Mesenchymal chest wall hamartoma – surgery is preferred

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Abstract
Objectives. Mesenchymal hamartoma of the chest wall (MHCW) is a rare benign lesion typically presenting at birth or in the first year of life with characteristically clinical, radiological and pathological features. The purpose for this study was to get a better understanding of the illness, its clinical appearance, treatment and course. Findings. 57 reports comprising 104 children were identified. The males to females ratio was 1.6:1. About 80% of children with MHCW were diagnosed prenatally or within the first 6 months of life. 84% of patients underwent surgery for MHCW. Follow up period was complicated by scoliosis in 13% of operated patients. 4 patients died, but surgery related death did not occur. The rate of complete resection was lower in patients with bilateral or multifocal as in patients with unilateral or unifocal disease (p < 0.05). The rate of resurgery was higher in case of previous incomplete resection compared to complete resection (p < 0.05). Conclusions. Physicians may misinterpret MHCW as malignant process. For large symptomatic MHCW surgical resection is the appropriate treatment. Complete resection seems to be superior to partial resection. Close observation may be justified, but only in case of small asymptomatic lesions. Careful follow up is necessary to allow early recognition of complications.
Key words: neonate, respiratory insufficiency, mesenchymal hamartoma, chest wall tumor

Introduction
Mesenchymal hamartoma of the chest wall (MHCW) is a rare lesion typically presenting at birth or in the first year of life with characteristically clinical, radiological and pathological features. The condition derives from the chest wall and may be single or multiple, bi- or unilateral. Death due to pulmonary compression is described [1, 2]. Despite the clinical appearance, the radiological picture and some histological findings are highly suggestive for a malignant process, MHCW is a benign condition. The optimal treatment for MHCW remains controversial, with some advocating early surgical intervention and others preferring conservative treatment [3-5].

To date about 100 cases are reported in the literature, mostly as case reports or small series with review of literature including up to 80 patients [6]. In order to get a better understanding of the illness, its clinical appearance, treatment and management we reviewed 103 children and children with MHCW published previously in the literature. Furthermore we present an additional case, a premature infant with a bilateral MHCW.

Methods
Search strategy
A PubMed MEDLINE search of the English and German literature was performed with use of the medical subject headings “hamartoma” and “chest wall”. All articles identified were searched for additional cross references. In addition an internet search using Google® was undertaken (mesh “hamartoma” and “chest wall”). Despite the reports noted above, one article in the French language was included [10].

Statistical analysis
We analyzed the following factors, that could possibly influence the clinical course: sex, age at time of diagnosis, side of MH, number of involved ribs, treatment modalities, time interval between diagnosis and surgery, extent of surgery. Statistical analysis was performed using SPSS® (Statistical Package for Social Sciences, SPSS Inc., Chicago, USA), Version 12.0. Comparisons between different groups were made using the Chi² test and the Fisher’s exact test. A p-value less than 0.05 was considered significant.

Case report
The need for Institutional Review Board (IRB) review is not required for case reports at our institution. A term male infant (gestational age 32/4 weeks, birth weight 2040 g) was born by caesarean section because of fetal distress and premature rupture of membranes. During the initial resuscitation an irregular shaped hard mass was noted in the right axilla. Chest radiography revealed a bilateral mass with deformations of the ribs and compression of the lungs. The intra-thoracic mass led to severe pulmonary compromise with the need for mechanical ventilation. Suggested diagnosis of MHCW was confirmed by biopsy at day 7. In the following months all extubation trials failed. At 6 months severe respiratory deterioration occurred and intensive mechanical ventilation was necessary. Chest computed tomography demonstrated tumor growth with compression of the right main bronchus. In order to avoid progressive obstruction of the right bronchus a large part of the right hamartoma was excised. Following surgery respiratory function promptly improved. Sufficient spontaneous ventilation was established within 22 days. At 30 months of age with the exception of a thoracic deformity, the boy is well without any signs of tumor progress, recurrence or scoliosis.

Results
Literature search
57 reports comprising 104 patients treated for MHCW were found in the literature [1-57]. We only identified 1 patient with diagnosis of MHCW as an adult [11]. The patient suffered
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from chest pain and age 47 and had bilateral multiple extrapleural round masses. Treatment was not undertaken. 13 years later the same patient is alive. Diagnosis of MHCW was made following partial tumor resection. The patient was excluded from the analysis.

Table 1. Characteristics of publications found in the literature search

<table>
<thead>
<tr>
<th>Number of included publications</th>
<th>56</th>
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<tbody>
<tr>
<td>included patients</td>
<td>103</td>
</tr>
<tr>
<td>case reports (≥ 2 patients)</td>
<td>29</td>
</tr>
<tr>
<td>series (≥ 2 patients)</td>
<td>17 (2-12 patients)</td>
</tr>
</tbody>
</table>

Information available regarding:

- age at initial diagnosis: 103/103 (100%)
- sex: 96/103 (93%)
- initial symptoms: 100/103 (97%)
- location of MH: 101/103 (98%)
- number of involved ribs: 77/103 (75%)
- treatment: 86/103 (83%)
- follow up: 72/103 (70%)

The remaining 56 reports were published between 1964 and 2006 and include 39 case reports and 17 series (≥ 2 patients). Further publications characteristics are given in table 1.

Clinical presentation

The median age at initial diagnosis for the 93 patients diagnosed postnatally was 1 month, the mean 8.8 months (range 0-156). In 10 of 103 (9.7%) cases diagnosis was made primarily by ultrasonography and in 44 (43%) cases within the neonatal period (Figure1). 37 of 96 (39%) patients were female and 59 of 96 (61%) male. Sex was not mentioned in 7 patients. Ratio of males to females was 1.6:1.

Information regarding initial symptoms were given in 100 of 103 patients. Characteristic symptoms leading to diagnosis of MHCW were respiratory compromise (n = 50, 50%) or a palpable mass at a deformity of the chest wall (n = 56, 56%). 14 of 100 (14%) patients presented with both, respiratory compromise and chest wall abnormalities (Fig. 1). Other first symptoms reported were fever (n = 2), scoliosis (n = 1), chest pain (n = 1) and incidental (n = 4).

Location

Information regarding the site of MH were available in 100 of 103 patients (98%). The MH was right sided in 54 patients (54%), left sided in 37 patients (37%) and bilateral in 9 patients (9%). Multiple lesions occurred in 23 patients. Unilateral, multiple lesions on the right side have been reported in 9 patients and on the left side in 5 patients (Fig. 2). The number of involved ribs was 1 in 13 patients, 2 in 31 patients, 3 in 13 patients and 4 or more in 13 patients. In 7 cases the number of involved ribs was declared as "multiple" and in 26 of 103 patients' information about the number of involved ribs was not available. Up to 2 ribs were in involved in 17 of 27 (63%) females and in 25 of 39 (64%) males (in 2 patients sex was not given). Age at initial diagnosis and side of MH in case of unilateral occurrence were not related to the number of involved ribs.

![Fig. 1. Age at initial diagnosis and clinical symptoms leading to initial diagnosis. Other (n): chest pain (1), fever (2), scoliosis (1), "incidental", not explained (4). In 3 patients information about the clinical presentation was not given](image)
Fig. 2. Location of the MHCW. Not shown (n): midline (1), not documented (2)

Fig. 3. Treatment modalities

**Treatment**

Treatment related informations were available in 86 of 103 (83%). At all, 72 of 86 (84%) patients received surgery, one of them in combination with chemotherapy [12]. In 2 patients [13, 14] chemotherapy was administered without surgery (figure 3). Information about the time interval between initial diagnosis and surgery were given in 71 of 72 (99%) cases. In 56 of 72 (78%) patients surgery was undertaken within 1 month following initial diagnosis. In 27 of 86 (31%) patients an approach of conservative treatment was choosen, but 12 of them received surgery within 6 months and further 3 within 6 years after initial diagnosis. The reasons for secondary surgery were growth of the MHCW and increasing respiratory compromise (n = 9), initial misdiagnosis (n = 2) and not specified (n = 4). Complete resection was done in 49 (68%) patients, partial resection in 20 (28%) patients. In 3 patients information about the extent of resection were not given. The time interval between diagnosis and surgery did not influence the rate of total resection. Because of excessive bleeding at time of surgery in 1 patient, it was not possible to remove the tumor and surgery was limited to biopsy [15].

**Follow up and outcome**

Information about the follow up were available in 72 of 103 (70%) and about the follow up period in 70 of 72 (97%) patients. Follow up period was between 1 day and 9 years (median 23.5 months, mean 45.6 months). Minimal given follow up time for survivors was 0.5 months. 2 patients died on day 1 of non treatable respiratory insufficiency [1, 2], 1 patient died on day 7 of severe sepsis during chemotherapy induced aplasia [13] and 1 patient died on day 14 of severe sepsis and pulmonary insufficiency [16]. 1 patient suffered from permanent brain damage following postoperatively respiratory arrest [17]. In 9 of 59 (15%) patients with surgery and follow up information resurgery was undertaken, in every case because of growth of MH [3, 18-23]. Resurgery was only required in the subgroup with previous incomplete resection (p < 0.03).

In 2 patients [4, 24] with significant upper airway obstruction a continued tracheotomy is necessary (last follow up for both with 6 years). Another patient developed significant airway obstruction due to growth of MHCW 3 month following initial diagnosis [25]. In this patient surgery was never done and he was well after a follow up of 125 months. Scoliosis was noted in 13 of 68 (19%) survivors with follow up. In 1 patient [20] a poorly differentiated sarcoma was diagnosed 35 months after the primary diagnosis of MHCW. A nearly total excision followed by chemotherapy and radiotherapy was done. At 126 months the patient had severe scoliosis.

**Risk factor analysis**

Following outcome parameters were used for comparison of possible risk factors: rate of complete resection, rate of scoliosis and rate of resurgery. Statistical analysis showed, that only the following factors significantly influenced outcome: The rate of complete resection was lower in bilateral or multifocal MH and also lower in case of more than 2 involved ribs (p < 0.03) and the rate of resurgery was higher following incomplete resection compared to the group with complete re-
The term MHCW is currently widely accepted, because it reflects the character of the lesion as focal disorder and self limiting overgrowth of normal skeletal components. Terms like osteochondrosarcoma [27], osteochondroma [23], chondroblastoma [28], malignant and benign mesenchymoma [14, 15, 59] have been used in the past, but imply a true neoplasm and should not be used for this non-neoplastic condition. Other terms previously used for MHCW are chondromatosus [7, 29], vascular and cartilaginous hamartoma [30, 31]. Along with other authors [1, 2, 17, 19, 29] we enclosed some reports, which describe the typical clinical, radiographic and pathologic appearance of MHCW, despite the authors [1, 22] originally had assumed a neoplastic process. Some of these authors were surprised about the long term survival of their patients.

The natural history of MHCW is not clearly understood. Even though MHCW are usually diagnosed at or shortly after birth with respiratory distress or a palpable chest wall mass, typically the lesion appears as a hard, immobile subcutaneous and extra pleural chest wall mass with deformations of one or more ribs. Respiratory distress and ventilator dependence may occur even in term or near term newborns. About 80% of all MHCW are diagnosed within the first 6 months of life. In patients with MHCW are usually diagnosed at or shortly after birth with respiratory distress or a palpable chest wall mass, typically the lesion appears as a hard, immobile subcutaneous and extra pleural chest wall mass with deformations of one or more ribs. Respiratory distress and ventilator dependence may occur even in term or near term newborns. About 80% of all MHCW are diagnosed within the first 6 months of life. In the second with skeletal cleft [36] and in the third with Duane's syndrome [4]. The prognosis of MHCW is excellent. Only 4 cases of deaths have been reported. 2 infants died briefly after birth because of respiratory insufficiency two further because of systemic infection.

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On chest radiography MHCW presents as an ipsilateral or bilateral mass with calcific density. The lesion obscures the ribs and leads to destruction of the chest wall. Reactive bone formation is common. Compression of the lungs and mediastinal shift may occur and can cause cardiorespiratory compromise. Chest CT

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Table 2. Risk factor analysis: only patients with given *sex, **age at time of diagnosis, ***side of MH, ****number of involved ribs, #treatment, ##time interval between diagnosis and surgery, ###extent of resection, +complete resection included or + + follow up information included

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Complete resection+</th>
<th>p</th>
<th>Resurgery++</th>
<th>p</th>
<th>Scoliosis++</th>
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<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>male/female</td>
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<td>0.25</td>
<td>5/4</td>
<td>0.56</td>
<td>8/5</td>
<td>0.95</td>
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<tr>
<td>age at time of diagnosis**</td>
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<td></td>
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</tr>
<tr>
<td>≤ 1 month/ &gt; 1 month</td>
<td>24/25</td>
<td>0.06</td>
<td>8/1</td>
<td>0.07</td>
<td>10/3</td>
<td>0.22</td>
</tr>
<tr>
<td>≤ 1 year/ &gt; 1 year</td>
<td>41/8</td>
<td>0.09</td>
<td>9/0</td>
<td>0.58</td>
<td>12/1</td>
<td>1.00</td>
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<tr>
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<tr>
<td>right/left</td>
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<td>0.79</td>
<td>1/5</td>
<td>0.39</td>
<td>6/6</td>
<td>0.51</td>
</tr>
<tr>
<td>unilateral/bilateral</td>
<td>48/0</td>
<td>&lt; 0.05</td>
<td>6/3</td>
<td>0.09</td>
<td>12/1</td>
<td>1.00</td>
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<td>&lt; 0.05</td>
<td>4/5</td>
<td>0.10</td>
<td>11/2</td>
<td>0.49</td>
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<tr>
<td>number of involved ribs****</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>≤ 2 ribs/ &gt; 2 ribs</td>
<td>27/12</td>
<td>&lt; 0.05</td>
<td>1/4</td>
<td>0.18</td>
<td>7/3</td>
<td>0.29</td>
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<td>1/12</td>
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<tr>
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<td>0.75</td>
<td>7/2</td>
<td>1.0</td>
<td>9/3</td>
<td>1.0</td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>complete/partial</td>
<td>n.d.</td>
<td>0/9</td>
<td>&lt; 0.05</td>
<td>11/1</td>
<td>0.26</td>
<td></td>
</tr>
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</table>
demonstrates heterogeneous rib lesions, extrapleural soft tissue masses with mineralization and regions of soft tissue attenuation [5, 9]. Haemorrhagic cavities and secondary aneurysmal bone cysts may be visible [37]. MRI can help to differentiate aneurysmal bone cysts and MHCW [38].

The various pathological and histological features of MHCW are described in detail by several authors [1, 7, 34, 39]. Briefly, despite its expansive growth the lesion is smooth surfaced. Cut section demonstrates solid and cystic areas with cartilaginous tissue as predominant elements. Often, but inconstant blood filled cysts are visible. Histologically highly cellular small round, oval or spindle mesenchymal cells, osteoelastic and multinucleated osteoclastic cells and fragments of hyalin cartilage have been described. Immunohistochemical staining may demonstrate the presence of S-100 protein in cartilaginous areas [19, 34].

The clinical appearance, the radiological picture and some histological features like actively proliferating fibroelastic and chondroid elements may suggest a malignant rather then a benign process [1] and provoke potential dangerous overtreatment. The main differential diagnoses of MHCW include aneurysmal bone cysts and primary bone tumors.

In this study 84% of evaluable patients received surgical intervention. These high proportions reflect the point of view of most authors, who prefer surgery. The prognosis following surgery is excellent, especially if complete resection was possible. Resulting chest wall defects can be closed primarily or with prosthetic materials or muscle flaps. Some authors advocate a wide en bloc excision of the involved portion of the chest wall including the involved ribs, intercostal muscles, underlying pleura and neurovascular bundle [3, 6, 20]. One of the reasons for this recommendation was the suspected possibility of malignant transformation [20] as discussed above. Because in MHCW malignant transformation or metastatic spread do not occur, in accordance with other authors [34] we suggest that surgery should be more conservative with clear margins if possible. Recurrence is rare and was only reported after incomplete resection, but as in our patient complete resection may be difficult, particularly with large multifocal lesions. In case of recurrence diagnosis should be checked. Irrespective of the treatment chosen, close follow up is necessary.

Other authors favour a conservative approach with close observation and surgery only in case of deterioration of clinical symptoms or growth of the MHCW, but as reported 15 out of 27 patients with primary conservative therapy required surgery within 6 years following initial diagnosis. However, usually MHCW stops growing within the first year of life and some patients may have an excellent outcome with conservative treatment alone [25]. Spontaneous regression has been observed in children even with bilateral MHCW [10].

The severity of the symptoms depends from the size and the location of the MHCW. Surgery may be the proper treatment for patients with large symptomatic MHCW. Observation may be appropriate for patients with small asymptomatic MHCW. Long term radiological and clinical surveillance is necessary for both groups. Chemotherapy as well as radiation is not indicated in the treatment of this non-malignant lesion.

The most important postsurgical complication is scoliosis, which appears in about 20% of patients [20]. The severity of scoliosis is related to the number of resected ribs and location of the resection. Resection of the posterior and lower ribs leads to a more severe scoliosis. [59]. Surgery related death was not reported, but 1 patient suffered respiratory arrest postoperatively leading to cerebral hypoxia and permanent brain damage [17].

MHCW is a rare lesion of infancy and early childhood. Physicians, who are not familiar with this diagnosis, may suggest a malignant rather than a benign process. In our literature study the majority of patients underwent surgery because of respiratory compromise or chest wall abnormalities. For large symptomatic MHCW surgical resection is the appropriate treatment. Complete resection seems to be superior to partial resection. Because of the tendency of MHCW to regress close observation may be justified, but only in case of small asymptomatic lesions. Careful follow up is necessary to allow early recognition of complications like renew growth of the MHCW or scoliosis.

References


