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Oncocytic carcinoma of the salivary glands: A Danish national study

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ABSTRACT

Objectives: To present a Danish national series of oncocytic carcinoma (OC) patients, including data on treatment, recurrence and survival.

Methods: From the national Danish database of salivary gland carcinomas, all patients diagnosed with OC from 1990 to 2005 were identified and data concerning demographics, tumor site, clinical stage and treatment profiles were extracted. A follow-up was carried out.

Results: Of the 15 cases of salivary gland OC, eight were female. The incidence was 0.02/100.000 inhabitants per year in Denmark, 13 patients presented with OC in the parotid gland and two patients with OC in the submandibular gland. Eight patients had nodal involvement at the time of diagnosis. None of the patients had distant metastases at the time of diagnosis. All patients were treated with primary surgery and seven patients received adjuvant radiotherapy. Half of the patients had recurrence. Six patients were alive at 5 years follow up and one patient was alive without recurrence at 10 years follow up.

Conclusions: This study is the first to report a national incidence of oncocytic carcinoma in the salivary glands. The results confirm oncocytic carcinoma to be a salivary gland carcinoma with a poor prognosis. All patients experiencing recurrence died of the disease. Treatment must be aggressive. National registries are necessary to achieve further knowledge for future treatment recommendations.

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1. Introduction

Oncocytic carcinomas (OC) of the salivary glands are extremely rare. OCs account for only 0.5% of all epithelial salivary gland malignancies and only 0.18% of all epithelial

salivary gland tumors [1]. In 1953, the first case was reported and described by Bauer and Bauer [2]. Until 2016, when a large study on OC was published [3], less than 100 cases had been reported in English-language literature [3–7]. Because of the relatively few patients it is difficult to obtain sufficient data on epidemiology, histopathology, treatment and prognosis. Due to the national Danish salivary gland carcinoma database it is possible to obtain knowledge on even rare subtypes. The database is the largest national unselected study group of salivary gland carcinoma [8].

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Most cases of OC have occurred in the parotid glands, but reports have also described cases that involved the submandibular gland and minor glands of the palate, nasal cavity, ethmoid and maxillary sinuses and retromolar area [4–7].

OC are composed of malignant oncocytes with adenocarcinomatous architectural phenotypes, infiltrative qualities and often invade muscle, lymphatics and nerves [9]. It is a high-grade tumor characterized by local recurrences and regional or distant metastases [4–6]. OC may arise de novo or from previous oncocytomas [9]. The long-term prognosis is poor [3,5,6].

The purpose of this study is to identify all patients diagnosed with OC in Denmark in the period of 1990–2005 and to present epidemiology, anatomical location, TNM-stage, treatment and survival data.

2. Material and methods

The study is a retrospective report on OC in Denmark in a period of 16 years. A national database was established in 2009 with registration of all patients with salivary gland carcinoma diagnosed in Denmark in the period from the 1st of January 1990 to the 31st of December 2005. Histological revision on all available surgical specimens was carried out by two experienced specialists in salivary gland pathology, and criteria for diagnosis according to WHO 2005 classification of Head and Neck Tumors were used [8,9]. Patients were identified from three Danish National Registries: The Danish Cancer Registry, The Danish Pathology Registry and The Danish National Patient Registry. Search criteria were based on ICD-8 and ICD-10 coding as well as combinations of topography and morphology codes [8]. Extracting data from all three registries ensured inclusion of carcinoma in both major and minor salivary glands. Data on patients diagnosed with OC were collected from the database. Extracted variables included: Age at diagnosis, gender, anatomical location of primary tumor, TNM-classification and stage at diagnosis, perineural and vascular invasion, surgical margins, surgical treatment of T- and N-site, radiotherapy, recurrence and survival.

Fifteen patients with OC were identified in the time period. Clinical data were available for 12 patients, whereas only data on gender, age and anatomical location were available on all 15 patients. Histological revision was possible in 11 cases. The follow-up time was calculated from the time of diagnosis until death or the end of data-collection (January 2016).

Surgical margins were defined as free when >5 mm, close when ≤5 mm or not free.

Primary tumors were staged according to the International Union Against Cancer (UICC 2002, 6th edition) classification [10].

The incidence rate was calculated as number of OC cases divided by total population in Denmark including Greenland and Faroe Islands. Numbers of total population were extracted from the National Statistics Databanks [11].

Data was stored in the DAHANCA (Danish Head and Neck Cancer Group) database. The study was conducted in accordance with the Danish law for scientific ethics committee and approved by the Danish Data Protection Agency.

3. Results

Fifteen patients (eight women, seven men) were identified during a period of 16 years, resulting in less than one new case per year in Denmark and an estimated incidence of 0.02/100.000 inhabitants/year. Data on age were available for all patients with a median age of 70.8 years [range 45.4–79.8 years].

Thirteen tumors presented in the parotid gland, only two tumors presented in the submandibular gland. All cases were unilateral. Since age, gender and anatomical location were the only available data on three of the patients, the remaining results are for 12 patients.

All patients presented with a mass in a major salivary gland. None of the patients presented with pain or facial nerve palsy.

Five patients had pathological class T1/T2 tumors and six patients had T3/T4 tumors in accordance with the TNM classification system [10]. One patient had an unclassified tumor (TX).

More than half of the patients (n = 8) had nodal involvement (N1–N3), while none of the patients had distant metastases at the time of diagnosis. Following this, nine patients presented with advanced disease (overall stage III and IV).

Data from histological records and revision showed perineural invasion in nine of the tumor specimens and vascular invasion in eight of the tumor specimens. There were free surgical margins after primary surgery in half of the patients (n = 6), close margins in one patient and involved margins in four patients. For one patient data on perineural invasion, perivascular invasion and surgical margins were not available.

All patients were treated with primary surgery. The two patients with tumor in the submandibular gland were treated with excision of the submandibular gland. Among the patients with tumors in the parotid gland nine patients were treated with total parotidectomy and two patients were treated with partial resection of the parotid gland. Concerning surgical treatment of the neck, four patients only had a single lymph node removed, while neck dissections to varying extents were performed in eight patients. In four patients neck dissection included level 1–5, in one patient level 2 and 3, and in three patients level 2, only.

Seven patients received adjuvant radiotherapy. Because of different treatment regimens and radiotherapy protocols in the country in the early time period, the patients received between 50 Gy and 66 Gy. None of the patients were treated with chemotherapy.

Last follow up was January 2016. Six patients were alive five years after diagnosis and one patient was alive 10 years after diagnosis which results in a 5-year and 10-year overall survival rate of 50% and 8% respectively. Six patients died of OC, five patients died from other causes. Two patients had recurrence in T- and N-site, three patients had recurrence in N- and M-site and one patient had recurrence only in M-site. Distant metastases were located in lung and liver in one patient, in lung and bones in two patients, and in bones and brain in one patient. All patients experiencing recurrence died of the disease.

Patient and tumor characteristics and data on follow up are summarized in Table 1a and b.

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