ISSN: 2395-6429

INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND PHARMACEUTICAL RESEARCH

IJCMPR

Available Online at http://www.journalcmpr.com

DOI: http://dx.doi.org/10.24327/23956429.ijcmpr20170104

CASE REPORT

MIXED ADENO-NEUROENDOCRINE CARCINOMA [MANEC] OF ASCENDING COLON A RARE OCCURRENCE: A CASE REPORT

Asmita Dhurve., Varsha.S.Barai and Aniket.B. Payagude*

Department of General Surgery, Government Medical College and Hospital Nagpur

ARTICLE INFO

Article History:

Received 26th March, 2017
Received in revised form 17th April, 2017
Accepted 11th May, 2017
Published online 28th June, 2017

Key words:

Mixed adenoneuroendocrine carcinoma, MANEC, ascending colon, immunohistochemistry.

ABSTRACT

Mixed adenoneuroendocrine carcinoma is an extremely rare tumour of gastrointestinal tract, classified by World Health Organisation 2010 as, malignant tumour with mixed adenocarcinoma and neuroendocrine components with at least 30% of each. MANEC's are highly aggressive tumour with poor outcome. The diagnosis is based on tumour histology and immunohistochemistry. We report here a case of 59 year old female which presented as vague abdominal pain, was diagnosed as with ascending colon malignancy on colonoscopy and tissue biopsy, underwent right hemi-colectomy and later diagnosed as MANEC on immunohistochemistry studies, positive for CK20, CDX2, MUC2, CD56, Chromogranin, Synaptophysin. Due to paucity of cases, little is known about optimal strategy for management of MANEC.

INTRODUCTION

Mixed adenoneuroendocrine carcinoma of gastrointestinal tract is a rare tumour with very few reported cases in medical literature. Till date only 7-8 cases in the caecum and 40 cases stomach have been reported mostly as individual case reports [1]. Only recently WHO 2010 defined dual nature of adenocarcinoma with neuroendocrine features as Mixed Adenoneuroendocrine neoplasm with each representing atleast 30% of the neoplasm [2]. Confirmation of MANEC is done by immunohistochemistry which stains positive for CK20, CDX2, MUC2, CD56, Chromogranin, Synaptophysin etc. Due to rarity of these neoplasms little is known about the adequate treatment options of these cases. We here report a case of mixed adenoneuroendocrine tumour of the ascending colon

Case report

A 59 year old female reported with complaints of vague abdominal pain over right side of abdomen since 4 months associated with altered bowel habits with intermittent loose stools and constipation, anorexia, weight loss. There was no history of vomiting, blood in stools, jaundice, fever or any other comorbidities/major surgery. There was no history of any addiction, patient was vegetarian. Family was complete, menopause attained 9 years back. Family history was not significant.

Patient was initially evaluated with routine blood investigation, including complete blood count, renal function test, Sr. electrolyte, liver function test, and USG Abdomen, which was inconclusive. Hence, CECT Abdomen was done which suggested moderate circumferential wall thickening involving ascending colon, caecum, IC junction and terminal ileum. Colonoscopy suggested large polypoidal ulcerated circumferential mass lesion causing luminal narrowing through which scope could not be negotiated any further, multiple biopsies were taken from the lesion. Histological features were of Well differentiated adenocarcinoma of colon grade-I. With this diagnosis, patient was further evaluated with pulmonary function test and 2D ECHO and prepared for major surgery. Right hemi-colectomy with ileo-transverse anastomosis was done. On cut section, a cauliflower like growth of size 5×5×3 cm, greyish white solid, was present involving caecum and just proximal part of ascending colon [Figure 1 A]. Two distinct pattern were identified one showing pools of Mucin with few floating tumour cells, signet ring and occasional tubular glands infiltrating into serosa. The other pattern showed nests and solid sheets predominantly in sub-mucosa infiltrating towards mucosa and deep into muscular propria, serosa and the fat surrounding it. Lympho-vascular emboli and peri-neural involvement was also seen [Figure 1 B]. Two lymph nodes were positive for malignant cells. Histological features were suggestive of Adenocarcinoma with carcinoid features. Immunohistochemistry confirmed the diagnosis.

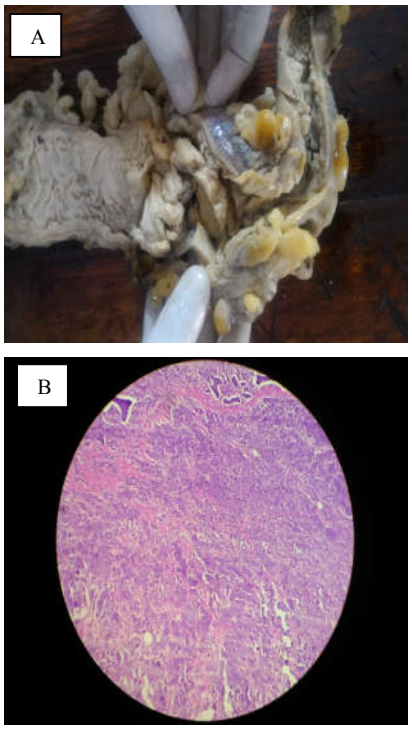
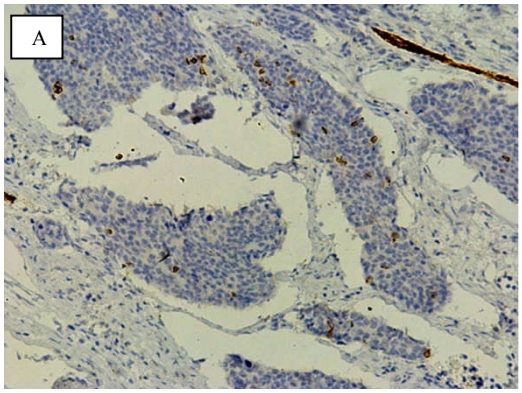
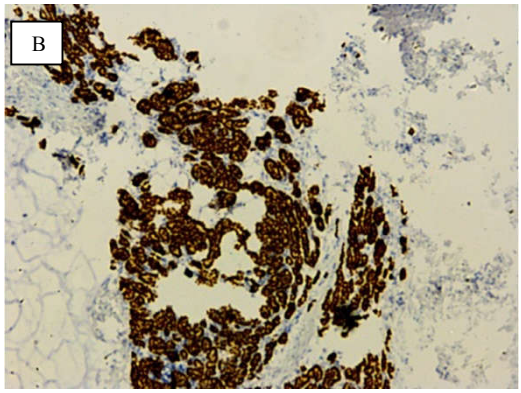
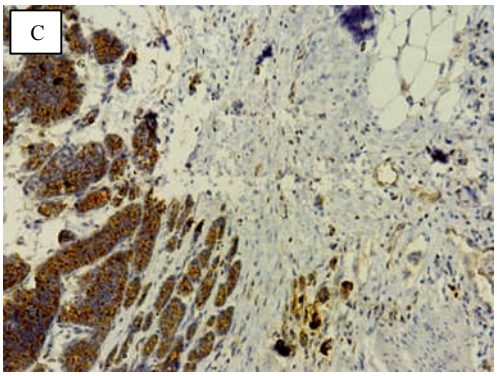


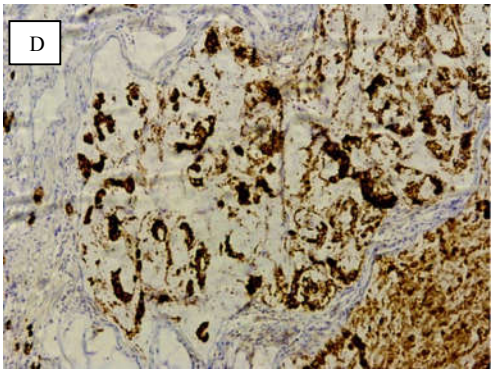
Figure 1 A gross specimen: On cut section, a cauliflower like growth of size 5×5×3 cm, greyish white solid, present involving caecum and just proximal part of ascending colon. B tissue stained with haematoxylin and eosin.

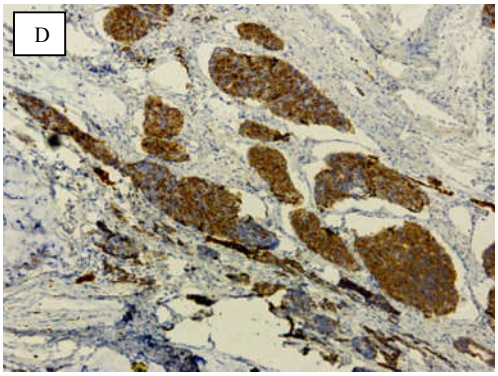
The neoplastic cells are positive for CK20, CDX2, MUC2 and focally for neuroendocrine markers like CD56, Chromogranin and Synaptophysin [Figure 2]. Based on this patient was started on postoperative chemotherapy (FOLFOX regimen) and is in follow up since 6 months with no recurrence and distant metastases.

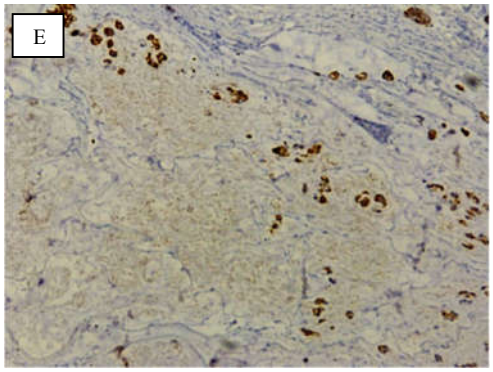


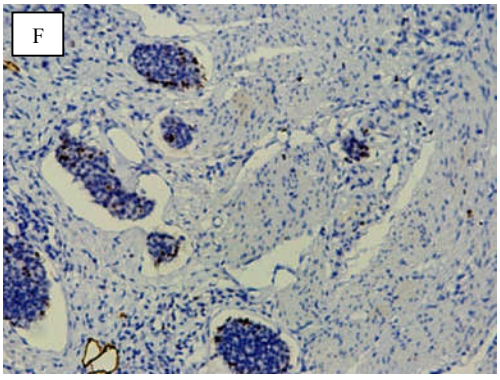












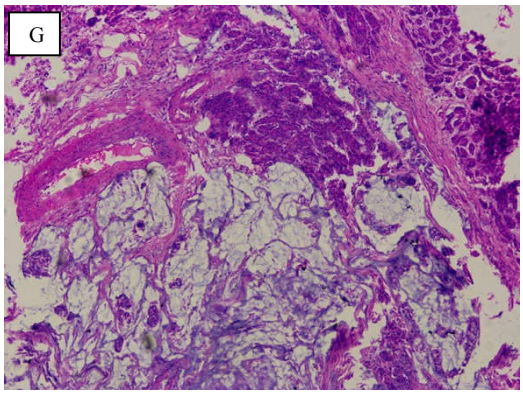


Figure 2 Immunohistochemistry expression of the ascending colon MANEC: A-C56, B-CDX2, C-Chromogranin, D-MUC2, E-Synaptophysin, F-Ki-67, G- Microscopic examination.

DISCUSSION

Cardier in 1924, first described the case of MANEC. Since then it has been reported with different names like composite carcinoid, Mucin producing carcinoids, argentaffin cell adenocarcinoma, goblet cell carcinoids, adeno-carcinoid, small undifferentiated carcinoma etc. [3]

More recently in 2010, WHO classified digestive neuroendocrine neoplasms into five categories. Classes 1-3 were identified as pure neuroendocrine tumours, class 4 as mixed neuroendocrine and non-neuroendocrine tumours and class 5 as pre-neoplastic either hyperplastic or dysplastic [2]. By definition mixed adenoneuroendocrine tumour of comprise atleast 30% of each component and are universally carry a poor prognosis as both the component of MANEC are malignant. Diagnosing MANEC may pose a challenge as frequently only one component of the neoplasm is identified leading to incomplete diagnosis and suboptimal treatment [4]. Therefore, diagnosis of MANEC should be based on histological findings and immunohistochemistry [5]. Atleast two out of three commonly used neuroendocrine markers synaptophysin, chromogranin A or CD56 must be expressed to define the tumour as high grade MANEC [6]. Ki-67 is usually very high between 60-90% [7]. In our case, neuroendocrine tumour was positive for all three Synaptophysin, Chromogranin A and CD 56. Ki-67 was 40%. The neoplastic cells were also positive for colonic markers like CK20, CDX2 and MUC2. Due to rarity of mixed-adenoneuroendocrine carcinoma, treatment strategies are not standardized and can be managed with palliative operation, adjuvant chemotherapy and somatostatin analogues [5].

Despite aggressive management, outcome of the MANEC is poor. In our case patient was initially diagnosed as well differentiated adenocarcinoma and managed with right hemi-colectomy with ileo-colic anastomosis. Later, immunohistochemistry evaluation suggested it to be a mixed adenoneuroendocrine carcinoma. Patient received post-operative chemotherapy (FOLFOX regimen) and is in follow up for 6 months with no recurrence and distant metastases with mild symptoms of nausea vomiting during the chemotherapy course.

CONCLUSION

As MANEC is highly malignant and carries poor prognosis, a thorough histopathological examination is must for diagnosis and further studies are required to throw light into its management.

References

1. Gurzu S, Kadar Z, Bara T, et al. Mixed adenoneuroendocrine carcinoma of gastrointestinal tract: report of two cases. *World J Gastroenterol* 2015; 21:1329-1333.
2. Rindi G, Petrone G & Inzani F. The 2010 WHO classification of digestive neuroendocrine neoplasms: a critical appraisal four years after its introduction. *Endocrine Pathology* 2014 25 186-192.
3. Kwok C-M. Mixed Adenoneuroendocrine Carcinoma of the Stomach. *Case Reports in Gastroenterology*. 2015; 9(2):241-245.
4. La Rosa S, Marando A, Sessa F, Capella C. Mixed Adenoneuroendocrine Carcinomas (MANECs) of the Gastrointestinal Tract: An Update. *Cancers.* 2012;4(1):11-30.
5. X.-J. Liu, J.-S.Feng, W.-Y. Xiang et al., "Clinicopathological features of an ascending colon mixed adenoneuroendocrine carcinoma with clinical serosal invasion," *International Journal of Clinical and Experimental Pathology*, vol. 7, no. 9, pp. 6395-6398, 2014.
6. Rindi G., Arnold R., Bosman F.T., Capella C., Kilmstra D.S., Kloppel G., Komminoth P., Solcia E. Nomenclature and classification of neuroendocrine neoplasms of the digestive system. In: Bosman F.T., Carneiro F., Hruban R.H., Theise N.D., editors. WHO Classification of Tumours of the Digestive System. 4th. IARC Press; Lyon, France: 2010. pp. 13-14.
7. Tanabe T, Nishimaki T, Kanda T, Nakagawa S, Ohashi M, Hatakeyama K. Esophageal composite carcinoma with tripartite differentiation: clinicopathological analysis of three cases. *Esophagus*. 2005; 2:91-96.

****