The Journal of Laryngology & Otology

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Nasal chondromesenchymal hamartoma: an update

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Review Article

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Cite this article: Saunders TFC, Bruijnzeel H, Ahmed S, Paruleka M, McDermott A-L. Nasal chondromesenchymal hamartoma: an update. *J Laryngol Otol* 2022;**136**:1140–1147. https://doi.org/10.1017/S0022215121002267

Accepted: 5 November 2020
First published online: 23 August 2021

Key words:
Endoscopy; Paranasal Sinuses; Otolaryngology

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Abstract

Objective. Nasal chondromesenchymal hamartoma is a rare pathology that can present with a myriad of symptoms to ENT, maxillofacial and ophthalmology departments. This study reviewed the literature on nasal chondromesenchymal hamartoma as well as adding three new cases to the reported literature.

Method. This study was an up-to-date review of the world literature with the addition of three new cases to provide the most comprehensive review to date.

Results. A total of 56 patients with nasal chondromesenchymal hamartoma were identified, ranging from children to adults. Nasal symptoms and ocular symptoms were most common, and surgical resection was the most frequent treatment modality.

Conclusion. This study advocates for increased awareness of the condition associations for nasal chondromesenchymal hamartoma, multi-specialty treatment and the role for the ENT surgeon in treatment of the condition.

Introduction

Nasal chondromesenchymal hamartoma is a rare pathology first described by McDermott *et al.* in 1998.[1] Embryologically, nasal chondromesenchymal hamartomas are derived from mesoderm. They are mostly benign, slow-growing lesions that have self-limiting proliferation. They do not regress following cessation of growth, and they cause local compression and obstruction necessitating complete surgical resection.

Nasal chondromesenchymal hamartoma has been linked to another important pathology: pleuropulmonary blastoma via the Dicer 1 gene.[2] Knowledge of this link is important for all specialties treating this condition.

The diagnosis, investigation, treatment and further management of nasal chondromesenchymal hamartoma cases should be known by all ENT clinicians who may diagnose and treat nasal masses. We present the most extensive literature review and analysis of nasal chondromesenchymal hamartoma cases as well as presentation of three new cases managed in a tertiary paediatric centre with multimodal surgical resections. This represents the largest series of infants and young children with nasal chondromesenchymal hamartoma reported since the original description in 1998.

Materials and methods

The literature was systematically reviewed to identify all nasal chondromesenchymal hamartoma cases presenting either with or without pleuropulmonary blastoma.

We reviewed the nasal chondromesenchymal hamartoma literature using PubMed, Embase, Scopus, Web of Science and Google Scholar databases. We composed a search syntax combining synonyms for nose, (chondro)mesenchyme and hamartoma. For PubMed, the search syntax was: (nasal[tiab] OR nose[tiab] OR 'Nose Diseases'[Mesh] OR 'Nose'[Mesh]) AND (chondromesenchymal[tiab] OR mesenchymal[tiab] OR 'Mesoderm'[Mesh]) AND (hamartoma[tiab] OR hamartoma[MeSH]).

For Embase the syntax was: (nasal:ti,ab OR nose:ti,ab) AND (chondromesenchymal:ti,ab OR mesenchymal:ti,ab) AND hamartoma:ti,ab.

We performed the literature review including all published articles between 1975 and the search date (1 June 2020). We screened reference lists of included nasal chondromesenchymal hamartoma cases to identify any additional relevant publications. No critical appraisal of the selected literature was performed. Data were extracted on the following variables: age at diagnosis, gender, presenting complaint, lesion site, performed diagnostics and treatment, nasal chondromesenchymal hamartoma recurrence follow-up length, and additional pleuropulmonary blastoma diagnosis. This report has been written according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[3]

Before the disease entity was formally called nasal chondromesenchymal hamartoma in 1998, it is speculated that nasal chondromesenchymal hamartoma was previously

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reported as a 'nasal hamartoma', a 'congenital benign mesenchymoma' or a 'chondroid hamartoma'. We decided to only include cases that were histologically classified as nasal chondromesenchymal hamartoma to avoid inaccurate data presentation; therefore, these diagnoses are not included in our report. For our own three cases, we retrospectively reviewed the clinical notes for presenting complaints, investigations, operative interventions, histopathology and follow up.

Results

The results from the literature review are presented in full in Table 1.[1,4–48] In total, we identified 56 individual cases of nasal chondromesenchymal hamartoma. Cases showing histological similarities that were not definitively labelled as nasal chondromesenchymal hamartoma were excluded. Duplicate cases were combined to give a clear picture of the actual number of reported cases. Although the vast majority of patients were paediatric, there were reported cases in adults, including one case where the patient was 70 years old.[4] The average age at diagnosis was 9.6 years (range, 5 days to 70 years). There were 23 cases in children under two years of age. The male-to-female ratio was 1.9:1 (Table 1).

As expected with an enlarging nasal mass, the common presenting symptoms were nasal obstruction (46 per cent) and ocular symptoms (29 per cent), most commonly ophthalmoplegia and proptosis. Other reported symptoms were dependent on the progression of the mass but encompassed headache, hydrocephalus, dental mobility and epistaxis. The lesions were predominantly in the nasal cavity, with a predilection for ethmoidal air-cell involvement and orbital extension, with occasional cribriform plate and skull base involvement. In terms of the common investigations for these cases, the mainstay has been computed tomography (CT) alone or CT and magnetic resonance imaging (MRI) in combination. Four patients had pre-operative angiography.[1,5,19,26]

By far the most common treatment modality was complete surgical resection. Only one patient underwent pre-operative embolisation before resection. One patient received radiotherapy, which resulted in regression of the mass.[1] Only one patient had a nasal chondromesenchymal hamartoma that underwent a malignant change, which was managed with post-operative chemoradiotherapy.[21] Residual disease post-surgical resection was seen in three cases and one patient who had persistent tumour growth. Recurrent disease was seen in 8 cases (14.5 per cent; Table 1). Table 1 demonstrates that there were 11 nasal chondromesenchymal hamartoma cases that were diagnosed in association with pleuropulmonary blastoma. Eight of these cases had pleuropulmonary blastoma before nasal chondromesenchymal hamartoma diagnosis.

Discussion

Along with the previous cases reported in the literature, we included the three cases we treated in our centre; this represents the largest case series in infants and young children since the first reported cases in 1998.[1] It is important that ENT surgeons recognise this rare condition as a potential cause of a myriad of symptoms related to the nose and eyes that can commonly present in out-patient settings. A thorough clinical examination and appropriate investigation choice of any intranasal mass is key to timely diagnosis before cases progress.

It is important to recognise that this is a condition that crosses the spectrum of age groups but particularly affects children. In terms of nasal obstruction in children, it is important to add nasal chondromesenchymal hamartoma to the working differential diagnosis, especially considering the associated condition of pleuropulmonary blastoma. This is important because of the poor prognosis of pleuropulmonary blastoma, which makes early diagnosis in its most curable stage preferable.[44]

Regarding the investigation of suspected nasal chondromesenchymal hamartoma or other nasal masses in children, our experience has been with the use of both CT and MRI to both establish the extent of local progression and involvement of local structures but also to plan complete surgical resection. This correlates with the majority of cases in the reported literature. We have not found it necessary to use angiography in our cases, and the available evidence suggests that this is not needed for successful treatment, unless there is an obvious vascular component.

Definitive diagnosis is only available with adequate histological findings because there are no specific pathognomonic features on imaging. Nasal chondromesenchymal hamartoma does display amorphous calcifications with rings and arcs, so-called 'popcorn' lesions, but this is also found in other chondroid lesions. Small tissue samples of this pathology can easily lead to diagnostic confusion, so adequate biopsies are essential for diagnostic accuracy.

The mainstay of successful treatment has proven to be surgical resection. All three of the cases in our unit have been treated either entirely or partially with a transnasal navigation assisted endoscopic resection. This technique can minimise the impact of the operation on the patient. Since the previous literature review,[11] the most recent reported cases have seen an increase in surgery utilising a transnasal endoscopic excision. It may be necessary to work with allied surgical specialties, especially neurosurgery and ophthalmology, when managing this condition.

The pre- and post-operative imaging results from two of our cases can be seen in Figures 1–6. Clinicians in ENT should particularly be aware of nasal chondromesenchymal hamartoma's association with pleuropulmonary blastoma. In our series one patient was found to have a Dicer 1 loss of function mutation on blood sample genetic analysis. Patients who test positive for this mutation should be made aware of the future risk of pleuropulmonary blastoma, and those patients who have previously had pleuropulmonary blastoma should be made aware of the future risk of developing nasal chondromesenchymal hamartoma. The exact risk of pleuropulmonary blastoma is not known, but patients with Dicer 1 mutations have a total neoplasm risk of 19 per cent.[44] In the out-patient setting, clinicians should take particular care in the presence of previous pleuropulmonary blastoma or Dicer 1 mutations. This involves a thorough nasal, neck and general examination in particular. This is not only because of the risk of nasal chondromesenchymal hamartoma but also the other Dicer 1 line tumours, such as pituitary and thyroid neoplasia or multinodular goitres.[6,44] Unfortunately, the testing of the nasal chondromesenchymal hamartoma patients in the literature is sporadic, so discerning the true prevalence is difficult.

https://doi.org/10.1017/S0022215121002267 Published online by Cambridge University Press

https://doi.org/10.1017/S0022215121002267 Published online by Cambridge University Press

Table 1. Cases of nasal chondromesenchymal hamartoma in the literature

Authors & number of cases	Year	Age	Sex	Presenting complaint	Site of lesion	Angiography	Treatment	Recurrence	Malignant	PPB	PPB type	PPB age
McDermott *et al.*,[1] 7 cases	1998	5 days, 12 days, 2 weeks, 2 months, 3 months, 7 years	Male & female	Nasal mass (5), choanal mass (1), hydrocephalus on prenatal ultrasound (1)	Nasal cavity (5 cases), intracranial fossa (2 cases), ethmoid sinus, (1 case), sphenoid sinus (1 case)	No (6), yes (1)	Resection (7), re-resection (2), ventriculoperitoneal-shunt (1)	No recurrence (5), remodelling tumour growth until age 16 months (1), residual tumour at 9 months (1)	No (7)	No (6), yes (1)	II–III, not otherwise specified	2.75 years
Kato *et al.*[5]	1999	4 months	Male	Intranasal mass, congestion conjunctiva, oculomotor disturbance	Nasal cavity, paranasal sinus, mid-portion frontal skull base & left orbital cavity	Yes	Subtotal resection, radiotherapy	No recurrence	No	n.r.	n.a.	n.a.
Chae *et al.*[45]	1999	3 months	Female	Nasal bleeding, obstruction	Nasal cavity, ethmoid sinus + cribriform plate	No	Resection	n.r.	No	n.r.	n.a.	n.a.
Hsueh *et al.*,[7] 2 cases	2001	New-born, 9 months	Male (2)	Nasal mass (2), respiratory difficulty (1), oculomotor disturbance (1)	Nasal cavity (2), sphenoid + ethmoid sinus involvement (1), maxillary sinus (1)	No (2)	Resection (2)	No recurrence (2)	No (2)	n.r. (2)	n.a.	n.a.
Itoh *et al.*[46]	2002	2 years	Male	Swelling of nose & buccal region, epistaxis, nasal obstruction, orbital deviation	Nasal cavity, involving ethmoid sinus + floor anterior cranial fossa, compressing left orbit with mild exophthalmos	No	Subtotal anterior craniofacial resection	No recurrence, residual tumour tissue around optic nerve	No	n.r	n.a.	n.a.
Alrawi *et al.*[47]	2003	16 years	Male	Asymptomatic nasal swelling	Nasal cavity	No	Resection	No recurrence	No	n.r.	n.a.	n.a.
Kim *et al.*[37]	2004	5 months	Male	Ptosis, flu-like symptoms	Nasal cavity, connected with the intracranial cavity + orbit	No	Resection	No recurrence	No	n.r.	n.a.	n.a.
Norman *et al.*[9]	2004	11 years	Male	Headache, proptosis	Ethmoid sinus, displacement nasal septum + orbital wall	No	Resection	n.r.	No	n.r	n.a.	n.a.
Shet *et al.*[36]	2004	1 year	Male	Proptosis, maxillary region swelling	Nasal cavity, involving ethmoidal & sphenoidal sinuses	No	Pre-operative CT, resection	Residual tumour at 18 months	No	n.r.	n.a.	n.a.
Ozolek *et al.*,[19] 4 cases	2005	11 years, 17 years, 25 years, 69 years	Male, male, female, female	Nasal cavity mass (2), chronic nasal congestion (1), intracranial aneurysms, chronic sinusitis (1)	Nasal cavity (2), mass posterior aspect of the vomer, continuing to hyoid level	No (3), yes (1)	Resection (4)	No recurrence (4)	No (4)	n.r. (4)	n.a.	n.a.
Tabatabaei *et al.*[14]	2006	23 years	Male	Anosmia, diplopia, proptosis, frequent epistaxis	Frontal sinus, extending to the right orbit, ethmoid cells & nose	No	Resection	n.r.	No	n.r.	n.a.	n.a.

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Low *et al.*[24]	2006	11 years	Male	Nasal blockage, intermittent epistaxis	Middle turbinate mass, obliterating ethmoid sinus + osteo-meatal complex	No	Resection	No recurrence	No	n.r.	n.a.	n.a.
Kang *et al.*[17], Cho *et al.*[49]	2007, 2013	14 years	Male	Facial swelling, tooth mobility	Maxillary sinus + partial destruction orbital floor + bone remodelling	No	Resection, orbital floor removal	No recurrence	No	n.r.	n.a.	n.a.
Johnson *et al.*[25]	2007	15 years	Female	Chronic sinusitis, facial pain, nasal congestion	Nasal cavity, extending into nasopharynx	No	Resection	No recurrence	No	Yes	II	1.8 years
Silkiss *et al.*[28]	2007	7 months	Male	Ptosis, strabismus, noisy breathing	Nasal cavity + exotropia, anisocoria, blepharoptosis	No	Resection	No recurrence	No	n.r.	n.a.	n.a.
Nakagawa *et al.*[39]	2009	12 years	Male	Nasal obstruction	Nasal cavity, extending to sphenoid & posterior ethmoid	No	Resection	Recurrence at 2 months	No	n.r.	n.a.	n.a.
Finitsis *et al.*[26]	2009	12 months	Male	Respiratory distress	Nasal cavity, extending into maxillary sinus + bony remodelling	Yes	Pre-operative embolisation, resection	n.r.	No	n.r.	n.a.	n.a.
Ganske & Faquin[29]	2009	14 years	Female	Nasal congestion, snoring	Anterior nasal cavity, extending to cribriform plate	No	Transnasal endoscopic excision	n.r.	No	n.r.	n.a.	n.a.
Kim *et al.*[33]	2009	19 months	Male	Nasal obstruction, rhinorrhoea	Nasal cavity, extending to anterior ethmoid sinus	No	Resection	Recurrence at 1 & 4 years follow up	No	n.r.	n.a.	n.a.
Sarin *et al.*[34]	2010	2.5 years	Male	Restricted ophthalmopathy	Maxillary, ethmoid & sphenoid sinus + cribriform plate erosion	No	Resection	n.r.	No	n.r	n.a.	n.a.
Priest *et al.*,[12] 2 cases	2010	10 years, 11 years	Male, female	Nasal congestion (2)	Bilateral intranasal polyps (1), nasal cavity (1)	No (2)	Resection (2)	No recurrence (2)	No	Yes (2)	III (2)	3.3 & 4.5 years
Mattos & Early[13]	2011	3 years	Male	Recurrent eye infection & congestion, proptosis, cheek fullness	Nasal cavity, ethmoid sinus, left orbit	No	Endoscopic resection, re-resection at 21 months	Recurrence at 21 months	No	n.r.	n.a.	n.a.
Jeyakumar *et al.*[48]	2011	7 days	Female	Proptosis right eye	Nasal cavity	No	Microdebrider, piecemeal resection	n.r.	No	n.r.	n.a.	n.a.
Eloy *et al.*[10]	2011	18 months	Male	Nasal obstruction, hypertelorism, proptosis, diplopia, nasal pyramid deformity, reduced extraocular motility, exophthalmia	Nasal cavity + anterior ethmoid mass with extension to endocranium + erosion lamina papyracea	No	Endonasal endoscopic approach, repair dural defect: fascia lata & Duraseal®	n.r.	No	n.r.	n.a.	n.a.
Yao-Lee *et al.*[18]	2011	Neonate	Female	Difficulty breathing	Nasal cavity with intracranial extradural involvement	No	Resection	Recurrence at 3 months, re-recurrence at 9 months	No	n.r.	n.a.	n.a.

(*Continued*)

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Table 1. (*Continued.*)

Authors & number of cases	Year	Age	Sex	Presenting complaint	Site of lesion	Angiography	Treatment	Recurrence	Malignant	PPB	PPB type	PPB age
El Behery *et al.*[35]	2012	11 years	Male	Nasal obstruction, nasal mass	Nasal cavity	No	Transnasal endoscopic resection	n.r.	No	Yes	n.r.	3 years
Uzomefuna *et al.*[32]	2012	8 years	Male	Frontal headache (throbbing)	Posterior ethmoid sinus & the anterior 2/3 of bilateral sphenoid lesion	No	Resection	No recurrence	No	n.r	n.a.	n.a.
Zulkifli *et al.*[22]	2013	47 years	Male	Reduced hearing, tinnitus, type B tympanometry	Lesion arising from the medial pterygoid plate abutting the left inferior turbinate	No	Resection, turbinectomy, myringotomy, grommet	No recurrence	No	n.r.	n.a.	n.a.
Li *et al.*[20]	2013	23 years	Male	Medial canthal lesion, proptosis	Nasal cavity with nasolacrimal sac extension	No	Resection	No recurrence	No	n.r.	n.a.	n.a.
Li *et al.*[21]	2013	40 years	Female	Nasal obstruction, bloody rhinorrhoea	Nasal cavity with extension to maxillary & ethmoid sinus	No	Resection	Recurrence at 3 months	Yes	n.r	n.a.	n.a.
Wang *et al.*,[31] 2 cases	2014	6 weeks, 5 years	Male, female	Nasal obstruction (2) + noisy breathing (1), nasal rhinorrhoea (1)	Nasal cavity (2), involving ethmoid sinus (1)	No (2)	Sub-total resection (1), total resection (1)	No recurrence (2)	No (2)	No (2)	n.a.	n.a.
Obidan & Ashoor[15]	2014	14 years	Male	Bilateral nasal obstruction, decreased sense of smell, snoring, sleep disturbance	Bilateral nasal polyps	n.r.	n.r.	n.r.	n.r.	Yes	II	6 years
Xia *et al.*[27]	2014	Newborn	Female	Shortness of breath, respiratory distress, mouth breathing, cyanosis while drinking	Nasal cavity, sinus tumour without invasion	No	Total resection & re-resection after 1 year of initial surgery	Recurrence at 1 year follow up	No	No	n.a.	n.a.
Chandra & Venkatahalam[30]	2014	12 years	Male	Nasal obstruction, snoring, mouth breathing, proptosis	Nasal cavity, involving the anterior & posterior ethmoids with extension into right orbit & maxilla & up to the hard palate	No	Resection (midfacial degloving approach)	No recurrence	No	n.r	n.a.	n.a.
Moon & Kim[38]	2014	9 months	Female	Inward deviation eye	Nasal cavity & maxillary sinus mass	No	n.r.	n.r.	No	n.r.	n.a.	n.a.
Mason *et al.*[11]	2015	49 years	Male	Right nasal cavity mass	Right nasal septum	No	Resection	n.r	No	n.r	n.a.	n.a.
Ünal *et al.*[40]	2016	13 years	Female	Nasal obstruction	Left nasal cavity	No, CT/MRI	Endoscopic resection	No	No	n.r.	n.a.	n.a.
Avcı *et al.*[41]	2016	5 years	Male	Nasal obstruction, recurrent sinusitis	Left nasal cavity	No CT/MRI	Endoscopic resection	No	No	n.r	n.a.	n.a.

Nakaya *et al.*[42]	2017	3 years	Male	Epiphora, proptosis, ophthalmoplegia	Right nasal cavity/ skull base	CT/MRI	Endoscopic resection	No	No	n.r.	n.a.	n.a.
Golbin *et al.*[43]	2018	25 months	Female	Nasal obstruction, feeding difficulty, microphthalmia	Sinonasal mass	CT/MRI	Excision	Yes	No	n.r.	n.a.	n.a.
Mirchia & Naous[44]	2018	70	Female	Chronic maxillary sinusitis	Right maxillary sinus mass	CT	Surgical excision	No	No	n.r.	n.a.	n.a.
Saunders *et al.*, (this paper) 3 cases	2021	18 months, 7 months, 7 years	Male, female, female	Enophthalmos/ ophthalmoplegia, enophthalmos/squint, nasal obstruction	Left nasal cavity/orbit & anterior skull base, left nasal cavity/orbit & clivus, nasal cavity/ paranasal sinuses	CT/MRI	Endoscopic excision all 3 cases	No, no, yes	Not known, no, yes	n.t.		n.a, n.a, years

PPB = pleuropulmonary blastoma; n.a. = not applicable; n.r. = not recorded CT = computed tomography; MRI = magnetic resonance imaging; n.t. = not tested

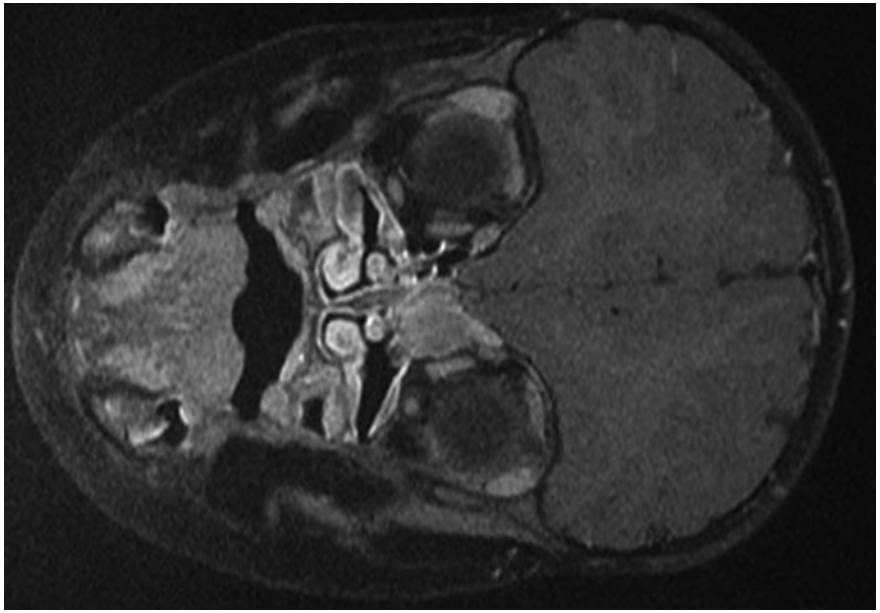


Fig. 1. Pre-operative coronal plane magnetic resonance image for patient 1.

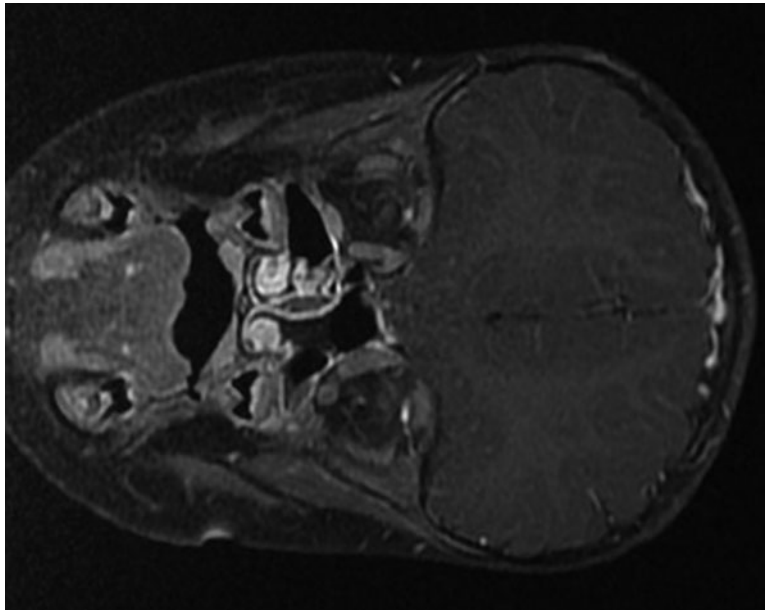


Fig. 2. Post-operative coronal plane magnetic resonance image at six months for patient 1.

https://doi.org/10.1017/S0022215121002267 Published online by Cambridge University Press



Fig. 3. Post-operative coronal plane computed tomography image at six years for patient 1.

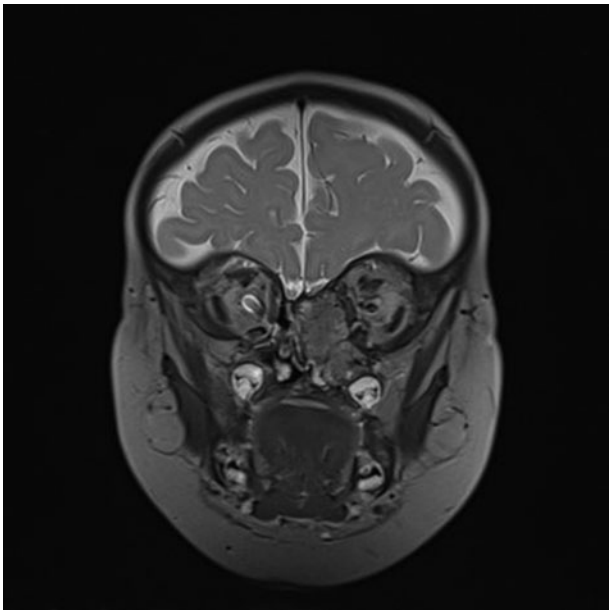


Fig. 4. Pre-operative coronal plane magnetic resonance image for patient 2.



Fig. 5. Pre-operative axial plane computed tomography image for patient 2.

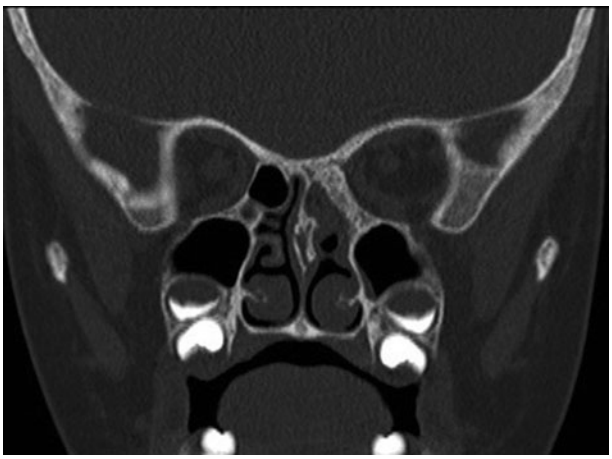


Fig. 6. Post-operative coronal plane computed tomography image at 18 months for patient 2.

Conclusion

This review of the literature, with the addition of the further reported cases over the last five years, has helped confirm the most useful management strategy for patients with suspected nasal chondromesenchymal hamartoma. Patients should be discussed at the paediatric skull base multidisciplinary team meeting following imaging of the paranasal sinuses and brain with CT and an MRI. Given the advances in endoscopic skills and equipment, the majority of cases have been able to be resected via the endonasal route, even very young patients. In order to effectively resect these tumours, giving the patient the best chance of disease-free survival and limiting local complications, a multidisciplinary approach should be considered.

Competing interests. None declared

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