

Mandibular ameloblastic carcinoma in a young patient

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Abstract

Ameloblastic carcinoma is a rare cause of jaw tumors, especially in children. This rare, rapidly growing, malignant tumor of odontogenic origin affects predominantly the mandible and maxilla. Hypercellularity, lack of differentiation, high mitotic index, vascular and neural invasion are its main histological features. Local destruction and distant metastases to the lungs, bones, liver and brain are common in ameloblastic carcinoma. Prognosis is poor, due to its low sensitivity to chemo- and radiotherapy. We report the case of an 8-year-old girl with ameloblastic carcinoma of the left mandible and extensive right pleuro-pulmonary and bone marrow metastases. Biopsies made from the mandibular tumor and lung tumor tissue obtained by bronchoscopy, showed the same histological features, that of ameloblastic carcinoma. Diagnostic and treatment challenges are shown in this uncommon pediatric solid tumor of the jaw. Carboplatin and etoposide treatment showed some therapeutic effect upon the primary tumor, but lung infiltrations were not influenced. Palliative treatment was initiated. Early detection of ameloblastic carcinoma, before massive distant metastases develop would be an option for long-term survival, which can be achieved with radical surgery followed by radiotherapy.

Keywords: ameloblastic carcinoma, mandible, lung metastasis, child.

Introduction

Tumors of the lower oro-facial region may be benign and malignant. Most frequently seen primary malignant lesions include soft tissue and hard connective tissue sarcomas, carcinomas of the salivary glands, especially squamous cell carcinomas (in 90% of the cases) and melanomas [1, 2]. Breast-, lung-, abdominal organs- and prostate-cancers can metastasize to lower-face structures. Benign lesions may have odontogenic or non-odontogenic origin, they are predominantly ameloblastomas [3–5]. Ameloblastomas, which represent 1% of all jaw tumors, are histologically benign odontogenic epithelial neoplasms, which exhibit an aggressive invasive local behavior [6].

Ameloblastic carcinoma (AC) is an extremely rare odontogenic epithelial malignant tumor, only 70 cases were reported in the English literature between 1984–2011 [7]. Eleven cases of AC in patients under the age of 20 have been reported so far [8]. Difficulties arose through time in finding adequate histopathological classification of AC to fulfill important features such as histopathogenesis, origin, cytologic characteristics of malignancy, clinical behavior [9–11]. “Primary ameloblastic carcinoma” has been classified recently by the World Health Organization (WHO) as a tumor that demonstrates the morphological features of ameloblastoma with atypia, regardless of the presence or absence of metastasis [12]. Two-thirds of AC are located in the mandible and only one third in the maxilla. Average age at diagnosis is 30 years, males are more frequently affected with a male:female ratio of

2.4:1 [13]. Clinical signs are rapidly growing tissue mass, ulceration, bleeding, fistula, pain, tooth mobility [7, 14]. Metastases appear most commonly in the lungs but brain and bone disseminations have also been seen. Histologically, features of ameloblastoma along with cytological atypia, high mitotic index, necrosis, neural and vascular invasion are the hallmarks of AC [14]. Wide local excision and cervical lymph node dissection followed by radiotherapy are the suggested treatment of AC. Chemotherapy has limited value, nor radiotherapy alone is a reliable treatment modality for AC [8]. Prognosis is poor, especially in cases when metastases are present. The extreme rarity of AC in general and in children in particular, adversely influences our knowledge about this disease entity.

Patient, Methods and Results

The 8-year old girl was admitted to the pediatric oncological ward because of painful enlargement of the left cheek, visible tumoral mass inside the oral cavity, fever, pallor, weight loss, respiratory distress with dry, irritative cough.

She had been complaining of left facial swelling and pain for two months prior her first examination in a dental practice, when an incision and draining was made for a suspected dental abscess. On check-up examination, it became obvious that the patient beside the left mandibular tumor was cachectic, feverish, dyspneic with dry irritative cough so that she was admitted to the pediatric pneumology ward for further investigations. Tuberculosis was ruled out and a bronchoscopy was

performed which showed a completely obstructed right main bronchus by a necrotic, friable, gelatinous mass, and a biopsy was carried out from the tumor mass. Simultaneously another biopsy was performed from the oral lesion and the patient was transferred to the Oncology Department.

Physical examination revealed a lean, pale child (18 kg weight, 120 cm height), with a 9×5 cm tumor mass in the left mandible, bulging into the oral cavity. The deep-violet colored, cauliflower-like endobuccal tumor mass-produced swallowing and breathing difficulties (Figure 1).



Figure 1 – Extension of ameloblastic carcinoma of the jaw into the oral cavity.

No enlarged lymph nodes were palpable. Signs of respiratory distress were obvious with intercostal retractions, distended nostrils, tachypnea, dyspnea, dullness over the whole right lung with absence of breath sounds. Tachycardic normal heart sounds (cardiac rate 120/min.) without murmurs were heard and her arterial blood pressure (118/60 mmHg) was slightly elevated. No hepato- or splenomegaly was found.

Paraclinical findings revealed an iron deficient anemia (hemoglobin 9.6 g/dL, hematocrit 31%, hypochromia, microcytosis, iron 2.3 μmol/L), infestation with *Ascaris lumbricoides*, mild tumor lysis (lactate dehydrogenase 1244 U/L) but no hypercalcemia. Plain chest radiography showed opacity over the right thorax with mild mediastinal displacement to the left (Figure 2).

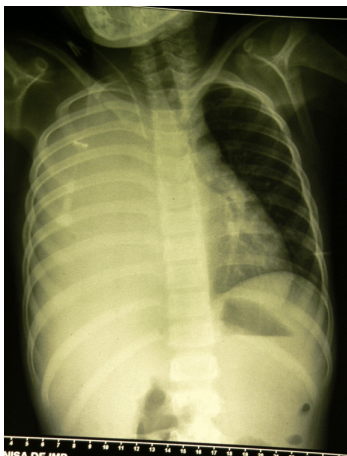


Figure 2 – Chest radiography of the minimal right pleural effusion and massive pulmonary metastasis provoked by ameloblastic carcinoma of the jaw; full opacity of the right lung, displacement of the mediastinum to the left.

Abdominal ultrasonography showed minimal fluid content in the Morrison space. Computed tomography of the chest showed a huge, solid tumor mass, which occupied the right hemithorax between the level of the sterno-clavicle joints and diaphragmatic arch. The tumor infiltrated the superior mediastinum and right side of the heart, which appeared to be dislocated to the left. The mass was inhomogeneous with hypodense areas due to possible intratumoral necrosis. A 27 mm

wide pleural effusion was noted on the right basal area. Computed tomography of the neck and head area revealed a bone tumor on the ascendant arm of the left hemimandible, which extended to the angular region and posterior side of the horizontal part. Multiple osseous extensions entered the masseter and internal pterygoid muscles, which were also enlarged by tumoral infiltration. Echocardiography showed pericardic reaction. Examination of the bone marrow aspirate revealed metastatic infiltration with tumor cells displaying basophilic cytoplasm, nuclei with fine chromatin content, some showing increased intercellular adherence.

The tumor pieces were represented by two biopsy fragments (lung and mandible), fixed in 10% buffered formalin and embedded in paraffin. Sections were stained with Hematoxylin and Eosin, Periodic Acid Schiff and Giemsa for the routine histopathological evaluation. The biopsy obtained from the mandible mass was identified as high-grade malignant tumor. Immunohistochemical stains were performed with LabVision and Dako reagents, using: LCA, panCK, EMA, CD56, VIM, NSE, synaptophysin and chromogranin bound antibodies were visualized using heat induced epitope retrieval method by the Ultra Vision LP Large Volume Detection System HRP Polymer detection system and DAKO EnVision™/HRP kit, followed by Hematoxylin counterstaining. The neoplastic cells formed nests of cells with the distinctive features of ameloblastic differentiation: peripheral pallisading of basaloid cells coupled with the dyscohesiveness of the cells in the middle of the nests created the typical stellate reticulum arrangement (Figure 3). Focal cystic degeneration in the middle of the cellular clusters left a rim of basaloid cells clinging to the stroma, also characteristic of ameloblastic tumor (Figure 4). The tumor cells were intense positive for Pan-Keratin (panCK) and EMA (Figure 5 and 6), while the vimentin, LCA and synaptophysin, chromogranin were negative. CD56 reaction was also negative (Figures 7 and 8). The degree of mitotic activity, presence of necrotic foci, and infiltrative characteristics of the tumor supported the malignant nature of this ameloblastic neoplasm.

Based on clinical, laboratory, imagistic and histological findings, the established diagnosis was left mandibular ameloblastic carcinoma with metastasis in the right lung, pleura and bone marrow.

The patient underwent five chemotherapeutic courses: two courses based on vincristine, endoxane and adriamycin with lack of clinical response and three courses based on vincristine, carboplatin and etoposide, with visible shrinking of the jaw tumor size (2×2 cm) but little or no efficacy upon the pleuro-pulmonary tumoral involvement. Paclitaxel based regimen was abandoned after severe allergic reaction. Respiratory function test results were under 50% of the estimate age-related values, which made impossible right pulmectomy. Palliative care was initiated in this patient. Eight months after the onset of symptoms, disease progression with worsening respiratory insufficiency lead to the death of the patient.

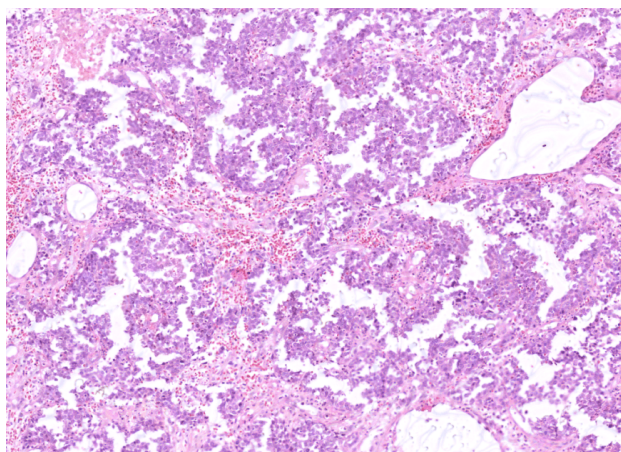


Figure 3 – Infiltrative tumor with neoplastic cells forming nests of cells with distinctive features of ameloblastic differentiation: peripheral palisading of basaloid cells (HE stain, ob. $\times 20$).

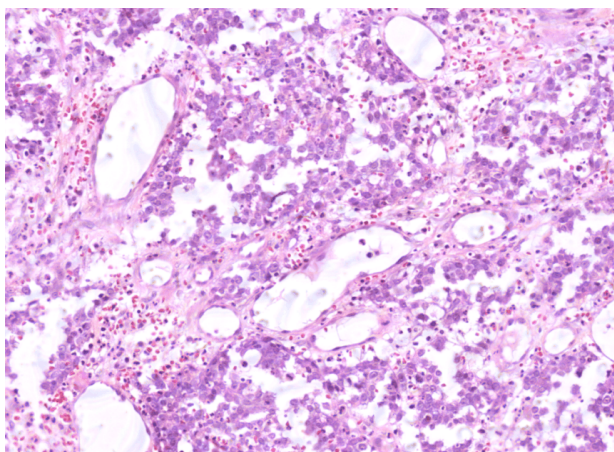


Figure 4 – Focal cystic degeneration in the middle of the cellular clusters (HE stain, ob. $\times 40$).

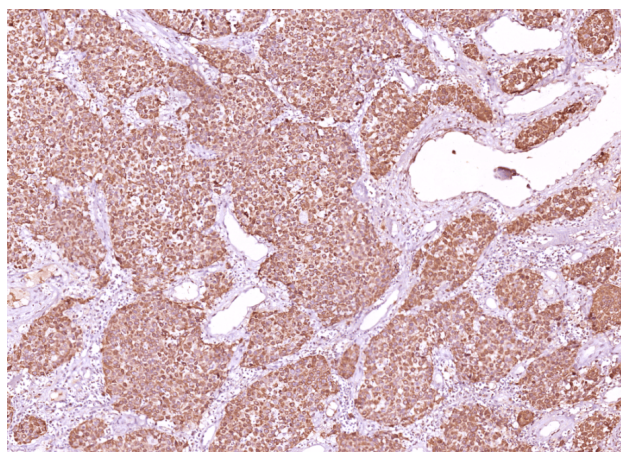


Figure 5 – Nets of tumor cells with peripheral basaloid cells (panCK immunostaining, ob. $\times 10$).

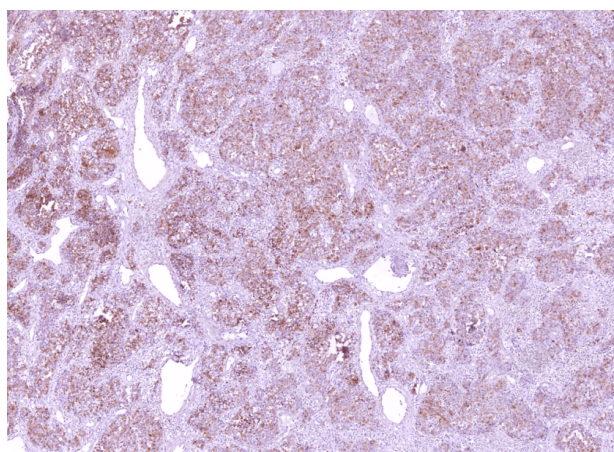


Figure 6 – Moderate immunostaining of EMA in ameloblastic carcinoma (ob. $\times 10$).

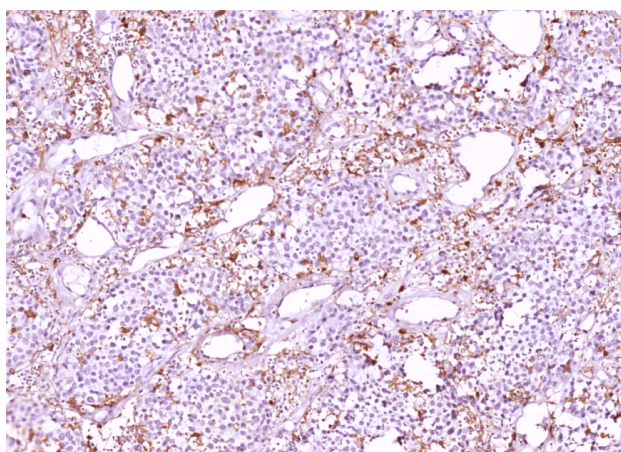


Figure 7 – Ameloblastic carcinoma: tumor cells without LCA expression (ob. $\times 20$).

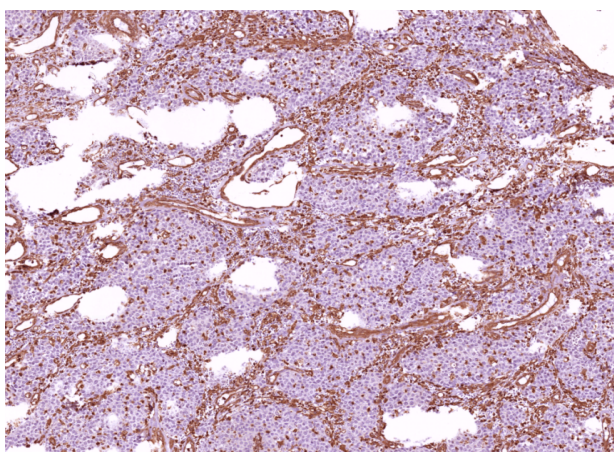


Figure 8 – Ameloblastic carcinoma: tumor cells without vimentin expression (ob. $\times 20$).

Discussion

Ameloblastic carcinoma (AC) is a rare, aggressive malignant epithelial odontogenic tumor. So far, about 65 cases have been reported in English literature and only a few cases in children [7, 14]. The common clinical presentation includes rapid painful swelling of the jaw, tooth mobility due to bone resorption, trismus.

In two thirds of the cases, the tumor is localized in the posterior mandible and in the remaining cases in the maxilla. Rare cases localized in the anterior skull and nasal cavity have been reported [15–17]. Peripheral ameloblastic carcinoma arising from gingiva and alveolar mucosal epithelia is very rare [7]. No age-group predilection have been noticed, however the average age is around 30 years and the tumor has been

rarely identified in children [8]. This aggressive, malignant tumor metastasizes most frequently into the lungs, bone, liver and brain [18–20]. An uncommon metastatic malignant ameloblastoma of the kidneys was reported by Hayakawa K *et al.* in 2004 [21]. The metastases may occur even in the absence of local recurrence. There is a male predominance; the male/female ratio varies according to authors between 1.4/1–2.4:1 [14].

Ameloblastoma is a benign tumor of the odontogenic apparatus, which constitutes 1% of tumors and cysts of the jaw in adults. The term “malignant ameloblastoma” has been used for tumors with histological findings consistent with ameloblastoma, which produce metastasis, despite benign histology. The term “ameloblastic carcinoma” was first used by Shafer WG *et al.*, in 1974 [11], for tumors with ameloblastic differentiation and signs of malignant cytological features, regardless of the presence of metastasis.

World Health Organization established a classification of odontogenic carcinomas in 1972, modifications were made on the recommendation of Elzay RP, in 1982 [9], and later by Slootweg PJ and Müller H [10]. Histopathologically ameloblastic carcinoma consists of foci and areas that are consistent with ameloblastoma and signs of malignancy: spindle-shaped cells or round epithelial cells with no differentiation towards the columnar cells of ameloblastoma, islands and sheets of epithelium absence or rare presence of stellate reticulum-like areas, hyperchromatism, large or atypical nuclei, increased mitotic index, necrosis, calcification, neural and vascular invasion [14]. Ameloblastic carcinoma may arise *de novo* or from preexistent ameloblastoma or odontogenic cyst.

Imagistic investigations are important in tumor assessment. Radiology may show poorly defined radiolucency, sometimes with focal radio-opacities. Computed tomography and magnetic resonance imaging offer more detailed information.

Differential diagnosis of jaw tumors in children includes metastases in jaw from visceral neoplasms; invasion of bone by an adjacent soft tissue tumor like rhabdomyosarcoma; Hodgkin and non-Hodgkin lymphomas; benign and malignant osseous tumors like osteosarcoma, Ewing sarcoma; leukemias, neuroblastoma, Langerhans' cell histiocytosis, xanthogranuloma, lymphangioma, hemangioma, benign and malignant odontogenic tumors and others [17, 22]. Application of a broad-range immunohistochemistry panel would be helpful for the establishment of a positive diagnosis.

Elective treatment for ameloblastic carcinoma is wide surgical excision with cervical lymph node dissection in case of adenomegaly. Radiotherapy and chemotherapy are of limited value, indicated in locally advanced or metastatic disease where operation is not an option. Osteonecrosis, secondary sarcomas may arise after radiotherapy. Yazici N *et al.* reports maxillary ameloblastic carcinoma in a child successfully treated with surgery and radiotherapy [8]. Cisplatin, adriamycin,

cyclophosphamide, paclitaxel, carboplatin have been used for chemotherapy, with best results achieved after paclitaxel and carboplatin therapy [23, 24]. In our patient, cyclophosphamide, adriamycin have little or no effect, while local shrinking of the primary tumor was noticed after carboplatin and etoposide treatment. The pleuro-pulmonary metastases were not influenced by chemotherapy.

☐ Conclusions

We presented this case because of the rarity of ameloblastic carcinoma in children and the differential diagnostic and treatment challenges it generated.

Acknowledgments

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