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CASE REPORT

Successful multimodal management of rhabdomyosarcoma and dento-facial sequelae of treatment

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Summary Rhabdomyosarcoma (RMS) is an aggressive malignant neoplasm associated with high morbidity. We describe a case of embryonal rhabdomyosarcoma treated successfully with combination radiotherapy and chemotherapy.

Introduction

Rhabdomyosarcoma (RMS) is a malignant neoplasm composed of neoplastic mesenchymal cells with varying degrees of striated muscle differentiation. It is the most common sarcoma in children, accounting for 4—8% of all cases of malignant disease under 15 years of age.[1] There is a pronounced predilection of RMS to children, most commonly affecting males.[2]

RMS commonly presents as persistent swelling which is often painful, though not exclusively so. Other reported symptoms of perioral RMS include dysphagia, trismus, and paraesthesia.[3] Anatomically RMS is divided into two subtypes: parameningeal (including RMS of the nasopharynx, paranasal sinuses, nose, infratemporal fossa, and pterygopalatine fossa) and nonparameningeal (including disease of the oral cavity, oropharynx, parotid gland, larynx, and parotid gland). Sites of predilection in the head and neck include the tongue and palate.

Head and neck RMS has a distinct prognosis and biologic behaviour. RMS has four distinct histopathological subtypes: embryonal, alveolar, pleomorphic and undifferentiated. The embryonal subtype

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is the most common subtype, tends to occur in young patients and frequently arises in the perioral region.[4]

Formerly, surgical excision was the only therapeutic modality available for RMS. However, combination therapy has replaced surgery as the standard of care with encouraging results.

This case report highlights the significant improvement in outcome offered by multimodal management of rhabdomyosarcoma. The turbulent nature of the active treatment phase aswell as the local sequelae of the combination therapy are also described.

Case report

An 8-year-old female was referred to the Oral and Maxillofacial Surgery Department by her medical practitioner with a three day history of a right-sided buccal swelling. The swelling had been unresponsive to empiric oral antibiotic treatment.

Initially, a dental origin was considered with the upper right first molar being tender to percussion, but responding positively to vitality testing. Oral antibiotics were continued for four further days. However, the swelling failed to resolve.

The patient was admitted for an examination under anaesthetic and incisional biopsy. On closer digital examination the mass appeared to extend into the right parapharyngeal space. The histopathology report described a tumour of small spindle cells in a loose myxoid ground substance. The appearance was consistent with embryonal rhabdomyosarcoma. Immunocytochemistry results confirmed this.

Further investigations were performed to decipher the precise location, spread and prognosis of the condition. A CT scan confirmed an extensive soft tissue tumour, measuring 3.5 cm × 3.5 cm in the right parapharyngeal space, buccal space and infra-temporal fossa (Fig. 1). Enlarged lymph nodes (>1 cm) were also noted in the parotid gland and superior mediastinum. A sub-pleural nodule was apparent on the chest CT scan.

The patient was referred to a paediatric oncologist. Treatment was commenced in accordance with an International Society of Paediatric Oncology (SIOP) protocol for management of high risk sarcomas. The patient was allocated to a 6 drug arm chemotherapy treatment strategy. Agents used included carboplatin, epirubicin, and vincristine (CEV) and ifosfamide, vincristine, and etoposide (IVE). Chemotherapy was administered over a 27 week period and adjuvant high-dose radiotherapy added at week 9.

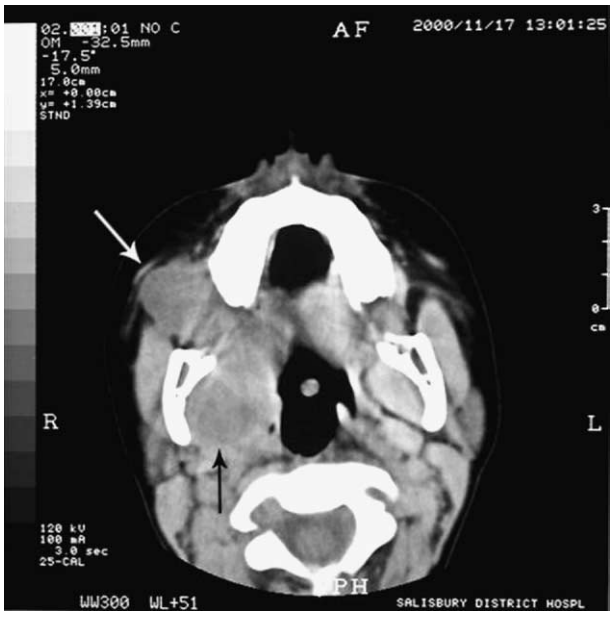

Figure 1 Pre-treatment CT scan.

During the active phase of treatment the patient developed a series of problems including painful radiation-induced oropharyngeal mucositis. This culminated in an inability to eat necessitating gastrostomy tube insertion. The patient was also admitted on two occasions with febrile neutropenia and developed right upper lobe pneumonia.

Within 2 months of completion of active treatment the patient had recovered significantly. She was improved systemically and began to regain weight steadily. Four years after completion of the active phase of treatment the patient has only minor residual problems including a degree of xerostomia and a generalized arrest of root development, particularly affecting the second premolars and second permanent molars (Fig. 2). The patient was also reassessed by a consultant maxillofacial

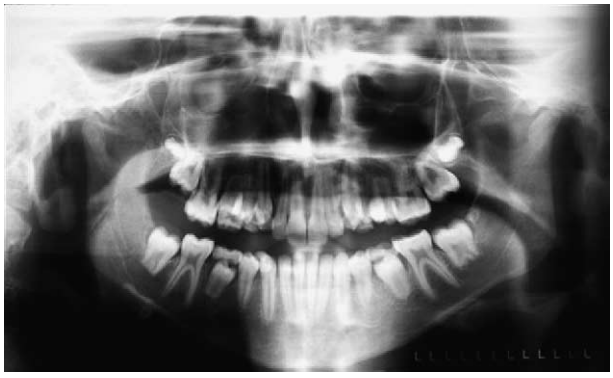

Figure 2 Post-treatment panoramic radiograph.

surgeon regarding underdevelopment of the right mandibular ramus. Intervention was felt unnecessary. Generally the patient is thriving with growth within the normal range for her age. There has been no evidence of local or regional tumour recurrence.

Discussion

RMS is a highly aggressive neoplasm capable of rapid local invasion and bony infiltration. The non-specific and somewhat unremarkable initial symptoms, including painless swelling, trismus and paraesthesia, often make early diagnosis difficult.[5] The time interval between onset of symptoms and correct diagnosis of head and neck RMS is estimated at 1–17 months.[6] Our patient sought treatment early ensuring a definitive diagnosis was made with in two weeks of onset of the swelling. The importance of biopsy of suspected inflammatory swellings if pus is not obtained after drainage is obvious.

Initially surgery was the sole therapeutic modality available for RMS.[7] Surgery tended to be radical and associated with significant morbidity if complete excision was to be achieved. Recurrence rates were high due to propensity of RMS to uncontrolled local invasion and metastatic spread. The condition carried an attendant poor prognosis.[8] The potential role of radiotherapy in management of recurrent RMS emerged.[9] Thereafter, the benefits of a multimodal approach involving combinations of surgery, chemotherapy and radiotherapy became clear.[10] A six drug combination in accordance with an international protocol for RMS was used, with adjunctive radiotherapy.[11] The possibility of surgical resection of the mass or part thereof was considered. In view of the size of the primary lesion, rapid tumour proliferation and metastatic spread the combination of radiotherapy and chemotherapy alone was deemed most prudent.

High-dose radiation and chemotherapy can independently provoke a plethora of oral complications including mucositis, xerostomia, loss of taste, opportunistic infection, trismus, erythema, and impaired dental and osseous development.[12] Concomitant use of both modalities exacerbates these difficulties. Radiotherapy in isolation may result in rampant dental caries, and can induce osteoradionecrosis as a consequence of hypovascular, hypocellular and hypoxic changes.[13] Our patient developed severe, painful oropharyngeal mucositis causing odynophagia, which ultimately necessitated gastrostomy placement. She also continues to complain of some xerostomia. However, her dental health has been maintained due to regular dental review, dietary changes, fluoride mouthrinsing and scrupulous oral hygiene. Generally, the susceptibility to post-treatment complications is reduced by prompt implementation of well-defined preventive regimes.[14]

The generalized arrest of root development is likely to be related to both treatment modalities, though primarily due to the high-dose radiotherapy.[15] Foreshortening and blunting of roots, incomplete calcification, premature apex closure, and tooth agenesis have also been attributed to radiotherapy and chemotherapy.[16] Immature teeth tend to be more susceptible to developmental disturbance than mature teeth.[17] This pattern is apparent in our patient. The absence of the mandibular third molars may also be related to the high-dose radiotherapy.

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