Synchronous Diagnosis of Angioimmunoblastic T-Cell Lymphoma and Lung Neuroendocrine Cancer in a Patient

Sir,

The synchronous occurrence of lymphoma and other tumours is extremely rare. In non-Hodgkin lymphoma patients, the incidence of synchronous solid tumours is approximately 0.8%.[1] Angio-immunoblastic T-cell lymphoma (AITL) and synchronous solid tumours are even rarer.[1] This study reports an extremely rare case of synchronous AITL and lung neuroendocrine cancer.

A 63-year-old male patient with bilateral submandibular, cervical, infraclavicular, axillary, supraclavicular, and inguinal lymphadenopathy and enlarged tonsils of Grade I was admitted on 8 April, 2020. Upon admission, pathological diagnosis from a left cervical lymph node excision biopsy was AITL with IgH rearrangement. Immunohistochemistry (IHC) showed LCA+, CD3+, CD20-, CD5+, CD10+ (few), bcl-6+ (partial), PD1+, CXCL13+ (partial), CD4+ (majority), background cells CD8+ (few), CD30+ (partial), PAX-5-, CD15-, MUM-1+ (partial), CD21 indicating follicular dendritic cell meshwork, Ki-67+ (40-50%), and occasional EBER1/2+ signals. Lymph node gene rearrangement identified IgH clonality without immunoglobulin (Ig^k) or TCRG amplification. Kristen rat sarcoma virus (KRAS) gene mutation was positive, however, RHOA G17V mutation was negative. Bone marrow aspirate and serum immunofixation electrophoresis were normal. Flow cytometry detected 0.2% clonal plasma cells. Whole-body-enhanced CT scan revealed enlarged lymph nodes in bilateral submandibular, cervical, infraclavicular, axillary, mediastinal, pulmonary hilum, inguinal, retroperitoneal, and diaphragmatic regions. No lung masses were observed. The patient was diagnosed as AITL and initiated on chemotherapy with cyclophosphamide, liposomal doxorubicin, vincristine, prednisone (CDOP) plus azacitidine, and chidamide. After six cycles, a follow-up CT on November 4, 2020, revealed a rounded mass (3.7×3.4 cm) in the right-upper lobe pleura, with heterogeneous enhancement, and enlarged lymph nodes in the right pulmonary hilum, mediastinum, and bilateral axilla. Enlarged lymph nodes were reduced in size in bilateral submandibular, cervical, and inguinal regions. CT-guided biopsy of the right lung mass confirmed small cell carcinoma, with IHC being positive for CK, TTF-1, Synaptophysin, CD56, and Ki-67 (60%), and negative for LCA, NapsinA, Chromogranin A, P40, P63, and Rb1 (sporadic cells+). The pathological diagnosis was small cell neuroendocrine carcinoma. The final diagnosis was synchronous primary AITL and lung neuroendocrine cancer. Due to recurrent bacterial, fungal, and COVID-19 pneumonia infections, the patient underwent 2 cycles of chemotherapy with etoposide and chidamide. Follow-up CT on 17 April 2021, revealed slight enlargement of the right-upper lobe pleural mass (4.3×3.4 cm). Radiotherapy was administered to the lung tumour site and positive lymph nodes on 24 June 2021. Follow-up CT on 5 August 2021, showed increased size of the right-upper lobe pleural mass (4.8×3.4 cm), increased extent of ground-glass opacities and consolidations in the right-upper and lower lobes, and enlarged lymph nodes in the right pulmonary hilum and mediastinum. The remaining lymph nodes showed no change in size. Further radiation therapy and chemotherapy were hindered by infection, and the patient remains alive at present.

Although rare, with the increasing use of multi-slice CT, PET/CT, PET/MRI, and endoscopy in lymphoma patients, the incidence of second primary malignant tumours (SPMTs) in lymphoma patients is gradually rising.[2] Pulmonary involvement by AITL is relatively rare.[3] In this case, after six cycles of treatment with CDOP plus azacitidine and chidamide, a newly developed lung mass and was diagnosed as primary lung small cell neuroendocrine carcinoma. Therefore, for rare sites of involvement by AITL (such as lungs, gastrointestinal tract, and nervous system), repeated screening for SPMTs is necessary. Optimal treatment strategies for patients with lymphoma and SPMTs remain challenging.[2] Typically, the treatment is directed towards the more aggressive malignancy.[2,4] In this case, despite initial reduction in lymph nodes with CDOP plus azacitidine and chidamide, the newly developed right lung mass progressed. Due to the patient's recurrent multiple infections, surgical resection of the lung neuroendocrine neoplasm or standard chemotherapy (such as etoposide plus cisplatin etc.) was not feasible, and a less aggressive approach with etoposide plus chidamide and localised radiotherapy to the lung neuroendocrine cancer and localised lymph nodes was chosen.[5] Unfortunately, the lung neuroendocrine cancer mass in this patient continued to grow, but the patient has survived for over 4 years, indicating no difference in survival rates between lymphoma with SPMTs and without SPMTs.

In conclusion, the authors report an extremely rare case of synchronous primary AITL and lung neuroendocrine cancer. When encountering rare sites of involvement by AITL (such as lungs, gastrointestinal tract, and nervous system), repeated screening for SPMTs is essential.

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