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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.

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 cartilagenous 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 Ifosfamida 2 g/m^2 equivalents of 4000 mg: D1-5 (first to fifth day) and Adriamicin 25 mg/m^2: 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

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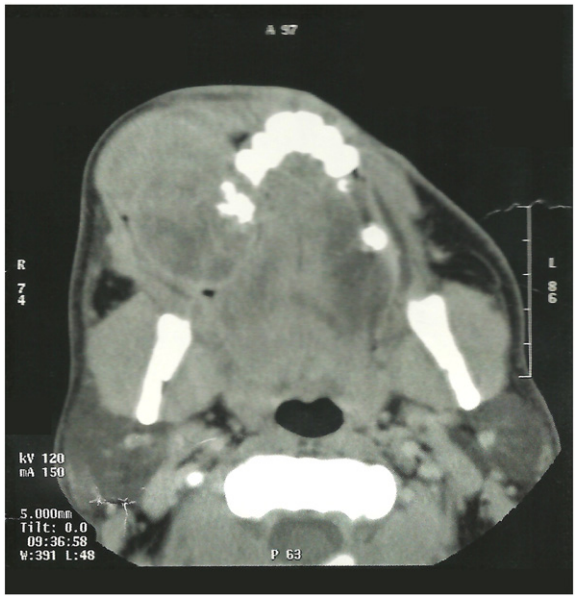

Fig. 1. CT demonstrating a tumor in the maxilla adjacent to the skin of the face.

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.

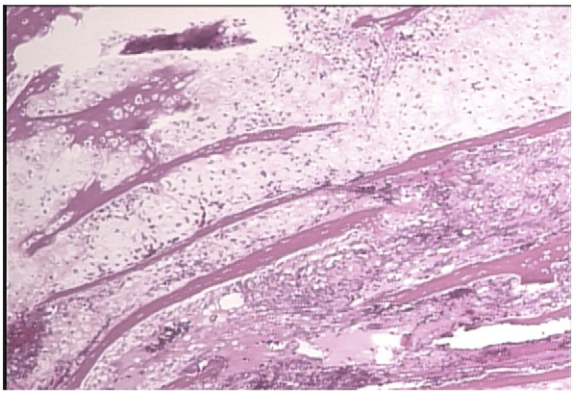

Fig. 3. Infiltration into the bone tissue by the neoplasia.

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

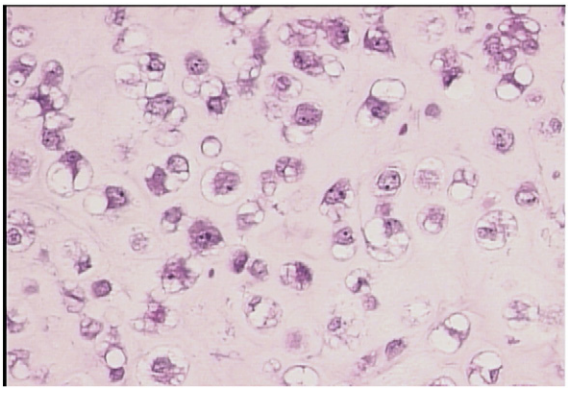

Fig. 2. Atypical cartilaginous cells in the middle of chondroid matrix.

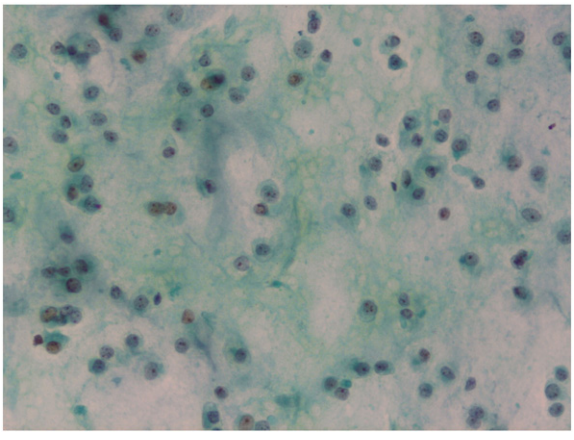

Fig. 4. Shorr stain of the malignant cartilaginous cells.