Metachronous occurrence of Squamous Cell Carcinoma of Hypopharynx in a case of Chronic Myeloid Leukaemia: A Case Report

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Abstract
Chronic Myeloid Leukaemia is a neoplasm originating from malignant transformation of pluripotent hematopoietic stem cells. It occurs in adults and characterised by various phases. CML diagnosed at chronic phase treated with chemotherapy will lead to improved survival and life expectancy. Which in turn increases the chances of second malignancy. Secondary malignancies are most commonly squamous cell carcinoma of skin and aero-digestive tract. The secondary malignancy arising in case of leukaemia is aggressive in nature and has more chances of recurrence. Squamous cell carcinoma of larynx and hypopharynx are rarest. Herein, we report a case of Squamous cell carcinoma of Hypopharynx presented as a secondary malignancy in a primary underlying Chronic Myeloid Leukaemia.

Keywords: Squamous cell carcinoma, Hypopharynx, Chronic Myeloid Leukaemia, Radiation therapy, Secondary malignancy.

Introduction
Chronic Myeloid Leukaemia is a Myeloproliferative neoplasm occurring in older patients, characterised by an initial chronic phase which is a stable phase, which will later end up in accelerated phase and blast crisis if untreated. Effective chemotherapy has led to prolonged survival of patients and increases the risk of secondary malignancies1. Squamous cell carcinoma of skin is most commonly reported as a secondary malignancy, followed by Squamous cell carcinoma of Aero-digestive tract1. Squamous cell carcinoma of Head and Neck is very rarely seen1,2. We have reported a case of 62-year-old Male who is being treated for Chronic Myeloid Leukaemia at our institute, diagnosed with a Squamous cell carcinoma of Hypopharynx as a second primary malignancy after 3 years.

Case Summary
A 62-year-old male patient was diagnosed as a Chronic Myeloid Leukaemia – Chronic phase in 2018 and started on Oral chemotherapy (Imatinib) since then. After 3 years of ongoing treatment he developed a complain of left side neck swelling, hoarseness of voice and dysphagia to solids. On clinical examination, neck swelling was palpable. Ultrasound of bilateral neck region showed 14 x 24 mm node in Left cervical level 4, possibility of metastatic node. USG findings were confirmed by Lymphnode biopsy which showed metastatic squamous cell carcinoma. CECT scan of PNS,
Neck, Thorax was done which showed 28 x 16 mm soft tissue lesion involving Left side of larynx, hypopharynx and cervical Lymph nodes at left level 4 - 17x18 mm and Right level 1b - 19x8 mm. EGD Scopy showed Ulcer proliferative growth at Post cricoid region extending to upper 2 cm of Esophagus from which biopsy was taken which was positive for Squamous cell carcinoma. After ruling out the metastasis, patient is planned for Radiation therapy 30 Gy in 10 fractions, 3 Gy per fraction daily for 2 weeks using antero-posterior parallel opposed fields. Initial Palliative approach was preferred to reduce symptoms. Repeat CECT scan was carried out after 4 weeks of completion of 30 Gy Radiation therapy, which showed reduction in the size of Primary lesion and Lymphnode (mild soft tissue thickening of 9 mm in Left AE fold and Pyriform sinus, 6 x 5 mm node in Left level 4 and 19 x 8 mm node in Right level 1b). Further Radiation therapy was given with conformal IMRT plan at 2 Gy per fraction upto a total equivalent dose of 60 Gy. Thus, after the full curative dose of Radiation therapy, patient has been kept on follow-up. Post radiation therapy patient was asymptomatic and clinically no abnormalities were found.

Discussion
In Chronic Myeloid Leukemia (CML), there is colonal expansion of hematopoietic stem cells involving myeloid, erythroid, megakaryocytic and sometimes lymphoid elements. It is characterised by a specific cyogenetic marker, the Philadelphia chromosome (Ph+), t(9;22). This translocation results in BCR-ABL fusion which has tyrosine kinase activity. Tyrosine kinase inhibitors, most commonly Imatinib is therefore effective in inducing and maintaining long term remission in both Chronic and Accelerated phases of CML. The aggressive chemotherapy prolongs the survival of CML patients which in turn increases the chances of secondary malignancy. The most common second primary cancers in haematological malignancy is cutaneous eg; squamous cell carcinoma of skin. The secondary solid tumors are rare to occur with the incidence of 1.1%. Squamous cell carcinoma of Head and Neck as a second primary malignancy in a case of hemato-lymphoid malignancy is extremely rare. Mucosal cancers of Head and Neck occurring in long term survivors of CML are aggressive, tends to recur and have poor prognosis. The exact cause and mechanism of head and neck squamous cell cancers in these cases remains unknown. But according to various studies, there are certain risk factors has been identified such as; genetic defect, mutations in tumour suppressor gene p53, chemotherapeutic agents, smoking and bone marrow remission causing decreased activity of Natural Killer cells (NK cells). Immune deficiency caused by leukaemia itself or chemotherapeutic agents can lead to secondary malignancies.

Management of this second primary squamous cell carcinoma Hypopharynx in patients with CML is concurrent chemo-radiation. The intent of treatment should be decided according to the stage of disease and symptoms related to the disease. In this case, due to aggressive nature of carcinoma Hypopharynx extending to Larynx, Palliative treatment with Radiation therapy was considered during the departmental discussion for palliation of symptoms followed by Additional Radiation to reach the total equivalent dose upto 60 Gy if there is response to initial therapy. The patients of CML should continue the treatment of underlying primary malignancy–leukaemia. Commonly used chemotherapeutic agents in Chronic Myeloid Leukemia are ABL Tyrosine Kinase Inhibitors (TKIs). Among TKIs, Imatinib is the commonest used agent nowadays as it is a relatively well tolerated oral medication with therapeutic efficacy in both chronic and accelerated phases of CML. Second generation TKIs like Dasatinib and Nilotinib can be used in patients who have developed resistance to Imatinib.

Conclusion
The reported second primary squamous cell carcinoma of Hypopharynx in a case of Chronic
Myeloid Leukaemia was treated with Radiation therapy and the best possible outcome is achieved. The patient has been kept on stringent follow-up.

Declaration of Patient Consent
Authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal.

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Conflicts of Interest
There are no conflicts of interest.

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