

Delay in Diagnosis and Referral Patterns of 646 Patients with Oral and Maxillofacial Cancer: A Report from a Single Institution in Hamburg, Germany

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Abstract. *Improvement in therapy for malignant diseases in the oral and maxillofacial (OMF) region rests mainly upon diagnosis at an early stage of the disease. This study performed an analysis of the delays between symptom onset and time taken for patients to seek medical advice and then their subsequent specialist referral to the Department of OMF Surgery at Eppendorf University Hospital. Patients and Methods: The files of 646 patients (males: 451, females: 195) with malignancies of the OMF region who were treated during an interval of 19 years were analysed retrospectively. Results: Localized swelling, pain and alterations of the mucosa were the predominant first signs and symptoms of disease. Stage grouping according to the TNM system (UICC, 1992) revealed advanced stages in the majority of cases (IV: 30%, III: 15%). The majority of patients were referred by residents in OMF surgery (31.7%) and dentists (28.8%) and were hospitalized within 4 months after notification of the first symptoms (66.9%). Conclusion: Both outreach work of public health institutions and continuous education during studies in both medicine and dentistry, and in further education play a key role in reducing diagnostic delay in OMF cancer.*

Therapy for cancer of the oral and maxillofacial (OMF) region in terms of overall survival has not improved over the last few decades, despite remarkable efforts in the field of reconstructive surgery allowing extensive ablation of advanced stage cancer. Many patients are admitted to hospital at an advanced stage of the disease, allowing only palliative treatment options. Much effort has been directed at improving diagnosis for head and neck cancer, including

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molecular biology-based screening techniques for malignant cells in smears of the mucosa of the upper aerodigestive tract, with modest results (1). Improvement in therapy mainly depends upon early diagnosis. However, symptoms are often not apparent in the early stages of OMF cancer, resulting in delays in diagnostic investigations (2). Thorough knowledge of the cancerous lesions in the OMF region by physicians is one important factor decreasing the time between when symptoms are first recognized by the patient and adequate medical treatment. Delays from the time of onset of signs and symptoms of OMF cancer to time of diagnosis have been repeatedly reported to be linked with the patient, the clinician, or both.

This analysis was performed to determine the disease stage of OMF cancer patients upon their arrival in the medical department and to disclose the referral patterns to a single institution, specialized in the field of treatment for OMF cancer.

Patients and Methods

The files of 646 patients with malignancies of the OMF region who were treated in a single institution over 19 years were retrospectively analysed. The analysis included: topography of tumour, staging for tumour size, involvement of regional lymph nodes and metastatic spread (TNM staging, UICC 1992), if applicable, grading of the tumour, time and type of first signs and symptoms, referral pattern to the hospital, occupation, smoking and drinking habits, and overall survival time.

Results

Mean age of all patients was 59 years. The mean age of females (62.5 years) was higher than in males (57.5 years). This difference proved to be statistically significant ($p < 0.05$, Mann-Whitney U -test). The male/female ratio was 2.3:1 (451/195). Localized swelling, pain and alterations of the mucosa were the predominant first signs and symptoms of the disease.

Localization. The files of 592 patients were evaluable for localization. Tumour locations were: oral cavity or oropharynx:

n=485 (75.1%), epipharynx: n=7 (1.1%), larynx: n=2 (0.3%) lips and facial skin: n=47 (7.3%), maxillary sinus: n=11 (17%) and parotid: n=15 (23%), not exactly classified: n=25, (3.9%).

Risk factors. The number of recognized smokers was 365 (56.5%), non-smokers 244 (37.8%) and smoking data were not evaluable in 37 (5.7%) cases. Alcohol abuse was admitted to by 274 patients (42.4%), denied by 313 (51.6%) and data were inconclusive in 59 (9.1%) cases. The combination of smoking and regular alcohol consumption was recorded in 231 patients (35.9%). Out of 494 patients (100%) with cancer of the upper aerodigestive tract, 314 (63.6%) were smokers and alcohol abuse was found in 241 (48.8%).

Tumour stage after diagnosis. Stage grouping according to the TNM system (UICC, 1992) revealed advanced stages in many cases (IV: n=192 (30%), III: n=97 (15%)), and lower stages in less than 30% (I: n=97, II: n=80). However, in 22% (n=180) the staging could not be determined due to first treatment in other institutions or incomplete data.

Symptoms and findings. The predominant symptoms and findings of OMF cancer were localized swelling (n=327) and pain (n=200), in few cases restricted to the temporomandibular joint (n=6). Other symptoms and findings were also noted: erythema 31 cases, bleeding 27 cases, altered taste 1 case, altered saliva 3 cases, altered musosa 17 cases, insufficient retention of prosthesis 50 cases, impaired swallowing 9 cases and, impaired wound healing 18 cases. Combinations of the 3 worst symptoms were found: swelling and pain (n=110), altered mucosa and pain (n=46), swelling and altered mucosa (n=71), all 3 symptoms simultaneously (n=21). Combinations of bleeding and swelling were apparent (15 of 27 cases). Impaired retention of dental prosthesis (n=50, 100%) was associated with localized swelling (n=26, 52%) and pain (n=17, 34%).

Impact of type of symptoms on the delay for seeking medical advice. Out of 327 patients (100%) with a localized swelling, 83 (25.4%) sought medical advice within 2 weeks of the onset of symptoms and a further 68 (21%) sought medical advice within 4 weeks. The number of patients who recognized but ignored their symptoms over a longer period was high (1 to 2 months: 51 (16%), 3 to 4 months: 42 (12.8%), 5 to 6 months: 22 (6.7%), 7 to 8 months: 7 (2.1%), 9 to 10 and 11 to 12 months: 8 (4.8%) each, >1 year: 27 (8.3%), not exactly determinable: 11 (3.7%).

Less than 1 in 4 patients with pain (n=200, 100%) sought medical advice within 2 weeks after the onset of this symptom (n=47, 23.5%). The number of patients that sought medical advice rose slowly after 4 weeks from onset of symptoms (n=39, 19.5%), 1 to 2 months (n=34, 17%) or 3 to 4 months (n=31, 15.5%) of pain history. However, suffering from pain

did not accelerate the desire seek for medical advice in many patients (5 to 6 months: 11 (5.5%), 7 to 8 months: 7 (3.5%), 9 to 10 months: 4 (2%), 11 to 12 months: 6 (3%), >1 year: 15 (7.5%), not exactly determinable: 6 (3%).

After notice of an alteration of the oral mucosa, 33 (19.8%) and 36 (21.6%) of this subgroup (n=167, 100%) sought medical advice within 2 weeks or 3 to 4 weeks, respectively. However, the mucosal alterations were apparent for a longer time in the majority of patients (1 to 2 months: n=24 (14.4%), 3 to 4 months: n=22 (13.2%), 5 to 6 months: n=10 (6%), 7 to 8 months: n=3 (1.8%), 11-12 months: n=5 (3%), >1 year: n=21 (12.6%), not exactly determinable: 13 (7.8%).

Impaired swallowing forced 18 patients (30.5%) to seek medical advice within 2 weeks, 13 (22%) sought medical advice after 3 to 4 weeks, and their number was reduced with a longer lasting course of this symptom (1 to 2 months: n=8 (13.6%), 3 to 4 months: n=4, (6.8%), 9 to 10 months: n=1 (1.7%), 11 to 12 months: n=3 (5.1%), or >1 year: n=1 (1.7%); n=59 (100%).

Fewer than 50% of patients who experienced an impaired retention of a dental prosthesis (n=50, 100%) in the course of oral cancer sought help from their dentist within the first month (within 2 weeks: n=12, (24%), 3 to 4 weeks: n=10, (20%)). Other patients accepted this discomfort for a longer period of time (1 to 2 months, 9 to 10 months, or 11 to 12 months: n=3 (6%) each, 3 to 4 months: n=11 (22%), 5 to 6 and 7 to 8 months: 1 (each) 2%, >1 year: n=5, (10%), not determinable: n=1)).

Erythema was an infrequently reported finding associated with OMF cancer diagnosis (n=31, 100%) and did not seem to be associated with earlier diagnostics (within 2 weeks: n=5 (16.1%), 3 to 4 weeks: n=7 (19.4%), 1 to 2 months: n=3 (9.7%), 3 to 4 months: n=6 (19.4%), 5 to 6 months: n=3 (9.7%), 7 to 8 and 9 to 10 and 11 to 12 months: n=1 (3.2%) each, >1 year: n=3 (9.7%), not determinable: 1).

Bleeding of the tumour site was reported to have first occurred more than 1 year before seeking for medical advice in 6 patients (22.2%). This subgroup is similar in size to the number of those patients who sought medical advice within 14 days after tumour bleeding (n=5, 18.5%). However, all time points of the evaluation scale were filled with numbers of patients who waited for a long time with a history of tumour bleeding prior to admittance (3 to 4 weeks or 1 to 2 months: n=4 (14.8%) each, 3 to 4 or 5 to 6 months: n=2 (7.4%) each, 7 to 8 or 11 to 12 months: n=1 (3.7%) each, not determinable: 2 (7.4%).

Impaired wound healing of the tumour site was noticed by 18 patients (100%), but was not taken seriously by the majority of those patients who sought medical advice in the following time periods: within 2 weeks or 3 to 4 weeks, n=2 (11.1%) each; 1 to 2 months, n=5 (27.8%); 3 to 4 months, n=4 (22.2%); 5 to 6 months, n=2 (11.1%); 11 to 12 months, n=1 (5.6%); >1 year, n=2 (11.1%); not determinable, 1 (5.6%).

Patients with complaints of their temporomandibular joints due to tumour extension were rare (n=6, 100%) but these patients sought medical advice quite rapidly (within 2 weeks: n=3 (50%) or were waiting for months (3 to 4 months: n=2 (33.3%)), leaving 1 patient who did not address this item adequately.

Alterations of saliva were noted by 3 patients as the only reason to seek medical advice (within 2 weeks: n=2 (66.7%), 3 to 4 months: n=1 (33.3%)).

The time that elapsed between the first symptoms and medical consultation varied considerably, and was within 3 to 4 months for the majority of patients (n=410, 63.5%; within 2 weeks: n=125 (19.3%), 3 to 4 weeks: n=117 (18.1%), 1 to 2 months: n=90 (14%), 3 to 4 months: n=78 (12%). A remarkable number of patients were aware of their symptoms but did not seek medical advice until: 5 to 6 months: n=39 (6%), 7 to 8 months or 9 to 10 months: n=15 (2.3%) each, 11 to 12 months: n=13 (2%), >1 year: n=63 (9.8%), no exact timing: n=91 (14.2%). The mean delay in notification of first symptoms was 6.26 months (minimum 0.5 months, maximum 103 months).

The time that elapsed between the first consultation with a doctor and diagnosis varied considerably (within 2 weeks: n=32 (5.8%), 3 to 4 weeks: n=88 (15.9%) 1 to 2 months: n=95 (17.2%), 3 to 4 months: n=137 (24.8%), 5 to 6 months: n=53 (9.6%), 7 to 8 months: n=31 (5.6%), 9 to 10 or 10 to 12 months: n=14 (2.5%) each), >1 year: n=88 (15.9%). The mean interval of time between attendance and diagnosis was 7.12 months (minimum: 0.5 months, maximum: 60.5 months).

Tumour stage and first consultation of a doctor (n=466). Out of 192 patients in the stage IV grouping, 32 (20.8%) and 40 (20.8%) had a contact with a doctor within 2 weeks or 3 to 4 weeks after first recognition of the findings, respectively (1 to 2 months: 25 (13%), 3 to 4 months (29, 15.1%), 7 to 12 months: 12 (6.3%), >1 year: 15 (7.8%)). However, the number of patients with inconclusive findings was high in this group (n=51 (26.6%)). The distribution of patients with stage III cancer (n=97) was similar to that of the other stages (within 2 weeks: 22 (22.7%), 3 to 4 weeks: n=16, (16.5%), 1 to 2 months: n=19, 19.6%), 3 to 4 months: n=9 (9.27%), 5 to 12 months: n=21 (21.6%), >1 year: n=10 (10.3%)). Nineteen patients (23.8%) with stage II cancer (n=80) consulted a doctor within 2 weeks (3 to 4 weeks and 1 to 2 months: 13 each (32.6%), 3 to 4 months (n=11, 13.8%), 5 to 12 months: 15 (18.8%), >1 year: n=9 (11.3%)). Twenty-two patients (22.6%) with stage I cancer (n=97) were referred to a doctor within 2 weeks (3 to 4 weeks: 12 (12.4%), 1 to 2 months: 14 (14.4%), 3 to 4 months: 11 (11.3%), 5 to 12 months: 25 (25.8%). >1 year: 13 (13.4%)).

Grading of tumour. Grading (G) of tumours differed (GI: n=146 (22.6%), GII: n=349 (54%), GIII: n=47 (7.3%), anaplastic: n=5 (0.8%), no grading: n=99 (15.3%). The

analysis of tumour localizations and grading revealed a statistically significant difference for well-differentiated cancer of the skin and lips compared to anaplastic carcinomas of the OMF regions ($p < 0.001$).

Referral. The majority of patients were referred by residents in OMF surgery (n=205, (31.7%)) and dentists (n=186 (28.8%)), followed by general practitioners (n=83 (12.8%)), otorhinolaryngologists (n=71 (11%)), dermatologists (n=61 (9.4%)), physicians (n=11 (1.7%)), general surgeons or ophthalmologists (n=5 (0.77%) each), or gynaecologists (n=2, 0.3%). The number of patients that were urged by their relatives to present themselves to a hospital was very low (n=2 (0.31%)). Self-referral of patients to a hospital was also low (n=9 (1.4%)). It was not possible to identify the route to the hospital in 9 patients. The majority of patients were hospitalized within 4 months after notification of the first symptoms (66.9%).

Discussion

Diagnosis of OMF cancer was made at a late stage of the disease in many cases. Residents with a qualification in dentistry, either as a dentist or as a maxillofacial surgeon, were the prevailing subgroup of medical specialists who referred the patient to our institution. In addition to outreach work of public health institutions, *e.g.* to inform about risk factors such as alcohol abuse and smoking as causative factors for oral cancer, continuous medical education during dentistry studies and in further education plays a key role in reducing diagnostic delay and optimizing treatment options in OMF cancer.

The data of this analysis are in accordance with data from earlier reports from other countries.

Shafer (3) reported the results of a study on 779 oral cancer patients of the United States whereby around 15% of patients (n=115) experienced a significant delay in diagnosis due to failure to recognise or suspect a malignant disease by physicians, dentists and patients. These findings have been confirmed by studies from Great Britain (4), the Netherlands (5) and Australia (6, 7). The combination of alcohol abuse and smoking is typical for cancer arising in the upper aerodigestive tract (8).

Several reports address the correlation of evolution time of cancer, as assessed by symptom history and the stage at the time of referral and diagnosis (9-11). Pitiphat *et al.* (9) found the length of delay was significantly associated with advanced stage cancer (and smoking). This association was not confirmed in a study from Brazil (10). McGurk *et al.* (11) also excluded any correlation between delay and stage or survival. In this study, the impact of signs and symptoms on the delay was analysed. Obviously, there is no close correlation between the signs and symptoms and the time of diagnosis.

Dentists and OMF surgeons were the largest groups of specialists that referred patients to the University hospital. Other specialists contributed in particular patients with facial cancer. This result is in accordance with current practice to teach dentistry students the signs and symptoms of oral cancer and to include OMF malignancies in the curriculum of medical students. However, oral cancer awareness in undergraduate medical and dental students remains poor (12), despite tremendous public and professional health care campaigns on oral cancer diagnosis (13), and this supports the call for further educational efforts in both the public and professionals (14, 15).

In a recent prospective study from San Francisco (16) on oral cancer diagnosis, the total time from a patient's first sign or symptoms to commencement of medical treatment was a mean of 205.9 days (range 52 to 786 days) and similar to the results of this study. These authors confirmed that the longest part of the delay was from the onset of symptoms to the initial consultation with a health care professional (mean time: 104.7 days). These authors concluded that public education on the subject and the encouragement of early self-referral of patients to the health care services to be the most adequate tool for improving diagnostics at an early stage, with strong impact on prognosis (17). On the other hand, the socio-economic status and the severity of life events in the patient's delay period have an impact on the time interval between the first signs and symptoms and seeking medical help (18).

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