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Collision tumor of metastatic carcinoma and lymphoma in the bone marrow: Report of an extremely rare and interesting case and review of the literature

Jayasudha Arundhathi Vasudevan, Rekha A Nair, Sindhu Nair P, Nileena Nayak, Sumod Mathew Koshy[1]

From, the Division of Pathology, Regional Cancer Centre, and [1]Division of Imageology, Regional Cancer Centre, Thiruvananthapuram, Kerala, India

Correspondence to: Dr Rekha A Nair, Division of Pathology, Regional Cancer Centre, Thiruvananthapuram, Kerala, India. Email: drrekhanair@gmail.com

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ABSTRACT

Collision tumors are composed of two or more histologically distinct tumor components occurring at the same anatomic location. Collision tumors composed of metastatic carcinoma and lymphoma in the bone marrow is an extremely rare occurrence which is not yet reported in literature. We are reporting a case of 61 year old male patient diagnosed as grey zone lymphoma in the oral cavity (B cell lymphoma unclassifiable with features intermediate between DLBCL and Burkitt lymphoma) and bone marrow showing collision tumor composed of metastatic carcinoma and lymphoma.

Keywords: carcinoma, lymphoma, collision tumor, grey zone lymphoma.

Collision tumor composed of carcinoma and lymphoma in the bone marrow is an extremely rare occurrence. Composite tumors are defined as tumours in which there are two different intermixed histologic types whereas collision tumors are defined as multiple synchronous tumours that are histologically distinct and in juxtaposition to one another without intermingling of tumours [1,2]. The close proximity of the two malignancies presents definite serious diagnostic and therapeutic challenges.

Synchronous occurrence of carcinoma and lymphoma in the bone marrow is not yet reported in the literature; although, there are case reports in other organs [1,2]. Immunosuppression may play a role. Further research is needed for the proper understanding of this rare association.

CASE REPORT

A 61 year old male presented with swelling in the oral cavity of two months duration which was rapidly increasing in size. On examination, there was a large fungating mass arising from hard palate with ulceration and palpable lymphnodes in the left cervical, left axillary, and bilateral inguinal region. Other systems were within normal limits. Routine blood investigations revealed normal blood counts, ESR of 105 mm in the first hour and normal LDH levels. CT neck showed a large enhancing mass lesion measuring 65x55 mm involving upper lip and upper alveolus with underlying bone destruction and cervical, right axillary and mediastinal lymphadenopathy (**Figure 1**). Suspicious pulmonary lesion measuring 15x25 mm was present in the left oblique fissure with mild

pleural effusion. Ill defined lytic area noted in bilateral posterior iliac bone and L4 vertebra.

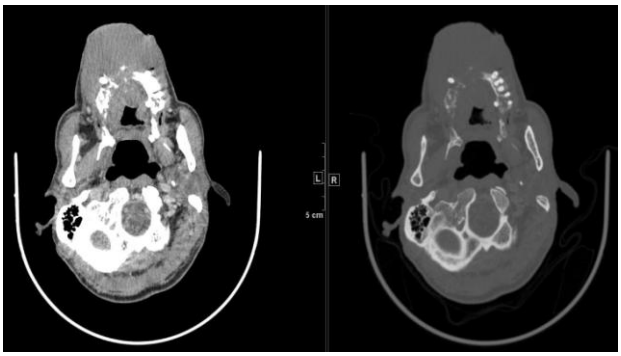

Figure 1 - Large enhancing soft tissue mass involving upper lip and upper alveolus at midline, the lesion is showing destruction of the upper alveolus, hard palate and nasal septum, superiorly the lesion is extending to the floor of the nasal cavity and inferiorly the lesion is projecting into the oral cavity, posteriorly the lesion is extending up to the anterior half of hard palate.

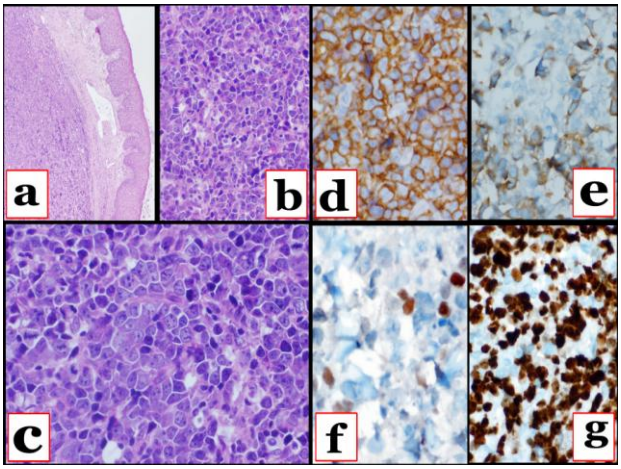

Figure 2 – a) Tissue lined by squamous epithelium and showing submucosal sheets of atypical lymphoid cells. (H&E, x40) b) Atypical lymphoid cells arranged diffusely, (H&E, x200) c) Tumor cells are medium sized to large with scanty cytoplasm and round to oval nucleus with multiple nucleoli, (H&E, x400) d) Tumor cells are CD 20 positive (IHC, x400) e) BCL 2 positive (IHC, x400) f) BCL6 positive (IHC, x400) g) MIB1 labeling index of around 100% (IHC, x400).

Incision biopsy of palatal mass revealed tissue lined by squamous epithelium with subepithelium showing a neoplasm composed of diffusely arranged cells which were medium to large sized with scanty cytoplasm and round to oval nucleus with multiple distinct nucleoli. Frequent mitotic figures and abundant cellular debris were also present. Immunohistochemistry revealed tumor cells to be positive for CD 20, LCA and BCL2 with focal positivity for BCL6. MIB1 labelling index was around 100%. The diagnosis of B cell lymphoma, unclassifiable with features intermediate between DLBCL and Burkitt lymphoma was given (**Figure2**).

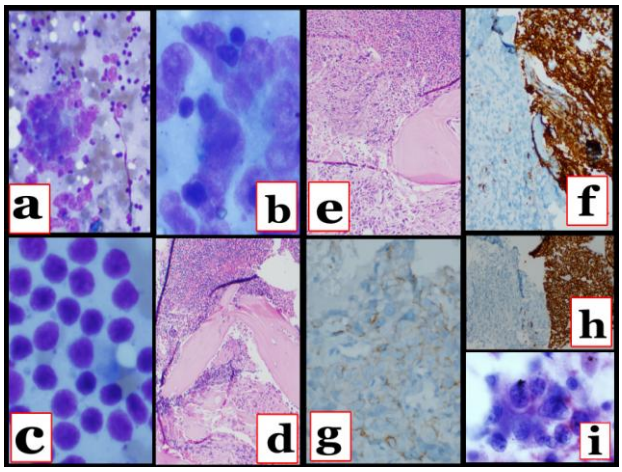

Figure 3 – a) Bone marrow imprint smears showing large atypical cells in clusters admixed with small lymphoid cells. (H&E, x400) b) Large atypical cells in clusters and vague glandular pattern admixed with small lymphoid cells (H&E, x1000) c) Small lymphoid cells (H&E, x1000) d & e) Bone marrow biopsy showing two histologically distinct tumor types with upper half showing the densely packed tumor cells and lower half showing tumor cells in a desmoplastic stroma (H&E, x100) f) LCA positive tumor cells (IHC, x200) g) Cytokeratin positive tumor cells in the desmoplastic stroma (IHC, x400) h) LCA positive tumor cells were also CD20 positive (IHC, x200) i) FNAC from the lung mass shows atypical large cells in glandular pattern, (Giemsa, x1000).

Bone marrow studies as a part of the staging work up revealed cellular imprint smears with clusters of large atypical cells with abundant cytoplasm and round to oval nucleus and focal sheets of small lymphoid cells. Bone marrow biopsy also showed the two populations of cells. Morphologically, it was presumed to be the large and small cell components of lymphoma. Immuno-histochemistry done on bone marrow biopsy showed the positivity of the large cells for cytokeratin and the small cells for CD 45, CD 20 (**Figure 3**) and negative for CD 5, BCL6, cyclin D1 and CD 23. Thus diagnosis of collision tumor composed of small B cell lymphoma and metastatic

poorly differentiated carcinoma was given CT guided FNAC of the lung showed cellular smears showing clusters of malignant cells in a necrotic background suggestive of non small cell lung carcinoma.

After discussing the treatment options and prognosis with the patient, he was planned on R- CHOP chemotherapy regimen for six cycles, but the patient did not opt for treatment and was lost to follow-up.

DISCUSSION

The synchronous occurrence of multiple malignancies in the same patient is a rare event. Synchronous carcinoma and lymphoma in the bone marrow is not yet described. Multiple malignancies presenting in the same patient within six months of diagnosis is referred as synchronous tumors. Lymphoproliferative disorders occur as a result of immune dysfunction and are often associated with epithelial malignancies. Interaction between immune system and development of carcinoma has been documented [3]. Collission tumors are reported in patients with colorectal cancer, non small cell lung cancer, gastric and breast cancer.

Several theories are proposed for the development of collision tumor including accidental colliding of two independently developed neoplasms, common carcinogen theory suggesting a single carcinogen responsible for the development of two colliding neoplasms, tumor to tumor carcinogenesis theory indicating that one tumor induces the development of a second primary tumour [4-6]. Common molecular pathways may be involved in the development of multiple tumors. Studies have shown that due to reduced immunological surveillance caused by lymphoma, patients are also predisposed to the development of adenocarcinoma [7]. Collision tumors of myeloma and prostate cancer and also myeloma and merkel cell carcinoma have been described [8,9]].

Some studies have pointed out that bone marrow microenvironment may play a crucial role. Microenvironment of myeloma and prostate cancer has shown the important similarities. Both depend on similar growth factors and similar chemoattractants for the metastasis to bone marrow. Merkel cell carcinoma is associated with secondary immunodeficiency affecting B and T cell function. Factors contributing to the multiple primary tumors may be environmental, genetic or immune system dysfunction. One of the primary tumor may cause cytokine dysregulation or reduced immune surveillance; thus, contributing for localized development of another malignancy.

Considering the rarity of occurrence of collision tumor, it is possible that they are just an accidental occurrence. Collision tumors are also difficult to diagnose as the lymphoid cells may be mistaken for reactive infiltrate. In our case, there was discordant infiltrate of lymphoma in the bone marrow. Discordant infiltrates may be clonally related or unrelated clonally distinct B cell neoplasms [10]. Due to the rare occurrence, there are no specific recommendations for the therapy. Some recommend treatment depending on the dominant tumour, but those treatment options appear to exacerbate the other tumour. Our patient did not take any treatment and was lost to follow up.

CONCLUSION

The synchronous occurrence of carcinoma and lymphoma in the bone marrow is an interesting rare occurrence and is also a diagnostic challenge. High index of suspicion is needed as the lymphomatous process may be judged as a reactive process secondary to epithelial malignancies. Association between immune system and development of malignancy can explain the pathogenesis of collision tumor. Further genetic studies are necessary to prove a common molecular pathway between these two cancers. Future studies may provide more information concerning the treatment approaches and prognosis of these patients.

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