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Second primary head and neck squamous cell cancers with aggressive behavior in patients with chronic myeloid leukaemia

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Abstract

Patients with chronic myeloid leukaemia (CML) are at considerable risk of developing second primary neoplasms. However, mucosal squamous cell cancers (SCCs) of the head and neck have not been reported. We review the data of 7 patients with mucosal SCC of the head and neck that presented as metachronous second primary tumours in patients with CML. All 7 patients were men (median age 48 years, range 31–67) (site:oral cavity $n=6$, hypopharynx $n=1$). The median interval between diagnosis of CML and head neck cancer was 6 years (range 2–15). Treatment was curative in 4 and palliative in 3. At median follow up of 14 months (range 2–44), 3 patients had died of head and neck cancer, 1 of CML, and 3 were alive and free of disease. Mucosal cancers of the head and neck can occur in long-term survivors of CML. They are aggressive and tend to recur.

Keywords: Chronic myeloid leukaemia; Head neck cancer; Squamous carcinoma; Hydroxyurea; Imatinib; Second primary

Introduction

Chronic myeloid leukaemia (CML) is a myeloproliferative disorder of older adults, which is characterised by an initial, relatively asymptomatic, stable phase, and invariably terminates in acute leukaemia. The risk of developing second primary tumours after treatment of haematological malignancies is well-known, and is seen particularly in long-term survivors treated with chemotherapy, or radiotherapy, or both.

Squamous cell carcinoma (SCC) of the skin has been reported in patients with CML after treatment with hydroxyurea or imatinib.[1,2] More often, SCC of the upper aerodigestive tract has been known to manifest after allogeneic haematopoietic stem cell transplant that follows chronic graft-versus-host disease.[3,4] Mucosal SCC of the head and neck region are extremely rare and we know of no reported cases. Here we report our data about SCC of the head and neck region that developed in patients with CML after treatment with hydroxyurea, or imatinib, or both.

Patients and methods

During a 15-year period (1994–2009) 7 patients were referred to our head and neck services for the evaluation of specific complaints. These included persistent hoarseness of voice

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Table 1
Details of patients, their treatment, and follow up.

	Case no. 1	2	3	4	5	6	7
Age (years)	49	52	41	67	35	46	31
Risk factors	Chewed tobacco; alcohol	None	None	Smoking; alcohol	Chewed tobacco; alcohol	Chewed tobacco; alcohol	Tobacco; alcohol
Site	Tongue (SCC) with calcaneal metastasis (biopsy)	Gingivobuccal sulcus[a]; recurred floor of mouth. Second primary recurred lower alveolus[b]	Tongue	Hypopharynx; oropharynx[a]	Buccal mucosa; neck node recurred after 3 months	Lower alveolus	Lower alveolus
Stage	T2N2cM1	T1N0M0	T4N2cM0	T2M0N0 and T4N0M0	T1N0M0	T4N1M0	T4N0M0
Interval between CML and cancer (years)	2	8	15	3	6	7	6
Intent to treat	Palliative	Curative	Palliative	Curative/palliative	Curative	Curative	Palliative
Treatment	Radiation × 2	Resection/resection + radiation	Radiation + chemotherapy	Radiation/support	Resection resection/radiation	Resection/radiation	Palliation
Follow up (months)	3	44	3	27	11	5	2
Condition at last follow up	Died of disease	Alive disease free	Died of disease	Died of disease	Alive disease free	Alive disease free	Died

[a] After 2 years.
[b] After 1 year.

($n = 1$) and progressive non-healing of oral ulcers ($n = 6$). After further investigation all these patients were diagnosed with SCC of the head and neck. We conducted a retrospective review of their case records, with attention to their personal details, presenting symptoms, clinical findings, radiological findings, histopathological investigations, and duration and details of treatment for CML (Tables 1 and 2). The follow up was calculated from the time between the date of diagnosis of cancer of the head and neck to the last date of follow up.

Results

Table 1 shows the clinical details of the patients. The interval until development of metachronous SCC ranged from 2 to 15 years with a median of 6 years. The site of head and neck cancers were oral cavity ($n = 6$) and hypopharynx ($n = 1$). The subsites in the oral cavity cases were oral tongue ($n = 2$), mandibular molar–premolar alveolar involvement with extension in the floor of mouth ($n = 3$), and buccal mucosa ($n = 1$). The details of the treatment for CML are given in Table 2. Six patients were in the chronic phase of CML while 1 patient had blast crisis at presentation for head neck cancer. The treatment was in the form of either HU or Imatinib, alone or given sequentially. Two patients received either only Imatinib or HU whereas the other patients received HU initially and subsequently started on Imatinib either when they developed second primary or when primary disease was not responding to HU. Duration of the drugs ranged from 2–12 years for HU, while for imatinib it was 1–3 years. The median follow up after detection of head and neck cancer was 14 months (range 2–44 months).

Discussion

To our knowledge this is one of the largest series of SCC of the head and neck in patients previously diagnosed with CML. The most common second primary cancers in patients with haematolymphoid malignancies are cutaneous.[5–7] The reported incidence of secondary solid tumours after primary aggressive treatment of haematological malignancies is only 1.1%.[8] The incidence of second malignancies increases as the duration of follow up increases. In a study of 2150 patients who were treated for haematological malignancies, the cumulative probability of development of solid tumours was 5.6% at 13 years, with a sharp increase after 8 years.[9,10] The incidence of SCC of the head and neck is extremely rare. We know of one report of development of SCC of the tongue during induction for acute myeloid leukaemia, but similar reports in patients with CML are not known.[11]

The mean interval between the diagnosis of the primary haematolymphoid malignancy and the development of a secondary solid tumour is 6.4 years with a range of 5–15 years. Secondary malignancies that develop earlier than these are almost always haematopoietic, with the mean interval after