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Case Report

Mandibular chondroblastic type osteosarcoma primarily diagnosed as chondrosarcoma as a result of radiation therapy: a case report

Alise Elizabete Rone[1,2]*, Ieva Bāgante[1,2], Irina Vasiļčenko[1], Jānis Zariņš[3,4], Renārs Deksnis[5], Sigita Hasnere[6]

[1]Department of Oral and Maxillofacial Surgery, Pauls Stradins Clinical University Hospital, Latvia
[2]Department of Oral and Maxillofacial Surgery and Oral Medicine, Riga Stradins University, Latvia
[3]Department of Hand and Plastic surgery, Microsurgery Centre of Latvia, Riga East University Hospital, Latvia
[4]Baltic Biomaterials Centre of Excellence, Headquarters at Riga Technical University, Riga, Latvia
[5]Department of Head and Neck surgery, Oncology Centre of Latvia, Riga East University Hospital, Latvia
[6]Department of Clinic of Oncology, Pauls Stradins Clinical University Hospital, Latvia

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***Correspondence:**
Dr. Alise Elizabete Rone,
E-mail: aliseelizabete.rone@rsu.lv

ABSTRACT

Radiation therapy is a recognized etiological factor for osteomyelitis, osteoradionecrosis and multiple sarcomas such as chondrosarcoma and osteosarcoma. Here we present a case of mandibular chondroblastic type osteosarcoma induced by radiotherapy which was primarily misdiagnosed as chondrosarcoma. A female presented with main complaint of pain at the extraction site following multiple teeth extraction and sequestrectomy on the right lower jaw. Medical history revealed stage IV squamous cell carcinoma of the base of the tongue which was treated by surgical excision, chemotherapy and radiotherapy ten years ago. Four recurring sequestrectomies were performed, but only histological material from the fourth sequestrectomy revealed grade 2 chondrosarcoma. This was followed by resection of the tumour and floor of the mouth, mandibular, lip and facial skin reconstruction and operation material through histology was again confirmed to be grade 2 chondrosarcomas. In a year's time, pathological nodule in thyroid gland was found on CT, surgery was performed. Operation material now revealed high grade chondroblastic type osteosarcoma and additional radiotherapy and chemotherapy was prescribed. This case illustrated chondrosarcoma and chondroblastic type osteosarcoma as a rare malignant incidence, with diagnostical difficulties and treatment. Differential diagnosis should be considered if no positive changes are observed after the designated therapy as well as importance of immuno histological evaluation. One treated malignancy does not exclude development of another unrelated malignancy.

Keywords: Chondroblastic type osteosarcoma, Lingual carcinoma, Mandibular chondrosarcoma, Radiation therapy

INTRODUCTION

Comprising about 0.2 percent of all head and neck malignancies are sarcomas.[1,2] Main histological subtypes of sarcomas are rhabdomyosarcoma, osteosarcoma, chondrosarcoma, vascular sarcomas and soft tissue sarcomas.[3] Most commonly, in head and neck area sarcomas are diagnosed around 50 years of age. Chondrosarcomas of the head and neck region affect male population more often than females and are less common in general than osteosarcomas. Pathogenetically they are a group of malignant bone tumours producing cartilaginous matrix, mostly found in flat bones.[4] In contrast, histologically chondroblastic osteosarcoma

typically appear with dominant amount of chondroid matrix and hyaline cartilage, but also exhibit non-chondroid elements as osteoid or bone matrix.[5] Only correct morphological diagnosis allows to choose the most appropriate treatment option.

CASE REPORT

At the beginning of July 2019, a 41-year-old Caucasian female presented to the outpatient department of P. Stradins Clinical University Hospital (PSCUH) with main complaint of pain at the extraction site following multiple teeth extraction and sequestrectomy on the right lower jaw. Medical history revealed that the patient was diagnosed with stage IV squamous cell carcinoma of the base of the tongue and metastasis of the neck lymph nodes. In the year of 2009 patient received resection of the tumour and neck dissection on the left side in April, followed by revision surgery on neck metastasis on the right side a month later, tumour was classified as T3N2M0. Patient received 8 cycles of chemotherapy and 27 fractions of radiotherapy, with no evidence of disease progression thereafter. However, in February of 2018, in private dental clinic, due to pathological mobility and pain, tooth #45 extraction was performed, in June of the same year wound revision and antibacterial therapy was performed without improvement. Therefore, patient was sent to Riga Stradins University Oral and Maxillofacial department and in September teeth #43,44,47 extraction and sequestrectomy was performed.

Tissue samples were sent for pathological examination. Histological conclusion showed unspecific purulent soft tissue inflammation and granulation, although bone structure was with normal architectonic. Unfortunately, with minimal improvement patient sought help in PSCUH and after consultation and examination patient was scheduled for surgery within one week. Local sequestrectomy was performed at the right side of mandible. Second time patient sought medical help in PSCUH in March, 2021 due to a lump in the region of tooth #47 and tooth ache of #37. Orthopantomogram and biopsy from soft tissues was performed (see Figure 1). Biopsy results revealed chronic inflammation and granulation tissue and was scheduled for another revision.

In April, 2021 tooth #37 extraction combined with sequesterectomy on the left side and lump excision on right side of mandible was performed with subsequent antibacterial therapy. Histological examination revealed on the right side - epulis and chronic inflammation on the left side. Third episode was in November of 2021, with complaints of mandibular bone enlargement and pain on the left side. Orthopantomogram concluded changes consistent with active osteomyelitis, another sequestrectomy was performed on left side of mandible and the cavity was filled with Platelet-rich fibrin (PRF) and patient again received antibacterial therapy. Biopsy material revealed grade 2 chondrosarcoma on the left side of mandible, a malignant cartilage-forming tumour. Following biopsy results patient was sent to department of Head and Neck Oncology Centre of Riga East University Hospital for further treatment. Following year, 2022, in March patient underwent radical tumour resection according to surgical principles of sarcoma – mandible, floor of the mouth, buccal mucosa, lower lip and facial skin was resected en-block. One stage functional reconstruction was done with a chimeric fibula flap and 2 local face flaps to reconstruct lost anatomical structures and maintain patient's functionality and aesthetic appearance (Figure 2). Biopsy results affirmed clear resection line, grade 2 chondrosarcoma with 10% of necrosis, vascular invasion, without invasion into the lymphatic vessels, but with extraoral spread and invasion in periapical, pulp and gum tissue and inferior lip tissue-T3NxM0L-V+Pa+RO. Computer tomography (CT) was performed but did not reveal any secondary dissemination. Recommendations included radiation therapy, but patient refused. Control CT scan was performed in November 2022, for abdomen, head, soft tissue of neck with intravenous contrast agent revealed no dissemination of the tumour. The next CT scans with intravenous contrast for head and neck, chest and abdomen were performed in March, April and July in the year of 2023. Pathological nodule with a cystic component and multiple calcified tissue fragments of the left lobule of the thyroid gland was detected in July's CT scans. In September supplementary magnetic resonance imaging (MRI) revealed marginal cricoid cartilage and tracheal cartilage infiltration of the left side. Ultrasound (US) controlled aspiration biopsy concluded malignant low differentiated formation with anaplastic cells and surgery was planned. In October, 2023, patient underwent surgery, where left hemithyroidectomy was performed with additional radiation therapy performed in November and chemotherapy appointed for January 2024. Surgery material results now revealed high grade 3 chondroid osteosarcoma. Due to different pathohistological diagnosis previous histological examination of mandibular tumour was re-evaluated and diagnosis was changed and proved as chondroblastic type osteosarcoma, which confirmed that thyroid gland nodule was metastasis of mandibular tumour.

In January, 2024, chemotherapy was started. Unfortunately, patient could not tolerate adverse effects of recommended dose, therefore, it was lowered from 160 mg Cisplatin to 35mg of Doxorubicin. Chemotherapy was performed between end of February and March. The next CT scan in May, 2024 showed a progression of the disease with a metastatic tumour with retro tracheal, parapharyngeal invasion and 2 metastatic processes in the left lung (Figure 3). Chemotherapy with doxorubicin /cisplatin was changed to second line of chemotherapy. Figure 3 showing extensive metastatic process progression in the thyroid gland, with further spread retro-tracheal, para-oesophageal and bilaterally into the subcutaneous soft tissues of the neck. At the beginning of July, 2024 patient was admitted due to oedema in the left hand after first course of second line chemotherapy.

Doppler ultrasound was performed and results revealed deep left axillary vein thrombosis with additional segmental pulmonary thromboembolism. Unfortunately, due to cardiovascular and pulmonary failure, patient's heart stopped.

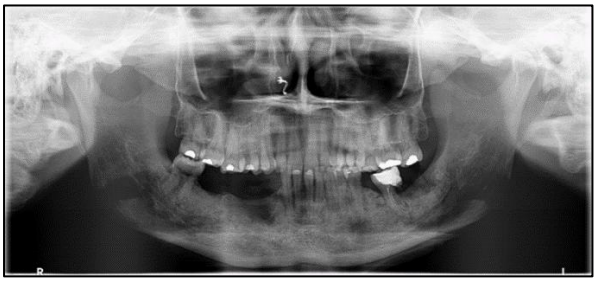

Figure 1: Orthopantomogram revealing sclerotic changes of bone structure and chronic periodontitis of tooth #37.

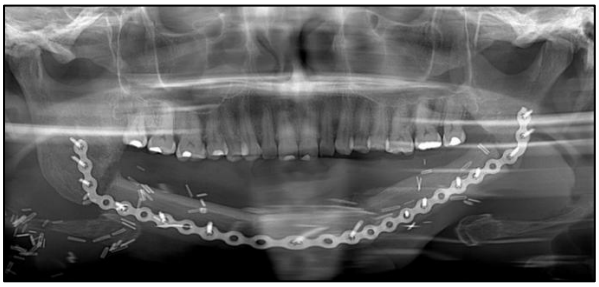

Figure 2: Orthopantomogram showing the full mandibular reconstruction.

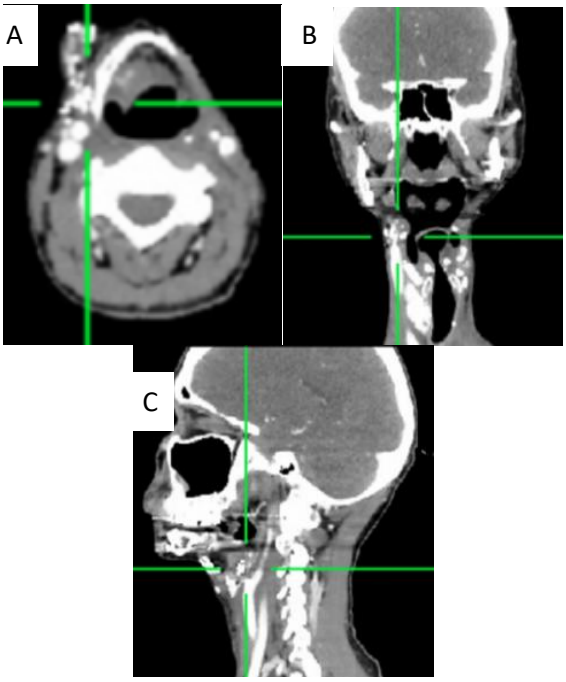

Figure 3: CT showing extensive metastatic process progression in the thyroid gland, with further spread retro-tracheal, para-oesophageal and bilaterally into the subcutaneous soft tissues of the neck.

DISCUSSION

Chondrosarcomas in the head and neck region predominantly affect molar region, but can also appear in ramus, condyle, symphysis or coronoid process.[6,7] This is in correspondence with our findings as the pathological material was found in the region of last molars at the left side of the mandible. High dose (>40 Gy) radiation therapy is recognized cause of sarcoma in the bone and soft tissue and are accountable for several percent of head and neck sarcomas.[8-10] In addition, other risk factors such as chronic irritation and trauma have been recognized as associated or predisposing risk factors as well.[11] Radiotherapy is also a risk factor for osteoradionecrosis as it acts by destroying neoplastic and normal cells, through devitalization of bone vasculature thus making it non vital and not able to remodel.[12-14] Study by Coşkun et al, revealed radiation therapy to be a risk factor for chondrosarcoma and patients had shorter survival rates.[15] This study correlates with our clinical findings as patient received 27 fractions of radiotherapy ten years ago.

Chondrosarcomas can be classified into 4 histological subtypes-conventional, clear cells, dedifferentiated and mesenchymal. Most important histological grading is for conventional chondrosarcomas as it will indicate clinical behaviour and prognosis of the disease.[2,16-18] Our case initially revealed conventional grade 2 chondrosarcoma, which is the most common type.

The incidence of osteosarcomas of the skull, similarly to chondrosarcomas, is rare. Osteosarcomas commonly present with painless or only mildly tender lesions as well. After diagnosis patients should receive neoadjuvant or adjuvant chemotherapy, resection of tumour and radiotherapy for more advanced or inoperable cases as it is relatively radiation resistant.[19] Osteosarcomas induced by radiation in the maxilla and mandible is an uncommon and aggressive tumour.[20,21] Study by McHugh et al, compared radiation induced and primary osteosarcomas, revealing that radiation associated osteosarcomas were more common high grade with more aggressive behaviour.[22] This is in correlation with our findings. Our case presented patient who had not only received radiotherapy but also chemotherapy in year 2009 following treatment of lingual carcinoma.

WHO has recognized several pathological subtypes of osteosarcomas-conventional, telangiectatic, small cell, low grade, parosteal, periosteal and high-grade surface.[23] Most common type is conventional which further divided by the dominant matrix can be osteoblastic, chondroblastic or fibroblastic.[24] Chondroblastic osteosarcoma histologically appear with dominant presence of chondroid matrix, exhibiting high level of hyaline cartilage and is associated with non-chondroid elements of osteoid or bone matrix.[5] Osteoid is one of the main components differentiating chondroblastic osteosarcoma from chondrosarcoma.[25] This single characteristic could explain why in the beginning our

clinical case was diagnosed as chondrosarcoma. Immunohistochemistry is a crucial tool in diagnostics as both pathologies exhibit vimentin and S100, but only chondroblastic osteosarcoma is positive for epithelial membrane antigen and cytokeratin.[25]

This rare case describes a patient who after receiving chemotherapy, radiation therapy and surgical excision prevented lingual carcinoma progression, but could have triggered different type of malignancy. After 9 years patient reported discomfort at the right side of the mandible, which was firstly associated with tooth ache, later progressed to the left side and was initially treated as radio-osteomyelitis. Histological evaluation of surgery material was recognized as grade 2 chondrosarcoma after mandibular sequestrectomy on left side.

Even after complete tumour resection and mandibular reconstruction, histological diagnosis remained as grade 2 chondrosarcoma. Only after appearance of pathological nodule in the thyroid gland and hemithyroidectomy, histological evaluation revealed high grade chondroblastic type osteosarcoma. This highlights the importance of histological evaluation and how it can be subjective. Hence for accurate diagnosis-two independent pathologists should evaluate slides and immunohistochemistry should be used.

Accurate and early diagnosis is a key element for treatment. At the early stages of a malignant process non-specific clinical signs and symptoms could be present, therefore accurate diagnosis is challenging. We benefitted from the preserved slides as it allowed to re-evaluate diagnosis and use them for scientific purposes.

CONCLUSION

This case illustrated chondrosarcoma and chondroblastic type osteosarcoma as a rare malignant incidence, with diagnostical difficulties and treatment. Differential diagnosis should be considered if no positive changes are observed after the designated therapy as well as importance of immuno histological evaluation. One treated malignancy does not exclude development of another unrelated malignancy.

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