



CASE REPORT

REVISED Case Report: Case report: A rare case of middle-ear Rhabdomyosarcoma in a 4-year-old boy [version 2; peer review: 3 approved]

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Abstract

We present a rare case of a four-year-old boy with a botryoid embryonal rhabdomyosarcoma of the right middle ear. Rhabdomyosarcoma is a soft tissue malignancy which is thought to originate from embryonic mesenchymal cells of striated skeletal muscle. It is a disease primarily of children and is exceptionally rare in parameningeal regions. The diagnosis is often delayed and easily misdiagnosed as aural polyp. Therefore, advanced disease is common at the time of diagnosis. A four-year-old boy presented with a four-month history of recurrent left ear blood and pus discharge, otalgia and fevers. He attended his GP three times and paediatric A&E 13 times where he received antibiotics for presumed otitis media and externa. He was eventually referred to the otolaryngology department and underwent an examination under anaesthesia of ear and excisional biopsy of a suspicious aural polyp. Staging chest CT and PET scan showed no loco-regional spread or distal metastasis. Magnetic resonance imaging demonstrated absence of invasion into adjacent organs. Histology confirmed embryonal rhabdomyosarcoma, botryoid subtype. Subsequent to the initial excision of the polyp, he was started on an ifosfamide, vincristine and actinomycin (IVA) chemotherapy regime in three weekly cycles for nine cycles with concomitant radiotherapy. Two weeks subsequent to his first chemotherapy dose he presented with a House-Brackmann II-III facial nerve palsy but no other middle ear complications. He was started on intravenous antibiotics and dexamethasone. The facial nerve palsy incompletely resolved with treatment.

Keywords

Rhabdomyosarcoma, middle ear

Open Peer Review

Reviewer Status

	Invited Reviewers		
	1	2	3
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- 1 **Max Cunnane** , Royal Sussex County Hospital, Brighton, UK
- 2 **Craig Hickson**, Leicester Royal Infirmary, Leicester, UK
- 3 **Adam Haymes** , Medway Maritime Hospital, Gillingham, UK

Any reports and responses or comments on the article can be found at the end of the article.

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REVISED Amendments from Version 1

Minor clarifications were made in response to reviewer comments.

Any further responses from the reviewers can be found at the end of the article

Introduction

Rhabdomyosarcoma is a rare soft tissue malignancy with unknown aetiology. It is thought to originate from embryonic mesenchymal cells of striated skeletal muscle. It is a disease primarily of children, with two-thirds of patients presenting under the age of six years¹. The commonest areas of the body to be affected are the head and neck, the bladder and reproductive organs. They are rare elsewhere and are exceptionally rare in parameningeal regions, including the ear and mastoid.

Symptoms depend on the location of the tumour. Aural involvement often has non-specific symptoms such as fever and otalgia. If the tumour is significant in size and protrudes through the tympanic membrane, then otorrhoea and hearing loss may result. Rarely, facial nerve palsy may occur. The diagnosis is often delayed and easily misdiagnosed as aural polyp. Therefore, advanced disease is common at the time of diagnosis.

We present a rare case of a four-year-old boy with a botryoid embryonal rhabdomyosarcoma of the right middle ear and review the literature.

Case report

A four-year-old boy presented with a four-month history of recurrent left ear blood and pus discharge, otalgia and fevers. He attended his general practitioner (GP) three times and Paediatric Accident & Emergency 13 times where he received oral, topical and intravenous antibiotics for presumed otitis media and externa. He had no relevant family history. He was eventually referred to the otolaryngology department after 19 months and was listed for an examination under anaesthesia of and excisional biopsy of a suspicious aural polyp 2 weeks after presentation to the otolaryngology department team. Intra-operatively, a large lesion extending from the middle ear through the tympanic membrane and into the external auditory canal was noted which was incompletely resected as only tissue lateral to the tympanic membrane was resected. The lesion was found to be highly vascular.

Histopathological findings were in keeping with embryonal rhabdomyosarcoma, botryoid subtype. This rare diagnosis required a second opinion from the Histology Department at the Royal Marsden Hospital. Immunohistochemical staining revealed sheets of rounded tumour cells with scant cytoplasm and inconspicuous nucleoli, which were distinguished by the formation of polypoid and grapelike tumour masses. Malignant cells in an abundant myxoid stroma were observed. Staining was positive for desmin and muscle-specific actin.

Magnetic resonance imaging (MRI) of the head was performed within two weeks of resection of the tumour, which demonstrated

absence of invasion into adjacent organs. Staging chest MRI showed no evidence of metastases and PET scan showed no loco-regional spread or distal metastasis. Bone marrow trephine and CSF were negative. The patient's haemoglobin levels were borderline anaemic but all routine blood tests were otherwise within normal limits.

At 5 weeks after initial presentation he was started on nine cycles of IVA chemotherapy: ifosfamide (3 g/m² on days 1 and 2); vincristine (1.5 mg/m² weekly during the first 7 weeks, then only on day 1 of each cycle); and Dactinomycin (at 1.5 mg/m² on day 1) in three weekly cycles with concomitant radiotherapy.

Two weeks subsequent to his first chemotherapy dose he was admitted with neutropenic sepsis and also presented with a House-Brackmann II-III facial nerve palsy but no other middle ear complications. He was started on paediatric doses of intravenous Piperacillin / tazobactam and gentamicin for 5 days as an inpatient prior to being discharged on a paediatric oral dose of ciprofloxacin for the remainder of his chemotherapy course. The facial nerve palsy incompletely resolved to a House-Brackmann I-II with a 2-week course of 3 mg dexamethasone twice daily. He is being followed up on the following schedule: 3–4 months in the first 2–3 years, then twice a year up to the fifth year. Disease free follow-up is 18 months.

Literature review

We searched EMBASE, MEDLINE, UpToDate, CINAHL, TRIP Database, BMJ Best Practice, Google Scholar, Cochrane Database of Systematic Reviews and NICE Evidence Search with the following search terms: rhabdomyosarcoma (RMS); ear; aural; middle ear; inner ear; ear canal, parameningeal; ear neoplasm in July 2018.

Inclusion criteria were: diagnosis of rhabdomyosarcoma of the middle ear; published in a peer reviewed journal; any geographical location or language; any publication date; any age of patient.

In total 11 case reports were found. Of these, there was an equal male-female split. The clinical presentations were similar throughout the case reports, mimicking recurrent otitis media/externa. The average survival across the case reports was 7.2 months. We summarise the case reports in [Table 1](#).

Discussion

Rhabdomyosarcoma of the middle ear and mastoid is rare². Around 30% of cases of paediatric rhabdomyosarcoma occur in the head and neck involving the orbits, base of skull, nasal cavity and nasopharynx³ but only 3% occur in the ear or mastoid⁴. In total, 63% of rhabdomyosarcomas occur in children under 10 years old, with a peak between 2 and 5 years old⁵.

Presentation often involves purulent or blood-stained discharge, hearing loss, aural polyps and granulation tissue. Clinical diagnosis is often delayed since the presentation is similar to that of chronic suppurative otitis media⁶. By the time of diagnosis, a facial nerve palsy is usually present and there is involvement of both the middle and external ear and petrous bone⁷. Metastases

Table 1. Summary of case reports.

Case	Authors	Patient sex	Age	Journal (year)	Symptom	Investigation	Subtype	Management	Prognosis
1	Phatak <i>et al.</i>	M	2	Indian Journal of Otol 1999	CNVII palsy	CT	Embryonal	Surgery + CRT	Alive at 18 mo
2	Hu <i>et al.</i>	M	3	Otol HNS 2002	Otorrhoea	CT	Embryonal	Surgery + CRT	Alive at 18 mo
3	Hu <i>et al.</i>	M	33	Otol HNS 2002	CNVII palsy + Otagia	CT	Embryonal	Surgery + CRT	Alive at 24 mo
4	Abbas <i>et al.</i>	M	3	ENT Jour 2005	Otorrhoea	CT	Embryonal	CRT	Died at 11 mo
5	Viswanatha	M	4	ENT Jour 2007	CNVII + CNVI	CT	Embryonal	Surgery + CRT	Died at 3 mo
6	Muranjan <i>et al.</i>	F	5	BMJ Case rep 2014	CNVII + Otorrhoea	CT + MRI	Anaplastic subtype of embryonal	CRT	Died at 5 mo
7	Vasiwala <i>et al.</i>	M	6	Med J Malaysia 2015	CNVII + Otorrhoea	CT	Embryonal	Surgery + CRT	Died at 7 mo
8	Bhargava <i>et al.</i>	M	31	J Surg Case Rep 2012	CNVII + Otorrhoea	CT	Embryonal	Surgery + CRT	Died at 6 mo
9	Salunke <i>et al.</i>	M	3	J Pediatr Neurosci 2012	CNVII + Otagia + H/Loss	CT + MRI	Embryonal	Surgery + CRT	Died at 6 mo
10	Vegari <i>et al.</i>	F	3	Case Rep Otolary 2012	Otorrhoea	CT	Embryonal	Surgery	Died at 12 mo
11	King <i>et al.</i>	F	2	Brachytherapy 2017	Mass	CT + MRI	Botyroid	Chemo + Brachy	Alive at 8 mo

commonly spread to the lungs, liver, bones and extremities, and are present in approximately 30% of cases³.

According to the International Classification of Rhabdomyosarcoma, these tumours are histopathologically classified into five categories: botryoid, spindle cell, embryonal, alveolar, and undifferentiated. Embryonal rhabdomyosarcoma is the most common, accounting for 70–80%, occurring mostly in the orbit and parameninges³. Alveolar is the second most common, usually presenting in the deep soft tissues of the extremities⁴.

Risk factors for rhabdomyosarcomas are poorly understood. Epidemiological studies have suggested a link with radiation and recreational drug *in utero*, lower socioeconomic status and use of antibiotics soon after birth⁸. Several genetic syndromes, including some commonly known to otolaryngologists such as Rubinstein-Taybi syndrome and Beckwith-Wiedemann syndrome, are associated with increased prevalence of rhabdomyosarcoma.

Historically, rhabdomyosarcomas were invariably fatal. Now, 5-year survival rates of around 80% have been reported⁹; however, surgical removal is often difficult in head and neck cases given the stage of the neoplasm and anatomy. Consequently,

the mainstay of treatment is often chemoradiotherapy. Parameningeal tumours, especially of the middle ear and mastoid, have a poor prognosis because of the proximity to the brain⁶. Of the categories, embryonal have the best prognostic factor and alveolar the worst and children have a better prognosis than adults⁴.

Conclusion

Rhabdomyosarcoma of the ear is a rare presentation but one which should be considered in young children with recurrent otitis media. If missed, facial nerve involvement is a common as well as local meningeal and distant metastasis. Multi-disciplinary involvement and patient education is mandatory in ensuring the highest survival rates. Treatment consists of a combination of surgery, chemotherapy and/or radiotherapy.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

Consent

Written informed consent for publication of their clinical details as obtained from the parent of the patient study.

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Reviewer Report 05 November 2019

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Adam Haymes 

Department of Otolaryngology Surgery, Medway Maritime Hospital, Gillingham, Kent, UK

This article describes a case of botyroid embryonal rhabdomyosarcoma of the right middle ear in a four year old child. It covers the clinical presentation, workup and subsequent management of this rare entity and reviews the pertinent literature of other case descriptions.

The case report is very well written, informative, covers an interesting and unusual topic, and adequately covers all of the objectives set out in the guidelines.

The background of the case's history and progression are described in excellent detail.

Description of the physical examination and workup of the patient are detailed and methodical, as are the descriptions of diagnostic tests, treatments and outcomes.

Emphasis is placed on the rarity of this clinical entity and thus it's contribution to the literature is a useful one. There were no novel treatments in this case report, however the description of the chemotherapy regimen will be useful for other clinicians. Description of the recurrent presentations to the GP and A&E departments are a sobering reminder of the need for these clinicians to recognise unusual clinical patterns, not rely on previous diagnoses and seek help from specialists early in such scenarios.

Images of the histology would have been a nice to see given the rarity of this clinical entity.

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Yes

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Otolaryngology, Rhinology, Head & Neck surgery, Tissue engineering, regenerative medicine

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 31 October 2019

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Craig Hickson

Leicester Royal Infirmary, Leicester, UK

This is a generally well written case report detailing a rare disease process in an unusual anatomical location. It covers pathogenesis, presentation, problems with diagnosis, treatment and prognosis.

It has multiple grammatical errors which need review and correcting:

'Recreational drugs in utero.'

The diagnosis is often delayed and easily misdiagnosed as AN aural polyp

'A four-year-old boy presented with a four-month history of recurrent left ear blood and pus discharge' - please revise to A four-year-old boy presented with a four-month history of recurrent haemo-purulent discharge from the left ear.

In addition I have the following comments/suggestions:

Intra- operatively, a large lesion extending from the middle ear through the tympanic membrane and into the external auditory canal was noted which was resected. The lesion was found to be highly vascular.

Was it totally resected? Via a tympanotomy? Or was the tissue lateral to the TM resected. If a tympanotomy was performed what was the status of the ossicles?

You say that the facial nerve palsy incompletely resolved. Please give details using House-Brackmann or

other suitable classification.

How do you arrive at '3% of paediatric rhabdomyosarcoma occurring in the head and neck involving the'?

There are only 11 cases reported. You would need $100/3 = 30$ cases or more to be able to state this?

Could intra operation images and high res CT image be included?

Please state the disease free followup to date of your patient.

Please comment on hearing outcome.

There is no mention specific mention of MDT discussion? You state a second opinion was sought but surely this case went through an MDT?

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Yes

Is the case presented with sufficient detail to be useful for other practitioners?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Otology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 11 Nov 2019

Richard Menzies-Wilson, Whipps Cross University Hospital, London, UK

Many Thanks for your comments. We have adjusted the manuscript to reflect your feedback.

Competing Interests: No competing interests were disclosed.

Reviewer Report 16 October 2019

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Max Cunnane 

Royal Sussex County Hospital, Brighton, UK

This is an interesting, concise and well-constructed case report and review of the relevant literature surrounding rhabdomyosarcoma affecting the middle ear. This is a rare entity and as such additional case reports are valuable in adding to the existing literature.

The case report contains adequate description of the patient and detail of the presentation and initial investigations, which would be in line with the reviewers own practice.

The case highlights the need for high clinical suspicion when treating non-resolving recurrent ear infections in children which is a useful message for clinicians.

The literature review results are presented clearly and contain all relevant information regarding the case's reported. However, there is a lack of detail surrounding which chemotherapy/radiotherapy regimes were used. It is also unclear if they were adjuvant or primary treatment modalities for the other cases described.

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Yes

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Working as specialist registrar in otolaryngology. Particular interest include paediatric ENT and laryngology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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