Nasal Chondromesenchymal Hamartoma (NCMH): a systematic review of the literature with a new case report

Katrina Anna Mason1*, Annakan Navaratnam2, Evgenia Theodorakopoulou1 and Perumal Gounder Chokkalingam2

Abstract

Background: Nasal chondromesenchymal hamartoma (NCMH) is a very rare, benign tumour of the sinonasal tract usually presenting in infants. We present a systematic review of NCMH cases alongside a case report of an adult with asymptomatic NCMH.

Methods: A systematic review was conducted in accordance with PRISMA guidelines. A PubMed, EMBASE and manual search through references of relevant publications was used to identify all published case-reports of NCMH. Data was collected from each case-report on: patient demographics, laterality, size and location of NCMH, presentation, co-morbidities, investigations, treatment and follow-up.

Results: The systematic review identified 48 patients (including ours): 33 male, 15 female. Mean age was 9.6 years (range: 1 day–69 years) with the majority aged 1 year or younger at presentation (n = 18). Presentations included: nasal congestion (n = 17), nasal mass (n = 15) and eye signs (n = 12). NCMH also involved the paranasal sinuses (n = 26), orbit (n = 16) and skull-base (n = 14). All patients underwent operative resection of NCMH. A small 2014 case-series found DICER1 mutations in 6 NCMH patients, establishing a link to the DICER1 tumour spectrum.

Conclusions: NCMH is a rare cause of nasal masses in young children and adults. In light of the newly established link between NCMH and DICER1 mutations surgeons should be vigilant for associated DICER1 tumours, as NCMH may be the ‘herald tumour’ of this disease spectrum.

Keywords: Nasal neoplasms, Hamartoma, DICER1 protein human, Review

Background

Nasal chondromesenchymal hamartoma (NCMH) is a very rare, benign tumour of the sinonasal tract. Forty-seven cases have been reported in the English literature and the vast majority of these presentations are in infants and young children often below the age of one. NCMHs have a mixed morphological structure comprised of predominantly mesenchymal and cartilaginous components. NCMH patients present with symptoms that are dependent on the location of the tumour in the nasal cavity or paranasal sinuses and their compression of local structures. These symptoms range from nasal obstruction to visual impairment and facial and dental pain. To date there have only been 6 cases of adult presentation of NCMH. Here we present the first systematic review of NCMH cases published in the literature to assess the patient demographics, presentation, management and prognosis of NCMH alongside a new and unusual case in an adult.

Case report

A 49-year-old man was referred to our outpatient clinic presenting with a small mass in his right nasal cavity. The lump, which the patient first noticed 5 years ago, had been growing insidiously over time and by the time of presentation had become visible at the right anterior nares. The patient did not complain of any symptoms but sought consultation as his wife was concerned by the cosmetic appearance of the mass.
Examination revealed a large firm mass arising from the right side of the anterior nasal septum with approximately 0.5 cm attachment to the anterior cartilage of the septum. The left and right nasal cavities were otherwise unremarkable. Clinically, the mass had the appearance of a papilloma confined to the nasal cavity with an attachment to the septum only and therefore further imaging was not undertaken. The differential diagnoses considered at the time of presentation were: nasal polyp, squamous papilloma or inverted papilloma.

The patient subsequently underwent excisional biopsy of the right nostril mass under general anaesthetic using a circumferential subperichondrial incision with a small margin. Intraoperatively, the mass had the macroscopic appearance of a 0.5 cm × 2 cm × 2 cm calcified nodule. Due to a small 0.5 cm base, subsequent healing was achieved by secondary intention aided by the routine application of topical antibacterial cream. Histopathological analysis showed the nodule to contain cartilage and aneurysmal bone covered in stratified squamous epithelium with keratinisation (Figs. 1 and 2). Histopathological diagnosis was made using a haematoxylin & eosin stain. These findings were consistent with a diagnosis of a nasal chondromesenchymal hamartoma.

The patient was followed up in clinic and was discharged after 2 years having shown no signs of recurrence. Furthermore, a telephone interview was conducted 4 years post operation and the patient reported no recurrence of the nasal mass. He confirmed that he had no postoperative complications and was happy with the outcome of the operation.

Methods
A systematic review was undertaken in accordance with PRISMA guidelines [1]. No systematic review protocol was used, however our systematic review methodology is described below and a four-phase flow diagram is represented in Fig. 3. All published case-reports of NCMH were included in the review. A PubMed search (MEDLINE) (1975 to May Week 2, 2015) was carried out using the following terms [(chondromesenchymal hamartoma) AND (nasal OR sinus OR maxillary OR ethmoid OR sphenoid OR frontal OR orbit OR cranial)]. An EMBASE search (1975 to May Week 2, 2015) was carried out using a best sensitivity-combination strategy. The PubMed search resulted in 32 citations of which 24 were relevant, 6 were not NCMH case-reports, one was a Chinese language case-report, and one case was a duplicate case-report publication [2]. An EMBASE search and a manual search through references of relevant publications yielded 11 further relevant citations. Of these only 6 were included in the analysis; one case was found to have been a duplicate case report [3, 4] and four other possible cases of NCMH were found through publication citation search, but were labelled as “Mesenchymal chondrosarcoma” [5] “nasal hamartoma” [6], “nasopharyngeal hamartoma” [7], and “congenital mesenchymoma” [8], and were therefore not included. Thirty-one publications that report 47 cases of NCMH were included in this systematic review. Data was collected on patient demographics (age, gender), laterality, size and site of NCMH, presentation, co-morbidities, investigations, treatment and follow-up. These were also the principle summary measures. Two
Fig. 2 Areas of osteoid formation (magnification x200, haematoxylin & eosin stain)

Fig. 3 Four-phase flow diagram of systematic review in accordance with PRISMA guidelines. * Two individual publications of single case-reports were excluded from analysis as these had previously been published, Schultz et al. [2] and Kang et al. [3]. ** See Table 1.
authors performed the database search, the manual search through references of relevant publications, and extracted the relevant data from the case-reports. Data was entered into an Excel 2013 Microsoft Office database which was used to carry out basic statistical analysis.

**Results of systematic review**

Forty-Eight NCMH patients (including our case) have been reported in the English literature (Fig. 3). Most cases presented in males; 33 male and 15 female, with a male to female ratio of 2.2:1 ratio. The mean age was 9.6 years (range: 1 day–69 years). A large proportion of these patients were aged 1 year or younger at presentation \((n = 18)\) and only 8 adult patients (including our case) have been described. Site of pathology was limited to the nasal cavity only in 10 patients, and involved the paranasal sinuses (maxillary, ethmoid, sphenoid) in 26 patients, the orbit in 16 patients, extending to the skull base in 14 patients, had intracranial extension in 8 cases, involved the nasopharynx in 3 patients and the oropharynx in 2 patients (see Table 1).

Clinical presentations of NCMH patients included: nasal congestion or obstruction \((n = 17)\), nasal mass \((n = 15)\), eye signs (proptosis, hypotropia, enophthalmos, strabismus, exotropia etc.) \((n = 12)\), facial swelling \((n = 8)\), headaches or facial pain \((n = 6)\), stertor or respiratory distress \((n = 8)\), ophthalmoplegia \((n = 4)\), recurrent sinusitis \((n = 4)\), rhinorrhea \((n = 3)\), otitis media \((n = 2)\), epistaxis \((n = 2)\), toothache \((n = 1)\), hyposmia \((n = 1)\), hydrocephalus \((n = 1)\) and 4 patients were asymptomatic or had no signs and symptoms documented (see Table 1).

All patients underwent operative resection of NCMH and the surgical approach was dependent on disease location. One patient had pre-operative chemotherapy due to initial misdiagnosis on biopsy as spindle cell sarcoma. One patient had pre-operative embolization to reduce operative blood loss. Follow up times were included for 24 patients, mean time for follow-up was 24 months, (range 2–156 months). Eleven patients were found to have persistent disease or disease recurrence on follow up, seven required further surgery, three patients were described as stable, and no further information was given on the other patient. Li et al. described the first and only reported case of malignant transformation of NCMH [9].

Thirty-six patients had no documented past medical problems. One adult patient had a history of multiple vascular aneurysms. Eleven of the patients had been diagnosed with pleuropulmonary blastoma (PPB) prior to NCMH detection. Of these 11 patients, 5 had other comorbidities including three with Sertoli-Leydig cell ovarian tumours, two with pulmonary cysts, one jejunal polyps, one papillary thyroid carcinoma, one cystic nephroma and one multinodular goitre.

A potential weakness of this systematic review is the possibility of reporting bias through publication bias both within individual case reports and across the review. This reporting bias is three-fold: firstly in the incomplete publication of all the clinical aspects of the case-reports by the original authors, for example not reporting follow-up times or co-morbidities etc. Secondly it is possible that there have been cases of NCMH that have not been reported in the literature and can therefore not be included in the systematic review. Thirdly the exclusion of case-reports of “Mesenchymal chondrosarcoma” [5] “nasal hamartoma” [6], “nasopharyngeal hamartoma” [7], and “congenital mesenchymoma” [8] alongside others, which are published prior to the first description of NCMH by McDermott et al. in 1998, may have resulted in an underreporting of true NCMH cases. However without being able to retrospectively assess and re-classify the histology of these cases we feel it is appropriate to have excluded them from our analysis and conclusions. These sources of reporting biases could potentially reduce the validity of conclusions drawn in terms of not fully representing or capturing all possible cases of NCMH.

**Discussion**

NCMHs are predominantly benign lesions that are locally destructive and because of their aggressive appearance can be mistaken for a malignant tumour. However NCMHs can be slow growing and therefore have a delayed presentation. Histopathologically these lesions are analogous to other mesenchymal hamartomas, and consist of islands of chondroid tissue such as hyaline cartilage, areas of calcification, and mesenchymal cellular elements such as spindle cells and myxoid stroma.

McDermott et al. were the first to recognise NCMH as a distinct clinic-pathological entity in 1998 when they described a case series of seven patients with a tumefactive process of the nasal passages and contiguous paranasal sinuses with a detectable mass in the nose [10]. In this case series, six of the seven patients were infants under the age of 3 months. As our systematic review demonstrates NCMH predominantly presents in young children and infants under the age of one, but there have now been seven case reports, including ours, of adults with NCMH up to the age of 69 [9, 11–14]. In 2013 the first and only reported case of malignant transformation of an NCMH was described in the literature [9].

In our case, the NCMH was initially thought to be a papilloma confined to the nasal septal wall and therefore further imaging was not undertaken prior to resection. However pre-operative imaging of these lesions provides valuable information regarding involvement of adjacent structures such as the paranasal sinuses, orbit and intracranial cavity. On computed tomography (CT) imaging,
| Author, Publication date | Case No | Age D/M/Y | Sex | Side & Size | Site | Symptoms | Co-morbidity | Investigations | Treatment | Follow Up/ |
|--------------------------|---------|-----------|-----|-------------|------|----------|-------------|---------------|-----------|-----------|
| (1) McDermot, 1998 [10] USA | 1 | 5 D | M | ND | 1. Nasal cavity | 1. Nasal Mass | ND | CT | Surgical excision | No recurrence at 2 years |
|                          | 2 | 3 M | F | ND | 1. Nasal cavity | 1. Nasal Mass | ND | MRI | Surgical excision | No recurrence at 2 years |
|                          | 3 | 3 M | M | ND | 1. Nasal cavity | 1. Choanal Mass | ND | ND | Biopsy then surgical excision Subsequent chemotherapy | No recurrence at 4 years |
|                          | 4 | 2 M | M | ND | 1. Nasal cavity | 1. Nasal Mass | ND | ND | Surgical excision | No recurrence at 18 months |
|                          | 5 | 12 D | F | ND | 1. Nasal cavity | 1. Nasal Mass | ND | CT | Surgical excision & further re-excision after 16 months | Unchanged persistent tumour in superior nasal cavity at 12 months |
|                          | 6 | 14 D | M | ND | 1. Nasal cavity | 1. Nasal Mass | ND | CT | Surgical excision VP shunt for hydrocephalus | Residual tumour in anterior cranial fossa at 9 months |
|                          | 7 | 7 Y | M | ND | 1. Nasal cavity | 1. Nasal Mass | PPB | ND | Surgical excision | No recurrence at 2 months NB later reported by Priest et al. 2010 [27] showed with multiple recurrences in first 3 years |
| (2) Chae 1999 Korea [30] | 8 | 3 M | F | Right Size: 3.5 × 7.5 × 2.5 cm | 1. Nasal cavity | 1. Epistaxis | ND | CT | Surgical excision | ND |
| *abstract only, Korean paper* | | | | | | | | | | |
| (3) Kim D 1999 [31] USA | 9 | 3 M | F | Right Size: ND | 1. Nasal cavity | 1. Nasal mass | None stated | CT MRI | Surgical excision with mid-facial de-gloving and bi-frontal craniotomy | No recurrence at 18 months |
|                          | 10 | 4 M | M | Left Size: ND | 1. Nasal cavity | 1. Nasal Mass | None stated | CT | Two stage surgical excision 1st intracranial/sinus | No recurrence at 13 years |
| Study Reference | Age | Gender | Side | Size | Symptoms | Findings | Treatment | Follow-up |
|-----------------|-----|--------|------|------|----------|----------|-----------|-----------|
| (5) Hsueh 2001 | 11  | M      | Left | ND   | Nasal cavity | None stated | CT MRI   | Radiotherapy post op |
| Taiwan (2 cases) |     |        |      |      | 1. Nasal cavity | 3. Ophthalmoplegia left eye | | |
| (6) Alrawi 2003 | 13  | M      | Left | 1.5 x 1.5 cm | Nasal cavity | None stated | CT MRI | Surgical resection with delayed reconstruction with forehead flap |
| Ireland |     |        |      |      | 1. Nasal cavity | 2. Left facial swelling | | |
| (7) Shet, 2004 | 14  | Y      | Left | ND   | Nasal cavity | Proptosis of left eye | Non stated | CT | Chemotherapy (VID) as biopsy suggested spindle cell sarcoma-30% reduction in tumour size. Then left maxillectomy and surgical excision |
| India |     |        |      |      | 1. Nasal cavity | 2. Left facial swelling | | |
| (8) Kim B, 2004 | 15  | M      | Left | ND   | Nasal cavity | Left eye ptosis | None stated | CT | Frontal craniotomy & trans-nasal surgical resection |
| Korea |     |        |      |      | 1. Nasal cavity | 2. Compression of left orbit | | |
| (9) Norman, 2004 | 16  | Y      | Left | ND   | Nasal cavity | Headaches left sided | None stated | CT | Endoscopic biopsy and anterior craniofacial resection |
| USA |     |        |      |      | 1. Nasal cavity | 2. Displacement left orbital wall | | |
| (10) Ozołek, 2005 | 17  | Y      | Left | ND   | Nasal cavity | Nasal mass | None stated | ND | Surgery and care undertaken in another hospital |
| USA (4 cases) |     |        |      |      | 1. Nasal cavity | 2. Ethmoid sinus | | |
| Case | Age | Gender | Size | Location | Symptoms | Treatments | Outcomes |
|------|-----|--------|------|----------|----------|------------|----------|
| 18   | 17  | F      | ND   | Nasal cavity | 1. Nasal obstruction | None stated | Surgical excision | ND |
| 19   | 25  | M      | Bilateral | 8 x 5 x 3.5 cm | 1. Nasal cavity | None stated | CT | ND |
|      |     |        |      |          | 2. Maxillary sinus | CT | Multiple surgical resections within one year including, tracheostomy and initial surgical resection, further surgical resection of bulbar mass and nasal tumour, then Le-Fort osteotomy and further surgical resection | |
|      |     |        |      |          | 3. Nasopharynx | CT |          | |
|      |     |        |      |          | 2. Oropharynx | CT |          | |
|      |     |        |      |          | 2. Chronic sinusitis | CT |          | |
|      |     |        |      |          | 1. Multiple intracranial vascular aneurysms | CT |          | |
|      |     |        |      |          | 2. Longstanding nasopharyngeal tumour- biopsy aged 13 ‘chronic inflamed polyp’ | CT |          | |
|      |     |        |      |          | 1. Respiratory distress from obstructing oropharyngeal tumour requiring emergency tracheostomy | CT |          | |
| 20   | 69  | F      | Right | ND | Nasal cavity | ND | Surgical excision | ND |
| (11) Low | 11  | M      | Right | ND | Nasal cavity | None stated | CT | No recurrence at 2 months |
| (12) Johnson, 2007 [29] USA | 15  | F      | Bilateral | ND | Nasal cavity | None stated | CT | No recurrence at 6 months |
| (13) Silkiss, 2007 [18] USA | 7   | M      | Right | 3.2 x 1.4 cm | Nasal cavity | None stated | CT MRI | Surgical resection-right lateral rhinotomy | No recurrence at 18 months |
| (14) Nakagawa, 2008 [34] Japan | 12  | M      | Left | 1.5 cm | Nasal cavity | None stated | CT | Endoscopic surgical resection and further endoscopic surgical resection after recurrence | Recurrence at 2 months No recurrence at 5 months post second surgery |
| (15) Finitsis, 2009 [35] Greece | 12  | M      | Left | 4 cm x 4.2 cm | Nasal cavity | None stated | CT MRI | Pre-operative embolization Then Surgical resection with midface de-gloving | ND |
Table 1 Summary table of systematic review of NCMH cases reported in the literature (Continued)

| Case No. | Year | Country | Age/Gender | Size | Location | Symptoms | Treatment | Outcome |
|----------|------|---------|------------|------|----------|----------|-----------|---------|
| (16) Kim J, 2009 [23] Korea | 26 | 19 M | M | Left 2.7 x 3.5 cm | Nasopharynx | 1. Nasal cavity 2. Orbital extension 3. Intracranial extension | 1. Watery rhinorrhoea 2. Nasal Obstruction | None stated | CT MRI | Endoscopic surgical resection x2 | Recurrence at one year, 2nd surgery. No recurrence 10 months after second surgery |
| (17) Priest, 2010 [27] USA *case previously reported by McDermont et al. 1998 **case previously reported by Johnson et al. 2007 (2 new cases) | - | 7 Y * | M | Initially unilateral, then bilateral | Orbital extension | 1. Sphenoid sinus 2. Left Nasal cavity 3. Bony erosion of posterior septum 2. Extending into nasopharynx | 1. Nasal Congestion 2. Left Nasal cavity 1. Chronic Sinusitis 2. Facial Pain | 1. PPB type II–III 1. PPB Type II 2. Sertoli-Leydig Cell Ovarian Tumour | Four resections over 3 years Surgical resection | Followed up for 13 years with multiple recurrences in first 3 years No recurrence at 51 months |
| | - | 15 Y ** | F | Bilateral | Intracranial extension | 1. Bilateral nasal cavities | 1. Nasal Congestion 1. PPB Type II 3. Congenital phthisi bulbi Stickler syndrome | Surgical resection | ND |
| (18) Sarin, 2010 [24] India | 27 | 10 Y | F | Bilateral Size: ND | Nasopharynx | 1. Bilateral nasal cavities 2. Extension to anterior skull base | 1. Nasal obstruction 1. Nasal obstruction | 1. PPB Type III CT Surgical resection | No recurrence at 21 months No recurrence at 4 months |
| | 28 | 11 Y | M | Right Size: ND | Nasopharynx | 1. Nasal cavity 2. Extension to anterior skull base | 1. Nasal obstruction | 1. PPB Type III ND Surgical resection | No recurrence at 4 months |
| (19) Eloy 2011 [25] Belgium | 29 | 2.5 Y | M | Right Size: ND | Nasopharynx | 1. Nasal cavity 2. Maxillary, ethmoid and sphenoid sinus 3. Erosion of middle wall of orbit | 1. Right eye oculomotor impairment | ND MRI | Biopsy and then lateral rhinotomy for excision | ND |
| (20) Jeyakumar 2011 [26] USA | 30 | 18 M* | M | Right 0.5 x 0.4 cm | Nasopharynx | 1. Nasal cavity 2. Ethmoid sinus 3. Extension into right orbit 4. Intracranial extension | 1. Nasal obstruction 2. Nasal mass 3. Hypertelorism, proptosis, diplopia 4. Nasal swelling *Symptoms 1st noticed at 2 months- delayed referral from Algeria to Brussels | None stated | CT MRI | Endoscopic surgical resection | ND |
| | 31 | 7 D | F | Right Size: ND | Nasopharynx | 1. Nasal cavity | 1. Nasal Mass 2. Stertor | None stated | CT MRI | Endoscopic surgical excision | ND |
| Case | Name | Age | Gender | Side | Size | Location | Symptoms | Treatment | Follow-up |
|------|------|-----|--------|------|------|----------|----------|-----------|-----------|
| (21) | Mattos | 32  | Y | M | Left | Size: ND | Nasal cavity | None stated | CT MRI | Endoscopic excision the further surgical excision | Recurrence at 21 months required further resection |
| (22) | Behery | 33  | Y | M | ND  | ND | Nasal Obstruction | 1. PPB | Surgical resection | ND |
| (23) | Uzomefuna | 34  | Y | M | ND  | Sphenoid sinus | 1. Frontal Headache | ND | CT MRI | Endoscopic surgical resection | No recurrence at 6 months |
| (24) | Cho | 35  | Y | M | Left | 5 cm × 5.3 cm × 4 cm | Nasal cavity | None stated | CT | Subtotal maxillectomy, removal of medial nasal mucous membrane. Reconstruction with iliac crest bone block | No recurrence at 4 years |
| (25) | Li Y | 36  | Y | F | Bilateral | Size: ND | Nasal Cavity | None stated | CT MRI | Complete radical resection | Recurrence at 3 months *Malignant transformation seen on histology |
| (26) | Li GY | 37  | Y | M | Left | 3.2 × 2.5 cm | Nasal cavity | None stated | ND | Endoscopic surgical excision | No recurrence at 3 months follow up |
| (27) | Moon | 38  | M | F | Right | Size: ND | Nasal cavity | None stated | CT MRI | Surgery and care undertaken in another hospital | ND Surgery and care undertaken in another hospital |
| (28) | Wang T | 39  | Y | M | Right | 2.5 × 3.6 × 4.3 cm | Nasal cavity | None stated | CT MRI | Surgical resection | No recurrence at 3 years |
| No. | Age | Sex | Side | Lesion Size | Sites | Clinical Presentation | Investigations | Treatment | Outcome |
|-----|-----|-----|------|-------------|-------|-----------------------|--------------|----------|---------|
| 40  | 6 W | F   | Left | 2.6 x 3.4 x 3.9 cm | 1. Nasal cavity | 2. Nasal obstruction | None stated | CT MRI | Surgical resection | No recurrence at 10 months |
| 41  | 14 Y | M   | Bilateral | | 1. Bilateral nasal cavities | 2. Pressure remodelling of adjacent bones | | | | |

(29) Obidan, 2014 [39] Saudi Arabia

(30) Stewart, 2014 [13] USA
**4 patients previously reported by Priest et al. 2010 [27] (4 new cases)**

- 7 Y*** M Initially unilateral, then bilateral | ND | 1. Nasal Congestion | 1. PPB | CT | Surgical endoscopic resection | ND |
- 15 Y*** F Bilateral | ND | 1. Chronic Sinusitis | 1. PPB | | Surgical resection | Multiple recurrences |
- 10 Y*** F Bilateral | ND | 1. Nasal congestion | 1. PPB | Surgical resection | No recurrence |
- 11 Y*** M Right | ND | 1. Nasal Congestion | 1. PPB | Surgical resection | No recurrence |
42  | 8 Y | M | ND | ND | ND | ND | 1. PPB | Surgical resection | No recurrence |

43  | 13 Y | F | Bilateral | ND | | ND | 1. ND | ND | Surgical resection | No recurrence |

44  | 8 Y | M | Bilateral | ND | | | 1. Chronic Sinusitis | ND | Surgical resection | No recurrence |
45  | 6 Y | F | ND | ND | ND | ND | | ND | Surgical resection | No recurrence |

46  | 21 Y | F | Right | ND | | 1. Nasal Congestion | 2. Septal deviation | | | Surgical resection | Recurrence at 4 years |
| Case | Age | Gender | Side | Size         | Location | Symptoms          | Imaging | Treatment       | Follow-up         |
|------|-----|--------|------|--------------|----------|-------------------|---------|-----------------|-------------------|
| Chandra 2014 [40] - India | 47  | M      | Right | ND           | 1. Nasal cavity | 1. Nasal Obstruction | CT MRI | Surgical excision | No recurrence at 5 months |
| Mason 2015 UK | 48  | M      | Right | 0.5 x 2 x 2 cm | 1. Nasal cavity | 1. Nasal mass | None stated | Surgical excision | No recurrence at 4 years |

*Years, M Months, F Days, Male, Female, ND not documented, PPB Pleuropulmonary Blastoma, CT Computed Tomography, MRI Magnetic Resonance Imaging*
NCMH are typically seen as non-encapsulated, poorly defined masses often with cystic components [15]. Magnetic resonance imaging (MRI) of NCMH demonstrates a heterogeneous mass on T1 weighted images and T2 weighted images show the presence of cystic components. MRI also has the advantage of superior tissue characterisation and delineation of invasion of adjacent structures in comparison to CT [16]. Due to rarity of NCMH, even after thorough clinical and radiographic examination NCMH can be misdiagnosed, and differential diagnoses include: inverted papilloma, aneurysmal bone cysts or ossifying fibromas, nasoethmoidal encephalocele, chondrosarcoma, nasal lymphoma, nasal glioma and rhabdomyosarcoma. Histopathological analysis following surgical resection is therefore needed for accurate diagnosis.

Patients with NCMH most commonly present with symptoms of nasal obstruction, nasal mass, or eye signs, which reflects the involvement of NCMH in the nasal passages and orbit. Ophthalmic signs include signs of globe displacement such as strabismus, extropia, hypertelorism, proptosis, enophthalmus and ophthalmoplegia, direct results of the intra-ocular extension of NCMH or ocular compression by NCMH [17–26]. There has also been a report of a patient presenting with intra-oral symptoms due to involvement of the oral cavity [4]. Patients can therefore present to otolaryngology, ophthalmology or maxillo-facial departments and doctors in these specialties should be aware of this rare pathology. In our case, the patient did not complain of any cranial, ophthalmic or nasal symptoms but was aware of a slowly enlarging nasal mass. This is most likely due to the relatively small size of the tumour at the anterior nasal septum which did not obstruct the nasal passage.

The aetiology of NCMH is thought to be due to an underlying genetic predisposition therefore accounting for the early presentation in the majority of cases. Priest et al. and Stewart et al. investigated patients with both NCMH and the rare paediatric dysembyronic sarcoma of the lung and pleura: pleuropulmonary blastoma (PPB) [13, 27]. In patients with NCMH and PPB Stewart et al. found germline DICER1 mutations in 6 out of 8 evaluated patients, and somatic DICER1 mutations in 2 out of those 6 patients with germline mutations [13]. This recent finding has established genetic proof of NCMH tumour association with DICER1 mutations and Stewart et al. therefore feel that NCMH should be considered part of the DICER1 tumour spectrum. The DICER1 familial tumour susceptibility syndrome confers an increased risk most commonly for pleuropulmonary blastoma (PPB) but also ovarian sex cord-stromal tumours; Sertoli-Leydig cell tumor [SLCT], juvenile granulosa cell tumour [JGCT] and gynandroblastomas. Less commonly the DICER1 tumour spectrum includes: cystic nephroma (CN), and thyroid gland neoplasia, multinodular goitres [MNG], adenomas, or differentiated thyroid cancers. The rarest observed tumours in this spectrum, alongside NCMHs, are ciliary body medulloepithelioma (CBME), botryoid-type embryonal rhabdomyosarcoma (ERMS) of the cervix or other sites, renal sarcomas, pituitary blastomas, and pineoblastomas [28]. Eleven patients in our systematic review had previous PPB and five of these also had other DICER1 tumours. Surgeons and physicians should therefore be aware of these disease associations and should be vigilant of a diagnosis of NCMH in patients presenting with sino-nasal or orbital symptoms who have a history of any of these tumours. Johnson et al. importantly also point out that due to its location, NCMH is more likely to present early in life than the other DICER1 tumours [29]. Surgeons and physicians should therefore either offer DICER1 mutation analysis if available, or ensure long-term follow up of these patients and be vigilant for associated tumours, as NCMH may be the ‘herald tumour’ of this disease spectrum.

There are also cases in the literature of children, adolescents and adults with NCMH who have had an asymptomatic infancy [9, 11, 12, 14]. This may imply that there are non-genetic components to NCMH pathogenesis. Alternatively it may simply reflect the insidious growth of the tumour or that some NCMH patients may only exhibit the phenotype later in life. However as this is an extremely rare pathology with only very recent formal association with the DICER1 mutation, the majority of the reported cases have not had formal DICER1 mutation analysis. Therefore an association or lack thereof in the non-tested cases cannot be inferred.

Successful management of NCMH entails complete resection in order to prevent recurrence. A complete excision however is not always technically feasible, especially in cases of intracranial extension of NCMH. An incomplete resection poses the risk of recurrence as well as the possibility of continued tumour growth and progressive symptoms. Nine patients in this systematic review were found to have disease recurrence, most likely from incomplete surgical excision.

**Conclusions**

We present an unusual case of NCMH in an adult without nasal obstructive symptoms due to the anatomical location of the NCMH attached to the nasal septum. A systematic review of the literature has highlighted that presentation is mostly related to tumour location, with nasal mass, nasal obstruction and ophthalmic signs being the most common forms of presentation. The majority of patients presenting with NCMH are children and infants below the age of one, but there have now been a few adult cases of presentation. Surgical resection is the treatment of choice with low recurrence rates in the
majority of cases. There has only been one reported case of malignant transformation and NCMH is still considered a benign tumour. NCMH’s association with the DICER1 mutation has very recently been established and therefore in light of this any patient with a DICER1-related tumour spectrum and new nasal or orbital symptoms should raise the suspicion of NCMH. Furthermore surgeons should subsequently be vigilant for associated DICER1 related tumours, as due to their location NCMHs may be the ‘herald tumour’ for this disease spectrum. This case and systematic review highlights the fact that NCMH can mimic other benign and malignant lesions and that surgeons and physicians should be aware of rare pathologies accounting for nasal masses.

Consent
Written consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editor-in-chief of this journal.

Abbreviations
NCMH: Nasal chondromesenchymal hamartoma; EMBASE: Excerpta medica database; CT: Computed tomography; MR: Magnetic resonance imaging; PPR: Pleuropulmonary blastoma; SLCT: Sertoli-Leydig cell tumour; JGCT: Juvenile granulosa cell tumour; CN: Cystic nephroma; MNG: Multinodular goitres; CBME: Ciliary body medulloepithelioma; ERMS: Embryonal rhabdomyosarcoma; DICER1: is not an abbreviation, but the name of gene located on chromosome 14 at position q32.13.

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
Contribution to conception and design: KM, AN, PC. Contribution to acquisition of data, analysis and interpretation: KM, AN, ET. Involved in drafting the manuscript & revising it critically: KM, AN, ET, PC. All authors read and approved the final manuscript.

Authors’ information
KM is a clinical teaching fellow with Barts and The London School of Medicine and Dentistry. ET is a clinical teaching fellow with Barts and The London School of Medicine and Dentistry. PC is a locum consultant at a regional teaching hospital where the case was encountered.

Acknowledgements
Thanks to Dr Ian Seddon (Consultant Histopathologist, Colchester Hospital University NHS Foundation Trust) for providing the histopathology images.

Author details
1 Barts and The London School of Medicine and Dentistry, The Blizard Institute of Cell and Molecular Science, 4 Newark Street, Whitechapel, E1 2AT London, UK.
2 Colchester Hospital University NHS Foundation Trust, Colchester, UK.

Received: 20 January 2015 Accepted: 1 June 2015
Published online: 03 July 2015

References
1. Mohler D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol. 2009;62(10):1006–12.
2. Schultz KA, Yang J, Doros L, Williams GM, Harris A, Stewart DR, et al. pleuropulmonary blastoma familial tumor predisposition syndrome: a unique constellation of neoplastic conditions. Pathology Case Rev. 2014;19(2):90–100.
3. Kang Jun HYO, Ahn Gueng H, Kim Young M, Cha Hee J, Choi H-J. Nasal Chondromesenchymal Hamartoma a case report. Korean J Pathol. 2007;41:258–62.
4. Cho YC, Sung IV, Son JH, Ord R. Nasal chondromesenchymal hamartoma: report of a case presenting with intraoral signs. J Oral Maxillofac Surg. 2013;71(1):72–6.
5. Roland NJ, Khine MM, Clarke R, Van Velzen D. A rare congenital intranasal polyp: mesenchymal chondrosarcoma of the nasal region. J Laryngol Otol. 1992;106(12):1081–3.
6. Tenss MH, Billman GF, Pransky SM. Nasal hamartoma: case report and review of the literature. Int J Pediatr Otorhinolaryngol. 1993;28(1):83–8.
7. Zarbo RJ, McClatchey KD. Nasopharyngeal hamartoma: report of a case and review of the literature. Laryngoscope. 1983;93(4):494–7.
8. Ludemann JP, Tewfik TL, Meagher-Villemure K, Bernard C. Congenital mesenchymoma transgressing the cribriform plate. J Otolaryngol. 1997;26(4):270–2.
9. Li Y, Yang GK, Tian XT, Li B, Li Z. Malignant transformation of nasal chondromesenchymal hamartoma in adult: a case report and review of the literature. Histol Histopathol. 2013;28(3):337–44.
10. McDermott MB, Ponder TB, Dehner LP. Nasal chondromesenchymal hamartoma: an upper respiratory tract analogue of the chord wall mesenchymal hamartoma. Am J Surg Pathol. 1998;22(4):425–33.
11. Ozölek JA, Cararo R, Barnes EL, Hunt JL. Nasal chondromesenchymal hamartoma in older children and adults: series and immunohistochemical analysis. Arch Pathol Lab Med. 2005;129(1):1444–50.
12. Li GY, Fan B, Jiao YY. Endonasal endoscopy for removing nasal chondromesenchymal hamartoma extending from the lacrimal sac region. Can J Ophthalmol. 2013;48(2):e22–3.
13. Stewart DR, Messinger Y, Williams GM, Yang J, Field A, Schulz KA, et al. Nasal chondromesenchymal hamartomas arise secondary to germline and somatic mutations of DICER1 in the pleuropulmonary blastoma tumor predisposition disorder. Hum Genet. 2014;133(11):1443–50.
14. Arai M, McDermott M, Orr D, Russell J. Nasal chondromesenchymal hamartoma presenting in an adolescent. Int J Pediatr Otorhinolaryngol. 2003;67(6):659–72.
15. Norman ES, Bergnon S, Trupiano JK. Nasal chondromesenchymal hamartoma: report of a case and review of the literature. Pediatr Dev Pathol. 2004;7(5):517–20.
16. Yao-Lee A, Ryan M, Rajaram V. Nasal chondromesenchymal hamartoma: correlation of typical MR, CT and pathological findings. Pediatr Radiol. 2011;41(5):675–7.
17. Kato K, Iinji R, Tanaka Y, Hara M, Sekido K. Nasal chondromesenchymal hamartoma of infancy: the first Japanese case report. Pathol Int. 1999;49(8):731–6.
18. Silkis RZ, Mudvari SS, Sether D. Ophthalmologic presentation of nasal chondromesenchymal hamartoma in an infant. Ophthalm Plast Reconstr Surg. 2007;23(3):243–4.
19. Moon SH, Kim MM. Nasal chondromesenchymal hamartoma with incontinent esotropia in an infant: a case report. Can J Ophthalmol. 2014;49(1):e30–2.
20. Mattos JL, Ehrly SV. Nasal chondromesenchymal hamartoma: a case report and literature review. Int J Pediatric Otorhinolaryngology Extra. 2011;6(4):215–9.
21. Shet T, Borges A, Nair C, Desai S, Mistry R. Two unusual lesions in the nasal cavity of infants—a nasal chondromesenchymal hamartoma and an aneurysmal bone cyst like lesion. More closely related than we think? Int J Pediatr Otorhinolaryngol. 2004;68(3):359–64.
22. Kim B, Park SH, Min HS, Rhee JS, Wang KC. Nasal chondromesenchymal hamartoma of infancy clinically mimicking meningocoelephalocele. Pediatr Neurosurg. 2004;40(3):136–40.
23. Kim JE, Kim HJ, Kim JH, Ko YH, Chung SK. Nasal chondromesenchymal hamartoma: CT and MR imaging findings. Korean J Radiol. 2009;10(4):416–9.
24. Sarin V, Singh B, Prasher P. A silent nasal mass with ophthalamic presentation. Orbit. 2010;29(6):357–9.
25. Eloy P, Tirgau H, Nastosge MC, Weynard B, Rombauts P. Nasal chondromesenchymal hamartoma: case report. Int J Pediatric Otorhinolaryngology Extra. 2010;6(4):300–3.
26. Jeyakumar A, McEvoy T, Fettman N. Neonatal nasal mass: Chondromesenchymal hamartoma. Int J Pediatric Otorhinolaryngology Extra. 2011;6(4):223–5.
27. Priest JR, Williams GM, Mize WA, Dehner LP, McDermott MB. Nasal chondromesenchymal hamartoma in children with pleuropulmonary blastoma–A report from the International Pleuropulmonary Blastoma Registry registry. Int J Pediatr Otorhinolaryngol. 2010;74(11):1240–4.

28. Doros L, Schultz RA, Stewart DR, Bauer AJ, Williams G, Rossi CT, et al. DICER1-Related Disorders. In: Pagon RA, Adam MP, Ardinger HH, Bird TD, Dolan CR, Fong CT, et al., editors. GeneReviews® Seattle (WA). 1993.

29. Johnson C, Nagaraj U, Ezquerra J, Wardahl D, Wurzbach D. Nasal chondromesenchymal hamartoma: radiographic and histopathologic analysis of a rare pediatric tumor. Pediatr Radiol. 2007;37(1):101–4.

30. Chae HJ SJ, Lee SK. Nasal Chondromesenchymal Hamartoma. Korean J Pathol. 1999;32:225–7.

31. Kim JW, Low W, Billman G, Wickersham J, Kears D. Chondroid hamartoma presenting as a neonatal nasal mass. Int J Pediatr Otorhinolaryngol. 1999;47(3):253–9.

32. Hsueh C, Hsueh S, González-Crussí F, Lee T, Su J. Nasal chondromesenchymal hamartoma in children: report of 2 cases with review of the literature. Arch Pathol Lab Med. 2001;125(3):400–3.

33. Love SE, Sethi RK, Davies E, Stafford JS. Nasal chondromesenchymal hamartoma in an adolescent. Histopathology. 2006;49(3):321–3.

34. Nakagawa T, Sakamoto T, Ito J. Nasal chondromesenchymal hamartoma in an adolescent. Int J Pediatric Otorhinolaryngology Extra. 2008;4(3):111–3.

35. Fintisis S, Gavrogliou C, Poti S, Constantinidis I, Mpaltatzidis A, Rachovitas D, et al. Nasal chondromesenchymal hamartoma in a child. Cardiovasc Intervent Radiol. 2009;32(3):593–7.

36. Behery RE, Bedmicej E, Lazenby A, Nelson M, Grove J, Huang D, et al. Translocation t(12;17) (q24.1;q21) as the sole anomaly in a nasal chondromesenchymal hamartoma arising in a patient with pleuropulmonary blastoma. Pediatr Dev Pathol. 2012;15(3):249–53.

37. Uzomefuna V, Glynn F, Russell J, McDermott M. Nasal chondromesenchymal hamartoma with no nasal symptoms. BMJ Case Rep. 2012;2012.

38. Wang T, Li W, Wu X, Li Q, Cui Y, Chu C, et al. Nasal chondromesenchymal hamartoma in young children: CT and MRI findings and review of the literature. World J Surg Oncol. 2014;12(1):257.

39. Obidan AA, Ashoor MM. Nasal chondromesenchymal hamartoma in an adolescent with pleuropulmonary blastoma. Saudi Med J. 2014;35(8):876–8.

40. Chandra Manis SN, Venkatahari VP. Nasal Chondromesenchymal Hamartoma: a case report and review of literature. JK-Practitioner. 2014;19:1–2.