Case Report

A Rare Case of Mixed Ductal Neuroendocrine Tumor of the Pancreas

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ABSTRACT

Collision tumors are tumors that have at least two types of tumors in the same anatomical site with no area of mixing within the transition zone. In 2010 WHO classification of neuroendocrine tumors consists of an adenocarcinoma component and a neuroendocrine carcinoma component in which each of the components accounts for 30% of the tumor. Such tumors are defined as mixed adenoneuroendocrine carcinomas. Occurrence of exocrine and endocrine tumors of the pancreas is extremely rare. The aim of our study was to describe a case in a 60 years old male who was diagnosed with this rare tumor. Gross, microscopic features and immunohistochemistry were used to diagnose this rare condition. Immunohistochemistry markers such as synaptophysin, chromogranin, EMA and Pan CK were used to come to a definitive diagnosis. Synaptophysin and chromogranin were found to be positive in the neuroendocrine component. EMA and Pan CK were found to be positive in the ductal component. Hence a diagnosis of mixed ductal neuroendocrine tumour (collision tumor) was made.

Keywords: Collision Tumor, Mixed, Rare, IHC

Introduction

Collision tumors are tumors that have at least two types of tumors in the same anatomical site with no area of mixing within the transition zone. In 2010 WHO classification of neuroendocrine tumors consists of an adenocarcinoma component and a neuroendocrine carcinoma component in which each of the components accounts for 30% of the tumor. Such tumors are defined as mixed adenoneuroendocrine carcinomas. Occurrence of exocrine and endocrine tumors of the pancreas is extremely rare. Pancreatic neuroendocrine tumors express markers such as synaptophysin, neuron specific enolase and chromogranin-A. Sometimes these tumors are associated with acute or chronic pancreatitis which may be due to obstruction of the pancreatic duct by the tumor. In this article we present a rare case of mixed adenoneuroendocrine pancreatic carcinoma

Case Report

A 60-year-old male patient came with chief complaints of pain abdomen more over the left hypochondrium and epigastric region since 6months which was associated with weight loss of 10kgs in 3 months. He did not have any history of vomiting, loose stools, chest pain, palpitations, Breathlessness. He was a known Case of diabetes mellitus since 18 months and is on regular treatment for the same. There was history of repeated attacks of pancreatitis in the past. No History of hypertension, bronchial asthma, T.B or thyroid disorders was found. Family medical history was not contributory in this case. Personal history the patient consumed mixed diet, had normal sleep, decreased appetite, normal bowel and bladder habits. Past history of alcohol consumption present.

On examination pulse rate was 70/min, Blood Pressure was 130/90 mm Hg, No pallor, icterus or pedal edema. Systemic examination showed mild epigastric tenderness and no palpable mass. The hematological parameters were as follows Hb- 12.6 g/dl, WBC- 5700 cells/ cumm3, Platelet count – 1.9 lakhs, Blood group – A positive, Urea – 37 mg/dl, S. Creat – 1.1 mg/dl, Na- 138 mmol/L, Potassium – 4.5 mmol/dL, Fasting blood Glucose – 156 mg/dL, T. Bilirubin – 0.7 mg/dL, SGOT – 38 IU, SGPT – 30 IU, ALP – 92 IU/L, Protein – 5.6 g/dL, Albumin – 3.9 g/dL, Serum amylase – 900 U/L, Serum lipase – 1600 U/L, HIV / HbsAg – negative. Only fasting blood glucose and serum amylase levels were found to be raised all other parameters were within normal limits. Chest X Ray showed normal radiographic study. ECG showed normal sinus rhythm. Echo showed ejection fraction of 60%, no regional wall motion abnormalities were noted. Mild concentric LVH was seen.

Endoscopic ultrasound guided fine needle aspiration cytology from pancreatic head mass showed only a few atypical cells which was reported as suspicious of malignancy.

CT of abdomen and pelvis showed severe atrophy of pancreatic parenchyma in the region of uncinate process,
head, body and tail with dilatation of main pancreatic duct. Poorly enhancing soft tissue in the region of the neck
and adjacent head of pancreatic parenchyma measuring 2 X 2.5 X 1.7cms in maximum diameter. The CT findings
suggested the possibility of pancreatic adenocarcinoma.

Ultrasound of the abdomen and pelvis showed fatty liver
along with borderline prostate enlargement.

Subsequent to this the patient was posted for Whipple’s
procedure that is Pancreatcico-duodenectomy along with
cholecystectomy and feeding jejunostomy under general
anaesthesia. Post-surgery the specimen was sent to Dept of
Pathology for Histopathological examination.

In our department the specimen received was studies for
both gross and microscopic features.

On gross examination the external surface of the pancreas
was greyish brown in colour. Cut surface was ill defined,
yellowish-white in colour, firm in consistency. Very scant
normal pancreatic parenchyma was seen (figure 1&2).

Microscopic examination showed a well differentiated
tumor predominantly composed of ductal invasive
component (figure 3&4) with approximately one
third of neuroendocrine component (figure 5&6). The
tumor was seen to extend into peripancreatic fat and the
adjoining duodenum (figure 7). There was no evidence
of Lymphovascular invasion but perineural invasion was
present (figure 9&10). The adjoining pancreas showed
features of chronic pancreatitis with fibrosis (figure 8). All
the surgical margins were found to be free of tumor. Four
lymph nodes were identified one of them was seen to be
involved by the tumor. One of the lymph nodes also showed
features of non-caseating granuloma. A diagnosis of mixed
ductal neuroendocrine carcinoma was made based on the
above microscopic findings. Immunohistochemistry was
performed to confirm the diagnosis. Synaptophysin and
chromogranin (figure 11&12) were found to be positive
in the neuroendocrine component. Epithelial membrane
antigen and pan CK (figure 13&14) were found to be
positive in the ductal component.

**Discussion**

We report an exceeding rare case of pancreatic
adenocarcinoma and neuroendocrine tumor. According
to WHO classification collision tumors are composed
of two different malignancies without histological
admixture. [1,3] Another terminology MANEC that is
mixed adenoneuroendocrine carcinoma was introduced
by WHO in 2010. Tumors with two different malignant
components with each tumor accounting for 30% of the
tumor are classified as MANEC.[2,7] Collision tumors have
been reported in various organs of the body such as breast,
uterus, colon and stomach. They most commonly occur in
the stomach and oesophagus. [1]

The pancreas is composed of both exocrine and endocrine
components. Pancreatic collision tumors are rare with
limited literature. Peak incidence of these tumors is between
30-60yrs. [3] Diagnosis of pancreatic collision tumors is
a post-operative diagnosis based on histopathological
examination.[1] Collision tumors appear to have a poor
prognosis with a median survival of 10 months. Surgical
treatment appears to be the treatment of choice.[1,2,4,5]

Little is known about the carcinogenesis of these tumors.
One hypothesis states that there may be dysfunction of

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**Fig. 1: Gross picture of the entire pancreaticoduodenectomy specimen.**

**Fig. 2: Gross picture of the tumor proper.**
C-22 Mixed Ductal Neuroendocrine Tumor of Pancreas

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Fig. 3: Low power view(10X) in Hematoxylin and eosin stain of Infiltrating, haphazard glands and surrounding desmoplastic stroma.

Fig. 4: High power view(40X) in Hematoxylin and eosin stain showing multilayering, nuclear atypia, Loss of polarity and focal prominent nucleoli.

Fig. 5: Scanner view(4X) in Hematoxylin and eosin stain of an area demonstrating components of neuroendocrine tumor (lower-most) and pancreatic ductal adenocarcinoma (upper).

Fig. 6: Scanner view(4X) in Hematoxylin and eosin stain of an area demonstrating components of neuroendocrine tumor (lower-most) and pancreatic ductal adenocarcinoma (upper).

Fig. 7: Low power view(10X) in Hematoxylin and eosin stain of infiltration into duodenal wall

Fig. 8: Low power view(10X) in Hematoxylin and eosin stain of chronic pancreatitis on background showing fibrosis, inflammation and fatty infiltration.
Fig. 9: Low power view (10X) in Hematoxylin and eosin stain of perineural invasion.

Fig. 10: High power view (40X) in Hematoxylin and eosin stain of perineural invasion.

Fig. 11: Synaptophysin positivity in the neuroendocrine component.

Fig. 12: Chromogranin positivity in neuroendocrine component.

Fig. 13: EMA positivity in the Glandular component.

Fig. 14: PAN CK positivity seen in adenocarcinoma.

Fitzgerald reported mixed type tumors as 0.2% of all tumors. [2] These tumors have been designated the term mixed ductal acinar tumors etc based on their components. Chang et al classified mixed tumors as amphicrine type, mixed type, collision type, solitary concomitant type and multiple concomitant type. [7]

Pancreatic neuroendocrine tumors can be functional and non-functional tumors. Functional tumors release active hormones in peripheral blood which are responsible for a particular syndrome. Non-functional tumors secrete functionally inert hormones which do not produce any syndrome. [5] Histopathologically non-functional tumors cannot be distinguished from functional tumors. However positive staining for chromogranin and synaptophysin confirms the diagnosis of non-functional pancreatic neuroendocrine tumors. [4,5]

Immunohistochemistry is very important for the diagnosis of pancreatic neuroendocrine tumors. Several markers are available such as neuron specific enolase, CD56, synaptophysin and other hormones. The malignant or metastatic potential of the neuroendocrine tumor can be determined by tumor size, expression of Ki67, vascular invasion and perineural invasion. [5,6] Most of these tumors are also associated with pancreatitis. In our study the association of chronic pancreatitis and neuroendocrine tumor seem incidental. [1]

In this article we report a case of mixed adenoneuroendocrine tumor or collision tumor. The exact method of tumorigenesis is unknown. When faced with a pancreatic mass with atypical radiological features and also ill-defined mass on gross examination a diagnosis of collision tumor needs to be considered. [1] The diagnosis can be confirmed by using additional immunohistochemical methods.

**Conclusion**

Pancreatic mixed adenoneuroendocrine tumors are extremely rare which raise important diagnostic and therapeutic decisions. Association with chronic pancreatitis is also noted which is not fully understood. Histopathology and immunohistochemistry remain the gold standard for the diagnosis of these tumors.

**References**


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