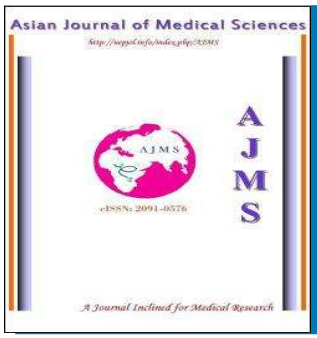

LARGE CELL NUEROENDOCRINE CARCINOMA OF LUNG METASTASIZING TO JEJUNUM- A RARE PRESENTATION WITH REVIEW OF LITERATURE

CASE REPORT & REVIEW OF LITERATURE, Vol-4 No.2

Asian Journal of Medical Science, Volume-4(2013) http://nepjol.info/index.php/AJMS

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ABSTRACT

Large cell neuroendocrine carcinoma of lung is not one of the commoner varieties of neoplasia found in the lungs. There are around 100 cases in literature which suggest the metastasis of various kinds of lung carcinomas to gastro intestinal tract (GIT). Metastasis of large cell neuroendocrine carcinoma to small bowel is rare. This is a rare case in which the primary neuroendocrine carcinoma of lung presented with metastasis and perforation of small bowel.

Key words: Large cell neuroendocrine carcinoma, metastasis, small bowel

"Small bowel large-cell neuroendocrine carcinomas are rare and aggressive tumors. Most are metastatic at presentation and primary in the lung be looked for. In such advanced cases, we must often rely on immunohistochemical markers in order to reach to a final diagnosis"

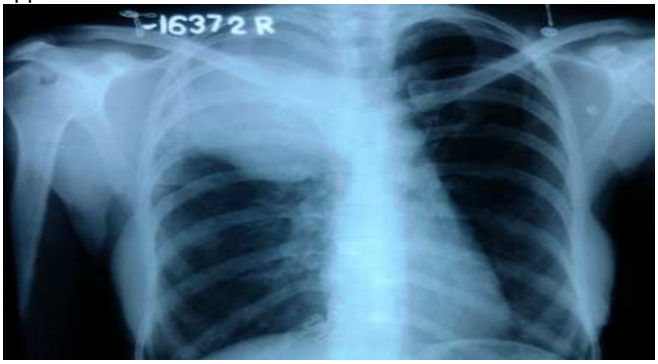
INTRODUCTION

LCNEC is an aggressive neuroendocrine tumor of lung with potential for early metastasis.Small bowel metastasis of LCNEC of lung is very rare. The immunohistochemical properties of the tumor help in characterization and also give the idea of the prognosis. Because of its aggressive clinical behavior and poor prognosis, large cell neuroendocrine carcinoma should be recognized as one of the poorest prognostic subgroups among primary lung cancers.

CASE STUDY

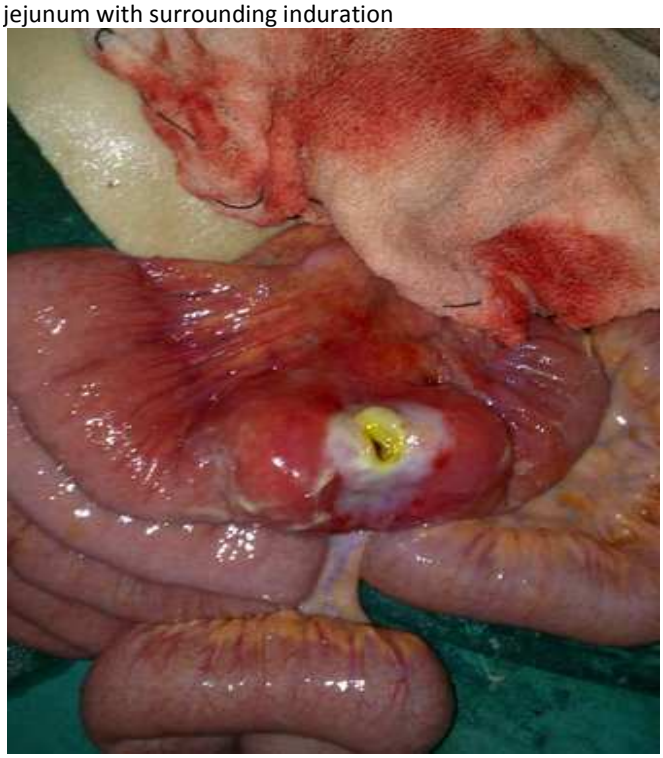
A 35 years old lady presented in surgical emergency with complaints of fever for 5 days, pain abdomen which was more in lower abdomen and colicky in nature for the last 3 days, non passage of flatus and feces for 2 days. There was no history of vomiting. There was no other significant past history suggestive of any co-morbidity. On general physical examination tachycardia and pallor was present. On systemic examination the air entry was reduced in right upper zone. Her abdomen was distended with tenderness and guarding present. Bowel sounds were absent. Blood and serum investigations showed raised urea, and normal electrolyte levels. The other routine investigations were unremarkable. Abdominal X-ray in erect posture showed multiple air fluid levels in small bowel, and no free gas under diaphragm. The chest X-ray showed a large radio opaque shadow over the right upper zone (Fig 1).

Fig.1 Chest X Ray (PA) View showing opacity in right lung upper zone



USG abdomen showed the dilated bowel loops with minimal free fluid in pelvis. On accumulating the clinical, laboratory and radiological findings diagnosis of acute intestinal obstruction was made and patient was planned for immediate exploratory laparotomy. Laparotomy findings revealed entangled loops of small bowel in left lumbar region. After the adhesiolysis of the entangled small bowel loop, there was 1cmx 1cm perforation over the ante mesenteric border of jejunum which was one and half feet distal to duodenojejunal junction, the area around the perforation was indurated with minimal pus in peritoneal cavity (Fig.2).

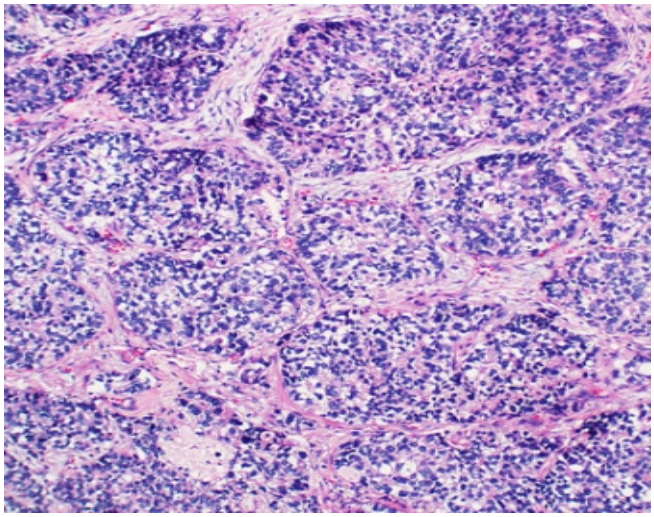
Fig.2 Intraoperative photograph showing perforation in jejunum with surrounding induration



The mesenteric lymph nodes were also enlarged. The resection of perforated segment of jejunum with 10 cm margin on either side of perforation, with end to end hand sewn anastomosis was done. The biopsy of the enlarged mesenteric lymph node was also taken. The post operative recovery of the patient was unremarkable. The gross finding of the resected jejunum showed an ulceroproliferative

growth of size 4cm x 5cm x 2cm around the perforation site. The histopathological examination of the ulceroproliferative growth was suggestive of large cell neuroendocrine carcinoma (LCNEC), which was reaching upto serosa (Fig: 3).

Fig.3 Large-cell neuroendocrine carcinoma displaying tumor cells with large and polygonal nuclei with vesicular chromatin and prominent nucleoli.



Both ends of the resected specimen of jejunum were free of tumor. The excised mesenteric lymph node was also negative for malignancy. The immunohistochemistry of the tumor was also performed which turned out positive for the neuron specific enolase (NSE), keratin, chromogranin and synaptophysin. Later on, on the post operative day 8, CECT scan of chest was done to know about the radio opaque shadow which was seen in chest x-ray, which showed a large heterogenous mass right upper lobe and hilum invading right bronchus and right upper lobe bronchus with mediastinal necrotic lymph nodes and superior vena cava thrombus. Fine needle aspiration (FNA) cytology from the chest lesion was positive for neuron specific enolase, keratin and Leu-7. The patient was then referred for chemotherapy.

DISCUSSION

The lung carcinomas are well known to metastasize to GIT. They usually present with perforation of GIT. In a study it has been reported that perforations occur most often in the jejunum (53%) followed by ileum (28%)[1]. There are various kinds of lung cancers which have been reported to metastasize to small bowel. Small bowel perforations were most often caused by adenocarcinoma (23.7%), squamous cell carcinoma (22.7%), large cell carcinoma (20.6%), and small cell carcinoma (19.6%). According to "the new WHO/International association for the study of lung cancer histologic classification of non-small cell lung carcinomas (NSCLC)" the LCNEC is a variant of large cell carcinoma[2]. LCNEC is now recognized as a histologically high-grade non-small cell carcinoma with very poor prognosis showing histopathological features of neuroendocrine differentiation as well as immunohistochemical neuroendocrine markers. The immunohistochemistry of LCNEC have been studied in a series of 35 patients and the results were as follows: neuron specific enolase (100%), chromogranin (80%), Leu-7 (40%), and synaptophysin (40%)[3]. Positivity for a neuroendocrine phenotype was determined by the presence of focal staining for at least one of these three markers [4]. The LCNEC, which is characterized by cells of large size, polygonal shape, low nuclear-cytoplasmic ratio (N:C), coarse nuclear chromatin, and frequent nucleoli, high mitotic and frequent necrosis with characterstic electron microscopic and immunohistochemical features [5]. These tumor cells have been shown to contain neurosecretory granules and occasional evidence of granular differentiation and intercellular junctions suggestive of squamous differentiation on electron microscopy. On immunohistochemistry, these tumors stain for neuron-specific enolase,

carcinoembryonic antigen (CEA), and keratin as well as variably stain for chromogranin, Leu-7, synaptophysin, and adrenocorticotropin hormone. These immunohistochemical properties have also been confirmed by Wick et al[6]. The 27% and 9%, 5 years and 10 years survival rate respectively has been described by Travis et.al for LCNEC in a study of 200 patients of neuroendocrine carcinomas of lung. The treatment for LCNEC in an early stage is complete surgical resection and adjuvant chemotherapy[7].

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