Primary lymphoepithelioma-like carcinoma of the lung

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Primary lymphoepithelioma-like carcinoma (LELC) of the lung is a neoplasm seen most commonly in the nasopharynx of individuals from south China and Taiwan, and is strongly associated with the Epstein-Barr virus. The case of a 62-year-old Chinese man with a rare primary lung T2N1M0 LELC of the left lower lobe is presented. The lesion was further notable because of the presence of necrotizing granulomatous inflammation. The patient was treated with surgical resection. After it was determined that the neoplasm was of primary lung origin, adjunctive chemotherapy was initiated. The role of adjunctive chemotherapy in this setting is discussed.

Key Words: *Epstein-Barr virus; Lung neoplasm; Lymphoepithelioma; Non-small cell carcinoma*

Carcinome pulmonaire primaire ressemblant à un lymphoépithéliome

RÉSUMÉ : Le carcinome pulmonaire primaire ressemblant à un lymphoépithéliome (LELC) est une tumeur observée le plus fréquemment dans le nasopharynx de personnes originaires du sud de la Chine ou de Taïwan et il est fortement associé au virus Epstein-Barr. Le cas d'un Chinois âgé de 62 ans souffrant d'un tel cancer T2N1M0 rare au lobe inférieur gauche est présenté ici. La lésion était en outre notable en raison d'une inflammation granulomateuse nécrosante. Le patient a été traité par résection chirurgicale. Après qu'il fut établi que la tumeur était d'origine pulmonaire primaire, une chimiothérapie d'appoint fut prescrite. Le rôle de la chimiothérapie d'appoint dans ce cadre est discuté.

Primary lymphoepithelioma-like carcinoma (LELC) of the lung is a neoplasm seen most commonly in the nasopharynx of individuals from south China and Taiwan. It is strongly associated with the Epstein-Barr virus (EBV) (1,2), and is rarely seen as a primary lung lesion (2-6). The treatment for primary lung LELC is multimodal and based on the treatment experience with LELC of the nasopharynx (7).

CASE PRESENTATION

A 62-year-old male smoker who recently emigrated from China to the United States presented with a three-month history of dry cough, patellar arthralgia and recent weight loss. A standard chest radiograph and a computed tomography scan (Figure 1) revealed a large mass on the medial aspect of the lower lobe with no associated lymphadenopathy. The

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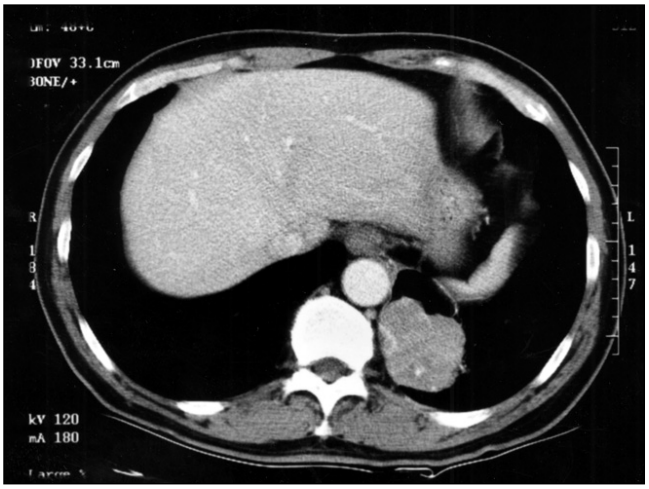

Figure 1) *Computed tomography scan revealing a large mass on the medial aspect of the left lower lobe*

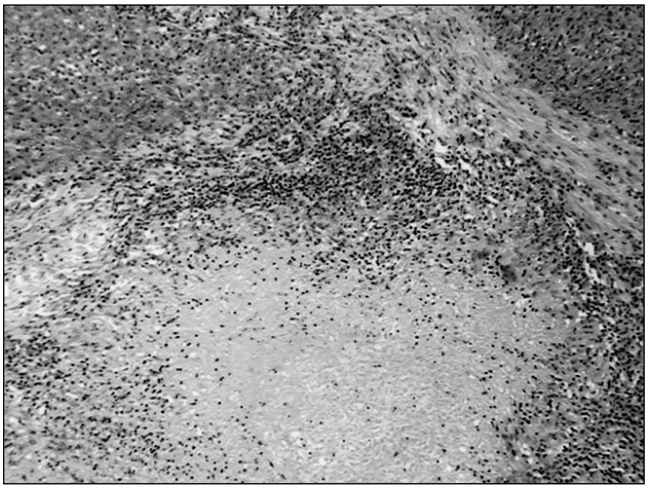

Figure 3) *Histological examination showing necrotizing granuloma. (hematoxylin and eosin stain, original magnification ×40)*

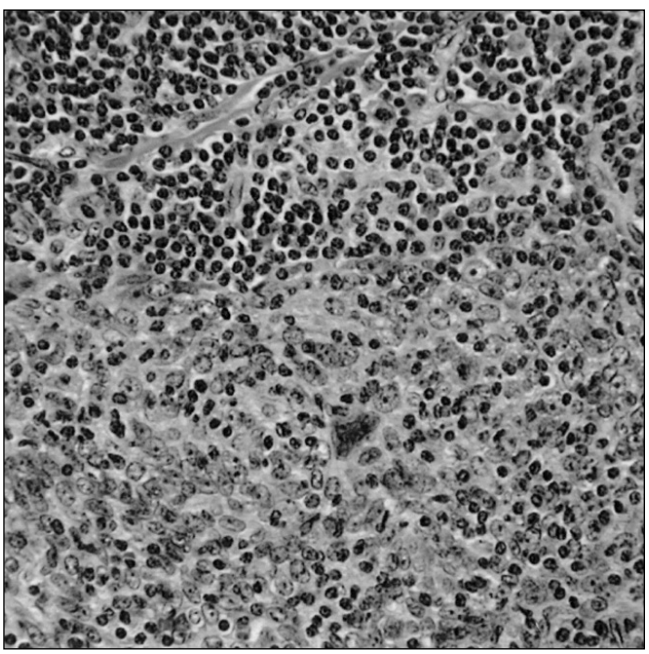

Figure 2) *Histological examination of a frozen section specimen revealing islands of epithelial cells surrounded by lymphocytes (hematoxylin and eosin stain, original magnification ×400)*

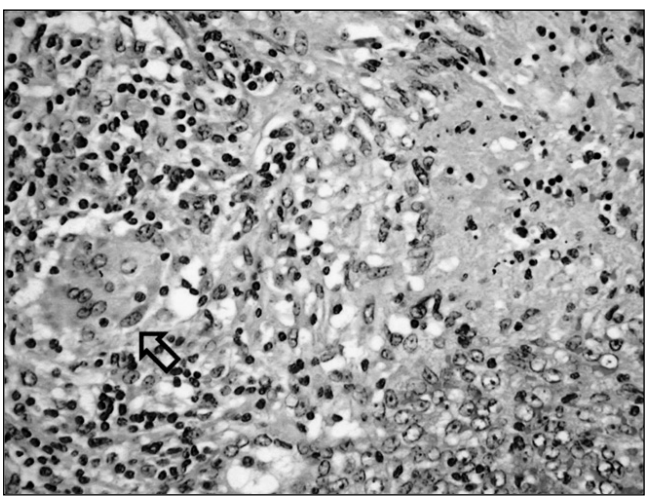

Figure 4) *Histological examination showing necrotizing granulomas (hematoxylin and eosin stain, original magnification ×100). Giant cell indicated by arrow*

patient underwent bronchoscopy and cervical mediastinascopy, which were negative. A left thoracotomy was then performed, and a frozen section of the lesion was sent for evaluation. On gross inspection, the mass was covered in pleura and was approximately 1 cm from the nearest bronchus. The lesion itself appeared to have an inflammatory component with local adhesions to the pericardium. The tumour itself was 6.0×5.5×4.0 cm in dimension. As a result of the frozen section pathology, a left lower lobectomy with systemic sampling of multiple lymph nodes was performed.

A histopathological examination of the tumour revealed features consistent with those described for LELC (2,3,8-11). Morphologically, the tumour was composed of nests and cords of undifferentiated neoplastic cells showing large nuclei and a vesicular chromatin pattern, completely invested by dense lymphocytic infiltrates (Figure 2). Plasma cells were also noted. Tumour cells showed no evidence of keratinization or glandular formation. Notably, the tumour showed numerous interspersed necrotizing granulomas, a feature that has not, to our knowledge, been previously described for LELC (Figures 3 and 4). Areas of necrotizing granulomatous inflammation were also noted in the parabronchial lymph nodes. The presence of granulomatous inflammation warranted examination for mycobacteria and fungi; however, acid-fast and methenamine silver stains were negative for microorganisms. The presence of EBV in the tumour cells was shown by their uniform reactivity on in situ hybridization of the deparaffinized sections to a complementary DNA probe to the EBER1 messenger RNA of EBV.

Further microscopic examination of the resection specimen revealed focal tumour infiltration within the visceral pleura elastica. The bronchial margin was free of tumour, and no angiolymphatic space invasion was identified within the pulmonary parenchyma. Two of the 20 submitted parabronchial lymph nodes showed metastatic tumour (N1 nodes); however, mediastinal nodes in stations 4R and 7 were free of metastatic disease.

On the basis of these findings, the patient underwent pharyngeal endoscopy and magnetic resonance imaging, which did not identify any pharyngeal lesions. Due to the presence of necrotizing granulomatous inflammation, the patient had a purified protein derivative skin reactivity test, which was negative. The patient then received five cycles of chemotherapy that included carboplatin area under the curve of 6 and paxlitaxel 175 mg/m^2. At five months follow-up, the patient was doing well, and a standard chest radiograph revealed no evidence of recurrent disease.

DISCUSSION

LELC of the nasopharynx is well documented in the literature, and is strongly associated with EBV and individuals from south China and Taiwan (2). The approach to managing primary lung LELC has only recently been documented and is based on the treatment experience with nasopharyngeal LELC (7). Nasopharyngeal LELC is typically treated with a multimodal approach including radiation therapy and adjunctive chemotherapy (12,13). In the case of primary lung LELC, the diagnosis is most often made after resection; therefore, radiation therapy is not warranted. It is important to rule out a primary nasopharyngeal lesion (14). In the past, adjunctive chemotherapy has involved cisplatin and 5-fluorouracil (2,7). Recently, Yeo and colleagues (15) documented the use of carboplatin area under the curve of 6 and paxlitaxel 135 mg/m^2 in a study involving 27 patients with nasopharyngeal carcinoma. The regimen had a response rate of 59%, with a total resolution of 11%. The side effects, based on 122 cycles, were grade 3 to 4 neutropenia (39%), grade 3 to 4 anemia (7%) and grade 3 to 4 thrombocytopenia (7%), with three episodes of neutropenic fever (15). This regimen has a more tolerable toxicity than the cisplatin and 5-fluorouracil regimen used in most cases of primary lung LELC. It is not clear to us what the etiology of the necrotizing granulomatous reaction associated with this tumour was; however, it might have been a vigorous immune response.

CONCLUSIONS

Primary lung LELC is an unusual lesion. It is important to rule out a primary nasopharyngeal tumour. On the basis of experience with nasopharyngeal LELC, adjunctive chemotherapy is warranted.

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