Case report: Chondrosarcoma of the head and neck

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Abstract

Chondrosarcoma originates in the bones of the head and neck. It is an unusual neoplasm that is slow-growing and represents only 1–3% of all cases of chondrosarcoma. Here, we report a case of a 45-year-old male Caucasian patient treated at Hospital Amaral Carvalho with a history of swelling of the face and a tumoral mass in the right maxilla with infiltration into the skin, which had been present for 4 months. A computerized tomography (CT) of the face and sinuses demonstrated a lesion in the right maxilla. A maxilectomia without orbital exenteration was performed. It was diagnosed as a grade III chondrosarcoma, with infiltration into the subjacent bone, anterior wall of the maxillary sinus and floor of the orbit. The patient presented with recurrence of the tumor after adjuvant therapies. A molecular study on the present case showed an unusually large number of abnormalities. This finding demonstrated extreme chromosomal instability, which was likely due to the undifferentiation of the tumor. Although there are no cases in the literature with which to compare, these findings may elucidate potential therapeutic targets for advanced tumors without other therapeutic options.

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1. Introduction

Chondrosarcoma originates in the bones of the head and neck. It is an unusual neoplasm that is slow-growing and represents only 1–3% of all cases of chondrosarcoma [1–2]. The maxilla is the most affected bone and usually has slow growth, but it can be locally aggressive with a high rate of recurrence. Other primary sites in the head or neck are the jaw, nasal cavity and maxillary sinus [3–5]. Its response to radio- and/or chemotherapy is poor. By definition, it is a locally aggressive or malignant group of cartilaginous matrix-producing neoplasms tumor and neoplastic osteoid should not be present according to the World Health Organization (WHO) [6–9].

1.1. Case presentation

A 45-year-old male Caucasian patient with a history of swelling of the face and a tumoral mass in the right maxilla with infiltration into the skin, which had been present for...
4 months, was treated the Hospital Amaral Carvalho on 10/28/2010. He received a diagnosis of “myxochondroid tumor” from another service with no slides to review. During a clinical evaluation, a deletion of the right nasolabial folds with a hardened injured right maxilla without hard palate infiltration was noticed. Computerized tomography (CT) of the face and sinuses demonstrated a lesion in the right maxilla (Fig. 1).

On 01/25/11, a maxilectomia without orbital exenteration was performed. The right part of the hard palate, anterior wall of the right maxillary sinus and part of the orbital floor were removed. Inside there was a large tumoral mass measuring 9.5 × 7 cm.

The tumor was diagnosed as a grade III chondrosarcoma with infiltration of the subjacent bone, anterior wall of the maxillary sinus and floor of orbit (Figs. 2 and 3).

The surgery was followed by adjuvant radiotherapy. The patient received conformational doses of 7000 cGy between 05/26/2011 and 08/10/2011.

A new CT performed on 10/20/2011 revealed a lesion in the right maxillary sinus. A fine needle aspiration biopsy (FNAB) was performed on the same day and received a diagnosis of consistent with infiltration by chondrosarcoma (Figs. 4 and 5).

Neoadjuvant chemotherapy was started. The patient received 3 cycles of Ifosfamide 2 g/m² equivalents of 4000 mg: D1-5 (first to fifth day) and Adriamicin 25 mg/m²: 50 mg D1-2. The patient tolerated this treatment, but had a non-oncological response. The patient was then submitted to an additional surgery on 02/27/2012 because of the infiltration of the floor of the orbit. After this procedure, he developed a large oro-facial fistula, returning to the clinical oncology department where he received three cycles of the same chemotherapy protocol. There was no response. The patient died on 06/09/2012. Another surgery was not performed because the tumor grew to the floor of the skull and rhinopharynx.

For investigating somatic molecular alterations, we screened 2855 hotspot regions defined by the Catalogue of Somatic Mutations in Cancer (COSMIC) of 50 cancer related genes using the Ion AmpliSeq™ Cancer Hotspot Panel v2 (Life Technologies). By sequencing the tumor and matched normal samples, we identified a total of 49 somatic mutations in 24 genes (Table 1). The majority of the alterations were missense mutations, and 6 were nonsense mutations.

2. Materials and methods

2.1. Cancer Hotspot Panel sequencing

We used the Ion AmpliSeq™ Cancer Hotspot Panel v2 (Life Technologies) for targeted sequencing. The panel is composed of 2855 hotspot regions defined by the Catalogue of Somatic Mutations in Cancer (COSMIC) of 50 cancer related genes. Libraries were prepared from 20 ng of DNA from the tumor and matched normal FFPE samples according to the Ion AmpliSeq™ Library Preparation protocol. Template preparation, emulsion PCR, and enrichment were performed using an Ion PGM™ Template OT2
200 kit (Life Technologies), according to the manufacturer’s instructions. Sequencing was performed using an Ion 318™ Chip and Ion PGM™ Sequencing 200 Kit v2 (Life Technologies) at Ion PGM™ Platform.

The sequencing reads were quality-filtered and mapped to a human genome reference (hg19) using Torrent Suite Browser 4.0.1. We obtained more than a 1000× coverage depth on average. More than 83% of the targeted regions were represented by more than a 200× coverage depth. Variants were called with a VariantCaller v4.0.r73742 plugin from Torrent Suite Browser and an in-house pipeline following a minimum coverage depth of 200× and minimum variant frequency of 10%. We selected somatic variants (detected in the tumor sample and absent in the normal sample) leading to amino acid changes, splice site variants or premature stop codons that were not present in dbSNP or with no described MAF (minor allele frequency).

3. Discussion

Chondrosarcoma of the head and neck is very rare. Only a few cases have been presented in the literature. The number of cases is usually small, and almost none of them demonstrate molecular findings. Chondrosarcoma is most common between the third and fourth decades of life [1,3,5,10,11]. Diagnosis is always a challenge because cartilaginous neoplasms have different histologic patterns, from benign chondroid tumors to malignant undifferentiated neoplasms.

We used the 2013 WHO [6] classification of bone tumors (grades I–III). We also add that in bone sarcomas, the histologic subtype often determines grade. For example, mesenchymal chondrosarcoma and the dedifferentiated chondrosarcomas are always considered high grade. In conventional chondrosarcoma, the grading system as proposed by Evans et al. [8] is still widely used. However, it is important to mention new category as per 2013 WHO classification-intermediate (locally aggressive) and new terminology low grade chondrosarcoma: atypical cartilagenous tumor/chondrosarcoma grade I that is considered intermediate (locally aggressive) as per new WHO classification [6]. Evans et al. [8] classified the tumors in question in 3 degrees, from I to III histological grades according to the cell density, nuclear differentiation, and size of the nuclei. Other authors prefer dividing cases into only high and low degrees, which provides a better correlation with prognoses and is easier for pathologists. A classification can drive the treatment options.

All chondrosarcomas, regardless of grade, show the histological characteristics of hypercellularity, pleomorphism, mitotic activity, intercellular myxoid matrix and cellular atypia. Low-grade tumors are typically well differentiated with moderate cellularity and very little cell pleomorphisms or atypia.

Like chondrosarcomas of other sites, tumors that arise in the head and neck region can show various histological types. The so-called “conventional” histological type is the most common. Other variants include mesenchymal, clear cell chondrosarcoma and dedifferentiated chondrosarcoma. The mesenchymal and dedifferentiated forms are known to have poor prognoses. The dedifferentiated chondrosarcoma represents the most aggressive subtype. Despite differences in the literature, the myxoid form is known to occur in soft tissue instead of bone tissue.

The molecular studies on the present case showed an unusually large number of abnormalities. This finding demonstrates an extreme chromosomal instability that is likely due to the undifferentiation of the tumor. There are no cases in the literature with which we can compare, but these findings may elucidate potential therapeutic targets for advanced tumors without other therapy options.

The consensus is that surgical treatment is the most effective therapy for chondrosarcoma. Dissection of the cervical lymph node is not routinely performed due to a low incidence of lymph node metastases. Generally, radiation is performed for palliative cases, unresectable cases or as an adjunctive therapy in cases of residual disease, but not as an initial or single treatment.

Chemotherapy has limited effect on chondrosarcoma. In high-grade mesenchymal chondrosarcoma cases with early local recurrence and aggressive behavior or potential metastasis, it can be employed as an adjuvant therapy.
The main prognostic factors are surgical resection, stage, grade and primary site. The mesenchymal and dedifferentiated forms are known to have poor prognoses. Tumor recurrence is relatively common and usually occurs due to an incomplete resection of the tumor. It also may be due to the local spread of the disease or surgical technique issues. In a

<table>
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<tr>
<th>Gene</th>
<th>Exon</th>
<th>Reference allele</th>
<th>Variant allele</th>
<th>Base coverage</th>
<th>Allele frequency</th>
<th>Variant type</th>
<th>cDNA change</th>
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<td>p.Q383*</td>
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<td>COSM3818350</td>
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<td>p.W446*</td>
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Table 1 Somatic alterations detected in chondrosarcoma of the head and neck.
study conducted by AC Camargo Hospital, Prado et al. observed recurrence in 4 of 10 previously treated patients. This figure is similar with other studies. Arlen et al. described 10 recurrences out 18 treated patients [4], and Mark et al. showed a recurrence rate of 44% [5].

This case was initially identified because the patient reported pain and swelling. Unfortunately, it took a long time to be formally investigated due to a variety of social conditions that affect the region and the low socio-cultural level of the population, which is unaware of the possible severity. Additionally, the education of the health professionals plays a major role in early diagnosis. Curative surgery can be performed in the initial stages to prevent local invasion and the dismal prognoses demonstrated in this present case.

References