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RESEARCH ARTICLE

A LARGE CELL NEUROENDOCRINE CANCER OF LUNG: A DIAGNOSTIC DILEMMA

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ABSTRACT

Large Cell Neuroendocrine Carcinoma (LCNEC) is a comparatively rarecarcinoma of lung with a poor prognosis. They are aggressive tumours and areincluded in the group of non-small cell carcinoma. Though aggressive in nature they respond to treatment more or less similar to small cell carcinomas of lung. We here report a case of 75year old man who presented with diffuse metastasis mainly to thoracic and lumbar spine, brain and liver.The primary was laterdiagnosed as LCNEC of lung through Computer Comography and cytological analysis.

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INTRODUCTION

LCNEC are rare and aggressive carcinomas of lung with a very poor prognosis accounting for approximately 1.6-3% of all lung cancer (Travis *et al*., 1991). The approximate life expectancy of patient with LCNEC and metastasis is around 6 months. They usually present as lung mass more frequently in the peripheral lung fields with less prominent respiratory complaints. Diagnosis of LCNEC usually require histological and cytological analysis. The neuroendocrine nature of the cancer can be diagnosed by the help of immunohistochemicalmarkers like CD56, chromogranin and synaptophysin (Rossi *et al*., 2004). The treatment regimen of LCNEC is almost similar to that of small cell carcinomas.

Case presentation

A 75 year old male admitted in our department with low back pain andconfusion since 1 month, he also had a weight loss of 6kg with in 2 month. Past history was relevant with chronic tobacco smoking and alcohol intake. NCCT of brain(Figure 1) and thoraco lumbar spine showed features highly suggestive of metastasis. Follow up chest x-ray (Figure 2) revealed rightperihilar opacityandsubsequent Contrast Enhanced CT (Figure 3) showed 5cm sizedperihilar soft tissue mass with surrounding collapse. Abdominal screening showed multiple hypo denselesion in liver associated with abdominal lymphadenopathy suggestive of metastasis. Bronchoscopic guided biopsy have been done and the histology of the lung mass (Figure 4) showed large tumour cells arranged in organised nests withprominent nucleoli, follow up immunohistochemistryrevealed cells staining positive for cytokeratin-7, chromogranin but negative for thyroid transcription factor 1[TTF-1] that is consistent with high grade large cell neuroendocrine carcinoma. Finally patient is diagnosed to be having extensive [stage 4] LCNCE with poor prognosis. He received chemotherapy with carboplatin & paclitaxel every 28 days followed by focal irradiation to brain and spine.

DISCUSSION

Large cell neuroendocrine carcinoma [LCNEC] is one of the rare primary lung tumors accountingfor 1.6- 3% (Travis *et al*., 1991). Usually presenting as a peripheral lung leision (Garcia-Yuste *et al*., 2000) centrally located primary pulmonary lesions as in our case is relatively rare. According to Paci *et al*. only 1 out of 48 LCNEC was found to originate from a central location (Paci *et al*., 2004). Large cell neuroendocrine carcinoma (LCNEC) is definedas "a large cellcarcinoma showing histological features suchas organoid nesting, trabecular, rosette-like and palisadingpatterns that suggest neuroendocrine differentiation (Sun *et al*., 2009) and in which the latter can be confirmed by immunohistochemistryor electron microscopy Nucleoli are frequent and often prominent.

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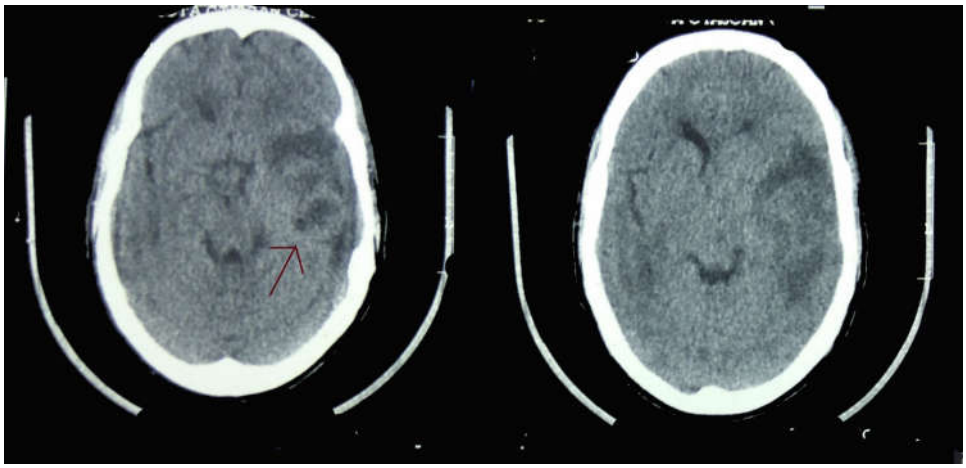

Figure 1. NCCT of brain showing multiple ill-defined hypodense intra cranial SOL with surrounding hyperdense rim highly suggestive of metastasis

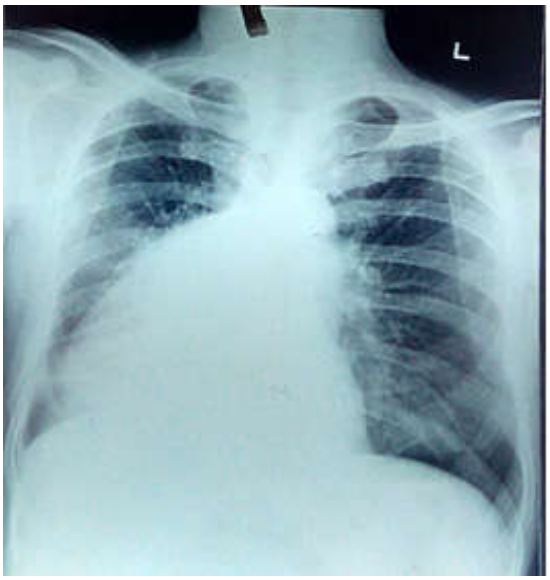

Figure 2. Chest x-ray revealed right perihilar opacity andsubsequent CTshowed 5cm sized perihilar soft tissue mass with surrounding collapse

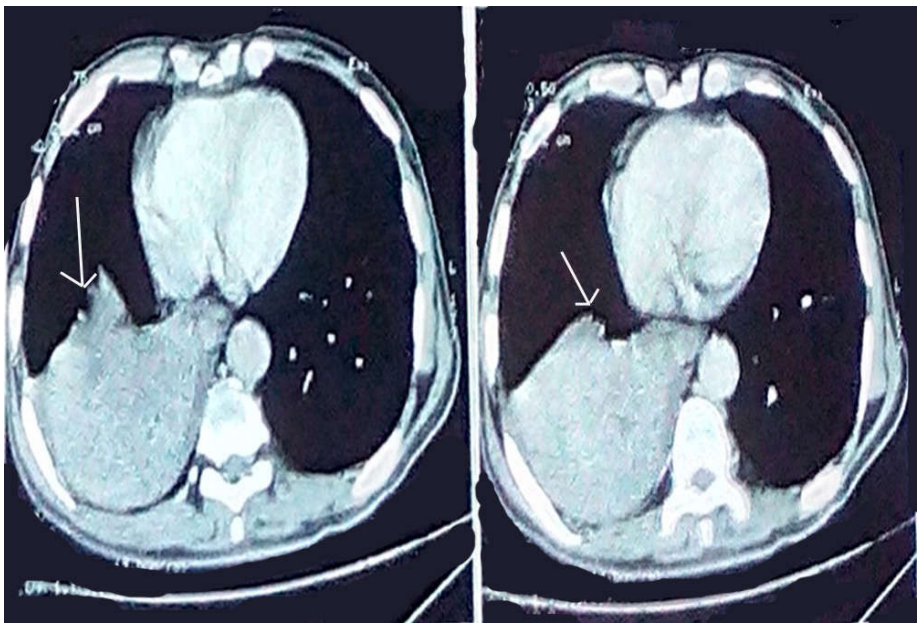

Figure 3. CT of chest with contrast in mediastinal view displaying 5 cm right perihilar soft tissue mass with surrounding collapse

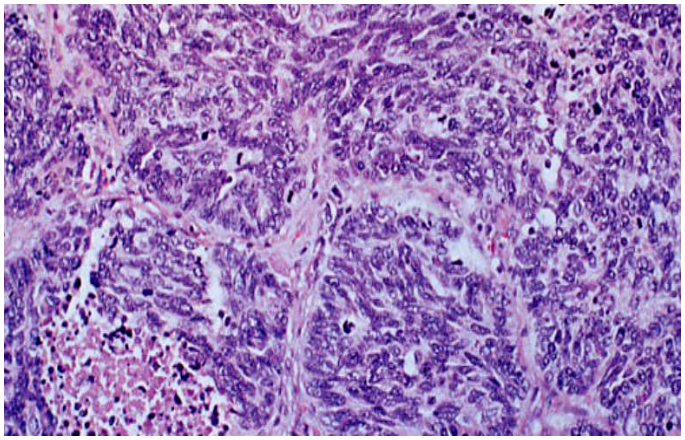

Figure 4. Histology of the lung mass showed large tumour cells arranged in organised nests withprominent nucleoli

The presence of nucleoli tends tobe a critical feature in theseparation from small cell carcinoma (Travis *et al*., 1991) neuroendocrine differentiationmust be demonstrated by ancillary techniques such asimmunohistochemistry. One of immunohistochemical marker should be positive amongchromogranin, synaptophysin, CD56 for confirming neuroendocrine origin (Rossi *et al*., 2004). In our case chromogranin was positive and TTF-1 was negative indicating poordifferentiation (Nakamura *et al*., 2002) Overall, prognosis of the present patient diagnosed as stage 4 LCNEC with distant metastasis was poor and having a life expectancy of only around 6 month. According to Travis *et al*. and Garcia-yuste *et al* overall 5 year survival rate for LCNEC are 27% and 21% respectively, irrespective of staging (Travis *et al*., 1991; Rossi *et al*., 2004).

However stage 4 LCNEC have a 5 year reported survival rate of 0% (Nakamura *et al*., 2002). Prognosis and treatment response to cisplatin –based chemotherapy are almost similar to that of small cell carcinoma (Gazdar *et al*., 1992; Graziano *et al*., 1989). Initially they will respond to chemotherapy but relapse are common with resistant to available regimen (Yamazaki *et al*., 2005).

Conclusion

LCNEC is a rare and aggressive neoplasm of lung with poor prognosis. This case was an atypical presentation of LCNEC diagnosed eventually with the aid of immunohistochemistry, which showed chromogranin and TTF-1 positivity confirming poorly differentiated LCNEC. Current treatment with chemotherapy and radiotherapy do not showing survival benefit in stage 4 LCNEC. This rare presentation on LCNEC reveals difficulties in early diagnosis, management and its poor outcome thus necessitating more advanced management option.

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