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The Number of 7 Patient's Clinical Analysis of Duodenal Neuroendocrine Neoplasms

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Abstract

Aim: The aim of this study was to report and analyze outcomes associated 7 patient's in-hospital evaluation and investigate of the cliniopathological features diagnosis and treatment of duodenal neuroendocrine neoplasms. So provide knowledge for further understanding of this condition.

Methods: The number of 7 consecutive patients who underwent duodenal (NEN) of the first affiliated hospital of Anhui medical university of December 2012 to 2015 were identified and included for analysis. Demographic and operative data, pathological findings and post-operative outcomes were entered into a computer database. Prognostic factors were analyzed by univariate and multivariate analysis.

Results: The number of 7 patients 3 cases was male and 4 were female; all cases underwent ultrasound and CT examination, 5 cases had endoscopy examination and 1 case had MRI examination. The imaging examinations showed that the tumor was located at descendant duodenum in 2 cases, at duodenal papilla in 1 case and at horizontal duodenum in 1 case. The endoscopy examination showed that the tumor was located at descendant duodenum in 1 case at duodenal papilla in 1 cases and at duodenal bulb in 1 case The 7 patients exhibited dissimilar clinical symptoms. Duodenal NEN was manifested as abdominal pain in 3 cases as jaundice in 2 cases and as headache and fatigue in 2 cases. All patients received surgical treatment, and their diagnoses were confirmed by postoperative pathological and immune histochemical examinations.

Conclusion: Duodenal NEN has low prevalence, insidious onset and usually without specific clinical signs and symptoms. Its diagnosis mainly relies on pathological biopsy and immunohistochemical staining, and surgery is the first option of treatment.

Keywords

Neoplasms; Duodenal neoplasms; Neuroendocrine tumors

Introduction

Neuroendocrine neoplasm (NEN) is derived from the neuroendocrine system, to generate peptides, and share common neuroendocrine tumor markers. Neuroendocrine tumor is a rare clinical disease, its good location is the stomach, intestine and pancreas [1]. Which occurred in the duodenum NEN, very rare, the literature of all gastrointestinal pancreatic neuroendocrine tumor (GEP - NEN) of 1.8% - 3.8% [2] according to the presence of hormone related clinical characteristic, divided into functional and non-functional duodenal NEN. Because most of these diseases have no characteristic clinical manifestations, clinical diagnosis rate is low, the author analyzed retrospectively during December 2012 - December 2015 were confirmed by surgery and pathology of patients with duodenal NEN, aims to further analyze the characteristics of the disease, improve the diagnosis of the disease and put forward reasonable treatment.

The second most frequent component of MEN1 is the development of NET of the duodenum or pancreas, 30% to 80% of patient with MEN1 develop clinically evident tumor. Gastronomy frequently occur within the wall of duodenum or in extra pancreatic site, The pancreatic duodenal tumor in patient with MEN1 produce symptoms caused by hormone over secretion or mass effect from the tumor growth itself.

The most common functional NET in patient with MEN1 is gastronomy, presenting sigh and symptom in patient with hyper gastrinemia, Zollinger Ellison syndrome(ZES) including epigastric pain, reflux esophagitis, secretory diarrhea and weight loss.

Gastronomy that develop in patient with MEN 1 are usually malignant usually (~ 80%), as indicated by the presence of regional lymph node or distant metastasis

Gastronomes occur frequently in the duodenal wall, combined with efforts to perform an extensive regional lymphadenectomy or even pancreaticoduodenectomy, and may improve the success rate of surgery for ZES in the setting of MEN 1. Total gastrostomy is rarely indicated for patient with gastronomy because medical therapy effectively prevents most of symptoms or complications resulting from the acid hyper secretion.

The second most common clinically evident pancreatic NETs in patient with MEN 1 are insulinomas, these are usually small (<2 cm) and occur with even distribution throughout the pancreas. Patient is typically present with the current symptoms of neuroglycopenia-sweating, dizziness, confusion or syncope. There is no ideal medical therapy for insulinoma, therefore the preferred treatment is accurate localization and surgical resection of the functioning tumor to correct life threatening hyper insulinemia.

Anatomy of Duodenum: The Duodenum is the shortest, widest

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and most fixed part of the small intestine. It extends from the pylorus to the duodenojejunal flexure. It is curved around the head of the pancreas in the form of letter "C". The duodenum lies above the level of the umbilicus, opposite first, second and third lumbar vertebrae.

The duodenum is about 25 cm long and 2.5 cm wide and it has four parts:

A) First part: by two parallel lines 2.5 cm apart extending from the pyloric orifice and to the right to meet second part

B) Second part: by similar lines on the right lateral vertical plane extending from the end of the first part downwards for 7.5 cm and reach the lower border of the third lumber vertebra, where it curves toward the left at inferior duodenal flexure, to continuous with third part.

C) Third part: this part is about 10 cm long. It begins at inferior duodenal flexure, on the right side of the lower border of the third lumber vertebra. It passes almost horizontal and slightly upwards in front of the inferior vena cava and end by joining the fourth part

D) Fourth part: this is about 2.5 cm long. It run upwards on or immediately to the left Of the aorta, up to the upper border of the second lumber vertebra, where it turn forwards to become continuous with the jejunum at the duodenojejunal flexure (Figure 1).

Data and Methods

General information

Collected in December 2012 - December 2015, the first affiliated hospital of Anhui medical university was confirmed by pathology of 7 patients with duodenal NEN, three male cases, female 4 cases, the ratio of men and women of 1:1.3 with Age 36- 72, at an average age of 52.

Diagnostic criteria: According to the 2010 WHO digestive system neuroendocrine tumor new classification (fourth edition) [3] for this group of duodenal NEN, naming and hierarchical classification.

Preoperative examinations: All patients were test CA19-9, < 37 U/ml; the patients were performed with ultrasound and C T examination, routine endoscopy, 1 routine MRI. Imaging prompt tumors located in 2 cases, duodenal descending department nipples in 1 case, level 1 case, endoscopic prompt tumors located in the fall of 1 case, nipple in 1 case, ball in 1 case.

Follow-up: The patients were followed up for 6-36 months, follow-up projects mainly for abdominal ultrasound, endoscopic index and tumor.

Treatment

Track of operative surgery is still the main method for the treatment of duodenal NEN. The treatment of duodenal.net preferred surgical resection, followed by endoscopic resection. Endoscopic mucosal stripping operation procedures were used (ESD), duodenal tumor resection, and resection of pancreas duodenum. Preoperative tumor location, tumor size, tumor infiltration depth, lymph node metastasis, tumor G preoperative staging is the main factor of clinical doctors decide model [4].

Some recent research suggests that for the relatively small size, diameter of < 1 cm and tumor growth in the region of the ampulla, lesions not assault and muscle layer, EUS, or CT examination no lymph node metastasis of duodenal NEN, tumor, feasible endoscopic excision [5-9], our group 1 underwent endoscopic lesion resection, cutting edge clean, follow-up asked lesions with no recurrence or metastasis. For 1-2 cm duodenal NEN, tumor diameter, beyond the sub mucosa, laparoscopic resection or laparotomy is the best choice [6], for > 2.0 cm in diameter, especially the EUS prompt tumor cells are seen around deep intestinal wall, tumor lymph node involvement, CT and (or) MRI prompt suspected cases of lymph node involvement, surgical radical excision of duodenostomy [10,11], Our group 1 line diameter is about 0.6 cm endoscopic mucosal decollement (ESD) treatment;1 case was 4.5 cm in diameter of duodenal tumor resection plus the left hepatic lobe resection;2 cases of 0.6 cm, 5.5 cm in diameter of duodenal tumor resection, this 5.5 cm huge bump because in the duodenum, nipple department is still far away, so the duodenal tumor resection;3 cases of 1.5-2.4 cm in diameter, treatment of pancreaticoduodenal resection. This group of 1 case of liver metastatic lesions of the patients, treatment for primary radical tumor resection combined resection of liver metastases. Timely treatment of liver metastatic lesions can not only inhibit the growth of liver metastases, also can improve the symptoms of carcinoid syndrome, improve patient quality of life and survival [9].

Non-surgical treatment for middle-late widely transfer cannot surgical treatment of patients can consider to use fluorouracil, more gentle than star, methotrexate, such as combination chemotherapy, biological therapy and molecular targeted therapy has shown good prospects for treatment, the application of somatostatin is a kind of cancer treatment milestone [12], but overall the duodenum.net is not sensitive to radiotherapy and chemotherapy.

Results

Clinical manifestations

7 patients have different clinical symptoms, there is a clear abdominal pain, abdominal discomfort complained of 3 cases of, 42.9% (3/7), dizziness, weakness in 2 cases (2/7, 28.6%), skin, sclera, mild yellow dye, 28.6% (2/7) in 2 cases.

Surgical treatment: 7 patients were treated with surgery, 1 underwent endoscopic mucosal decollement (endoscopic sub mucosal dissection, ESD) treatment; 1 duodenal tumor resection of the left hepatic lobe resection, 2 routine duodenal tumor resection;3 resection

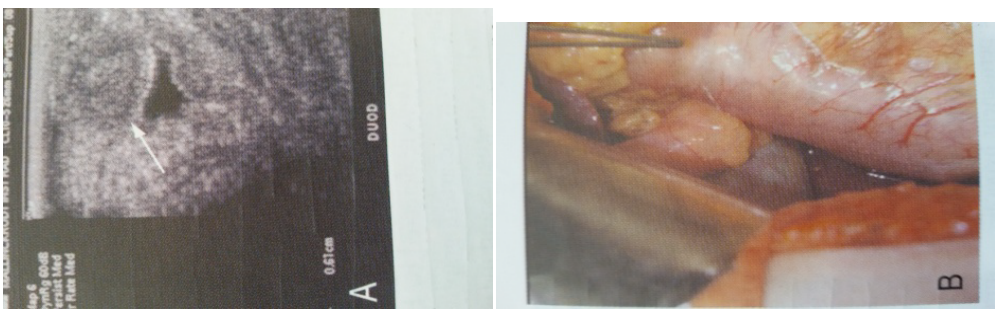

Figure 1: Gastronomy in the duodenal wall from patient with MEN1. **A**) Intraoperative ultrasound demonstrating a circumscribed hypoechoic tumor in submucosa of the duodenal wall, demonstrated just superior to the duodenal lumen. **B**) Gross appearance of the duodenal wall tumor from the serosal surface.

of pancreatic duodenal tumor treatment. Operation time was 2.5- 6 hours, intraoperative bleeding is 100 ~ 400 mL, intraoperative blood transfusion in 1 case, postoperative gastrointestinal function recovery time 4-6 d, length of hospital stay of 12 ~ 20 d, has not been postoperative anastomotic fistula, pancreatic fistula, biliary fistula, intestinal fistula.

Pathology results: This group of 7 cases of duodenal NEN is solid, diameter 0. 6 to 5.5 cm, 3 cases of > 2 cm, 2 cases, and 1-2 cm < 1 cm 2 cases, 4 cases of invasive growth. New classification according to the WHO 2010 digestive system tumors (fourth edition) [3], the G1 stage 5 cases (5/7, 71.4%), 2 G level 2, 28.6% (2/7). This group of 7 cases of patients with surgical specimens immune histochemical results and special dyeing results are as follows: chromaffin granule proteins (CgA) positive in 7 cases, synapse (Syn) Yang 7 cases, creatine kinase (CK) positive in 7 cases, nerve cell adhesion molecules (CD56) positive in 7 cases, insulin (insulin) staining positive in 1 case, wool protein (villin) staining positive in 1 case (Tables I-III).

Follow-up results: For follow-up in all 7 cases, follow-up time was 6 ~ 36 months, the median surial was 21.4 months, specific survival are shown in Table Il. Has not been all patients postoperative chemotherapy, median follow-up time, higher quality of living, no obvious discomfort complained of.

Prognoses

At present, all the NEN is has the potential of malignant tumor, should be long-term follow-up [13]. All the patients followed up, all the long-term survival. Follow-up results suggest the duodenum NEN malignant degree is low, a satisfactory curative effect after the surgery, should be early surgical treatment after diagnosis of duodenal NEN. Even in the liver, pancreas, under the condition of patients can tolerate surgery, still should actively surgery. Duodenal NEN the prognosis depends on many factors: the primary site of tumor, pathologic type, stage, differentiation, cell proliferation index Ki - 67 and the onset of patient's age, physical condition, etc.

Above all, the past duodenal low prevalence of NEN cause clinicians understanding of its progress is slow, the misdiagnosis rate and missed diagnosis were higher, in recent years, with the improvement of diagnosis and treatment level, especially the progress of the imaging and endoscopic ultrasonography and different molecular targeted drugs in clinical treatment success, understanding of duodenal NEN is continuously deepened, but there are still many clinicians understanding insufficiency, therefore the research of diagnosis and treatment of duodenal NEN, characteristics and is the task of every clinician is urgently needed, believe that the future can be better diagnosis and treatment of the disease, of course it needs more medical workers continue to study.

Discussion

Clinical characteristic

In recent years, the incidences of NEN rise year by year, probably because of endoscopic technology and the development of the imaging diagnostic techniques [14,15]. Neuroendocrine tumor in 1907 by the German pathologist Obemdorfer first reported; although histologically similar to malignant tumor, but biology behavior tend to be more benign lesions. Duodenal neuroendocrine tumor originated in the duodenum mucosa Lieberkuhn deep intestinal crypt sample chromaffin cells (Kulchitsky) [16], the cells from the embryonic neural crest, is the most widely distributed in the gastrointestinal tract, the largest number of neuroendocrine cells can secrete a serotonin, histamine, 5 slow excitation peptide, kallikrein, and more than 20 kinds of material such as prostaglandins, cause skin flush, diarrhea, abdominal pain, dyspnea, cardiovascular abnormalities, such as clinical syndrome, namely the carcinoid syndrome. Patients with carcinoid syndrome is the NEN, characteristic of literature reports the duodenum NEN carcinoid syndrome rate was only 9% [17]. The patients had no carcinoid syndrome, which is consistent with the literature reported low incidence of carcinoid syndrome. It is worth noting that when patients with carcinoid syndrome occurs, the lesion has shift, prompt

Table I: Clinical data about 7 duodenal NEN patients and their prognosis.

Cases	Gender	Age	Tumor site	Tumor site(cm)	Infiltrating Depth	Surrounding the violation	Treatment	Survival (month)	Ki-67 index (%)
1	Male	52	Descend	0.6 cm	Sub mucosa	No	Duodenal tumor resection	8	<2
2	Male	59	Descend	2.4 cm	Serous fat outside	Pancreatic head	Pancreatic duodenal resection	22	5
3	Female	53	Descend	4.5 cm	Serous fat outside	Liver	Pancreatic duodenal resection	6	<2
4	Female	42	Papilla	1.5 cm	Serous fat outside	Common bile duct	Pancreatic duodenal resection	36	<2
5	Male	72	Bulb	0.6 cm	Sub mucosa	No	ESD	12	<2
6	Female	36	Papilla	2.0 cm	Plasma muscular	No	Pancreatic duodenal resection	33	3
7	Female	48	horizontal	5.5 cm	Serous fat outside	No	Duodenal tumor resection	33	<2

Table II: Results of immune histochemical and special staining of the surgical specimens from the 7 duodenal NEN patients.

Cases	Syn	CgA	CD56	CK	Insulin	Villin
1	(+)	(+)	(+)	(+)	(–)	(–)
2	(+)	(+)	(+)	(+)	(–)	(–)
3	(+)	(+)	(+)	(+)	(–)	(–)
4	(+)	(+)	(+)	(+)	(–)	(+)
5	(+)	(+)	(+)	(+)	(–)	(–)
6	(+)	(+)	(+)	(+)	(–)	(–)
7	(+)	(+)	(+)	(+)	(+)	(–)

Table III: Histologic classification of surgical specimens from the 7 duodenal NEN patients.

1	2	3	4	5	6	7
G1	G2	G1	G1	G1	G2	G1

the liver cannot be neuroendocrine tumor peptides secreted, amine metabolism; similarly, when the liver metastatic liver function abate, neuroendocrine tumor peptides secreted, amine substance with portal venous blood, the increased incidence of carcinoid syndrome.

This group of data on the issue of onset age and gender ratio of 1:1.3, the onset age 36- 72, the average age of 52, domestic scholars jian-jun zhao [18] reports such as the average age of 54, male to female ratio is 1.14:1, xing-yu liu etc. [19] reported as the average age of 57 years of age, the sex ratio is 1. 2:1, the data and the results of this study are basically identical.

About risk, foreign scholars reported in proximal duodenal [10]. This group of patients with duodenal drop 3 cases, nipple department in 2 cases, the ball in 1 case, level 1 case, domestic and foreign researchers report data generally consistent [19-21].

Duodenal NEN is a kind of peptide can neurons and neuroendocrine cells originated from the heterogeneity of cancer, according to whether the associated with hormone related clinical features, it can be divided into functional duodenal and no functional duodenal NEN. Functional duodenal NEN, often have obvious hormone related characteristic clinical manifestations, easy diagnosis, for the most common and stomach secrete insulin tumor melanoma; Non-functional duodenal NEN, most onset hidden, slow progression, lack of characteristic clinical symptoms, or tumor can be detected by physical examination often increase compression symptoms surrounding organs and see a doctor. This group of data, abdominal discomfort complained of 3 cases of, 42.9% (3/7), dizziness, weakness in 2 cases (2/7, 28.6%), skin, sclera, mild yellow dye, 28.6% (2/7) in 2 cases. Therefore, consider duodenal NEN, no typical clinical symptoms, and functional duodenal NEN, and a lower incidence of carcinoid syndrome [7], to the doctor diagnosis of duodenal NEN, puts forward the higher request.

Essentials of diagnosis

The diagnosis of duodenal NEN, rely mainly on endoscopy and imaging examination. Ultrasound, CT and MRI can be found that the tumor >1 cm in diameter, check out the positive rate was 60% ~ 90%, and in the evaluation of tumor relationship with the adjacent organs, blood vessels, and peripheral lymph node metastasis, feasibility of operation, preoperative staging, etc. Surya Narayan Bayar, MD. (endoscopic ultrasonography, EUS) combined endoscopic technique and real-time ultrasound, clearly shows the layers of structure of digestive tube wall, clear lesions origin, size, infiltration depth, echo intensity and local blood supply situation, help determine lesion features, differential diagnosis and choosing the appropriate treatment. Endoscopic ultrasonography for duodenal NEN positioning has a special advantage, can detect the diameter <1 cm tumor, diagnostic sensitivity is as high as 80% ~ 90% [22].

The pathological features

Pathological diagnosis consensus views according to the 2013 edition of China [22-24], CgA, Syn for neuroendocrine markers must detect project, and CD 56 may choose a project. This group of data also inspected the CK, as well as insulin dyeing and villin. This group of data of CgA were 100%, Syn positive rate 100%, CD56 positive rate 100%, CK were 100%, 14.3% insulin dyeing, dyeing 14.3% villin, reflects the Cg A, Syn, CD56, CK all have high positive rate, insulin positive staining can directly reflect the presence of insulin secretion. NEN, rely on proliferation activity of classification, the fission and Ki - 67 positive index of two indicators, in most cases, the fission and Ki - 67 positive index were positively correlated, a few cases may be inconsistent, USES hierarchical higher at this time as a result, whether in which indicators, are recorded in the pathological report specific values.2010 WHO new standards [3] according to Ki-67 in level of Neuroendocrine cancers can be divided into three groups, namely the low level (G1, Ki - 67 <3%), the level (G2, Ki - 67 is 3% ~ 3%) and high level (G3, Ki - 67 > 20%), the new standard is not recommended to use a Neuroendocrine tumor (Neuroendocrine tumor.net) G3 level classification, because. net G3 has belongs to Neuroendocrine carcinoma (Neuroendocrine carcinoma NEC), and NET are defined as high differentiation. This group of data, the.net G grade 1 in 5 cases (71.4%), NET G level 2 in 2 cases (28.6%). Reflects the duodenum NEN, high differentiation of mild atypical neuroendocrine tumor.

Conclusion

Based on our studies the utilization of Duodenal NEN has low prevalence, insidious onset and usually without specific clinical signs and symptoms. Its diagnosis mainly relies on pathological biopsy and immune histochemical staining, and surgery is the first option of treatment. Given the overall rarity of complications that require surgery familiarity with the published data and sound clinical judgment are key to successful patient outcomes.

Conflict of Interest

Authors have no conflict of interests to declare.

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