpation, with an overall five-year survival rate of approximately 86 per cent, compared with only 30–50 per cent in patients undergoing incomplete resection.[6]

The overall three-year failure-free survival rate is greater than 80 per cent for patients with the embryonal subtype, and less for other subtypes.[17]

The standard treatment is multimodality therapy with surgery and chemotherapy with or without radiotherapy. The Intergroup Rhabdomyosarcoma Study IV advocated a combination of vincristine, actinomycin D and cyclophosphamide, with or without radiotherapy.[17]

Conventional radiotherapy uses X-rays (photons), which eradicate neoplastic tissue by causing DNA damage.[18] Conventional radiotherapy causes damage to healthy tissue, resulting in morbidity.

Proton beam therapy is a form of charged particle therapy. Protons have very rapid energy loss in the last few millimetres of penetration, which results in a sharply localised peak radiation dosage known as the Bragg peak (Figure 4). The penetration depth of the proton beam is directly related to the initial energy of the charged particle, and this can be

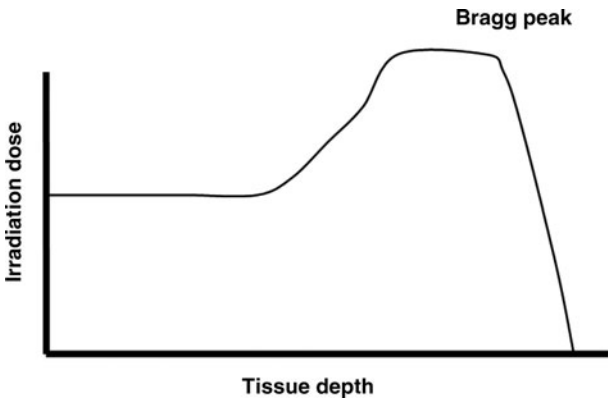

FIG. 4
Graphical representation of the Bragg peak: a sharp reduction in ionisation which reduces distal tissue irradiation.

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predetermined during treatment planning, avoiding damage to critical structures deep to the target. This was of particular value in our patient as it limited the irradiation of the spinal cord.

Conclusion

Embryonal rhabdomyosarcoma is a rare form of paediatric cancer. To our knowledge, only three cases of rhabdomyosarcoma of the trachea have previously been reported. Our patient represents the first reported such case to be treated with proton beam therapy.

Rhabdomyosarcoma requires management with multimodality therapy co-ordinated by an experienced MDT. The risks of conventional radiotherapy in paediatric patients cannot be ignored. Current guidance for the treatment of paediatric malignancy suggests that appropriate patients should be considered for proton beam therapy.

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