Original Article

Prevalence of Diagnostic Methods and Treatment Modalities in Vipoma Patients: A Rare Cause of Hormone-Mediated Diarrhea

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Abstract

Introduction: VIPoma is a neuroendocrine tumor that secrets vasoactive intestinal peptide and produces a well-defined clinical syndrome characterized by watery diarrhea, hypokalemia, hypochlorhydria and metabolic acidosis. The aim of this study to investigate clinical studies about diagnostic and therapeutic modalities of vipoma patients. In this retrospective study, all patients of vipoma were investigated. Clinical features, laboratory data at initial presentation, management and outcomes were collected. **Subjects and Methods:** The paper has written based on searching PubMed and Google Scholar to identify potentially relevant articles or abstracts. Categorical variables as percentage and continuous variables were reported as mean ± standard deviation (SD). **Results:** All the patients presented with watery diarrhea (30/30, 100%) and dehydration was reported in 33.3% of them. Prevalence of laboratory findings in these patients were assessed for hypokalaemia (25/30, 83.3%), metabolic acidosis (9/30, 33.6%), hypochloremia and achlorhydria (2/30, 6.6%). Elevated VIP levels have been seen in 73.3% patients with mean values of 882.85 ± 1134.87 pg/ml. Prevalence of diagnostic methods included CT scan in 19 patients (19/30, 63.3%), ultrasonography (15/50, 50%), and somatostatin receptor scintigraphy (8/30, 26.6%). Medical treatments included somatostatin and analogues in 18 patients (18/30, 60%). Surgery included less percentage of treatment in these patients. **Conclusion:** CT scan can be used as a reliable modality for diagnosis of vipoma and somatostatin analogues can be used as the most effective treatment in vipoma patients. Surveillance of these patients needs to close monitoring of patients via history, physical examination, laboratory and imaging.

Keywords: Diarrhea, hypokalemia, multiple endocrine neoplasia1, OctreoScan, somatostatin analogues, Vipoma

Introduction

Neuroendocrine tumors are neoplasms that exhibit neuroendocrine phenotypes such as the production of neuropeptides, large dense-core secretory vesicles, and a lack of neural structures. Pancreatic neuroendocrine tumors (pNETs), a group of endocrine tumors arising in the pancreas, are among the most common neuroendocrine tumors (NETs). pNETs are classified as functioning or non-functioning depending on whether they cause hormonal hypersecretion syndrome.[1] Functioning pNETs include gastrinomas, glucagonomas, somatostatinomas, or and vasoactive intestinal peptide tumors (VIPomas).

Subjects and Methods

Data source and search

The paper has written based on searching PubMed and Google Scholar, Cochrane library and Embase databases to identify potentially relevant article titles or abstracts.

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Terminology of search

The mentioned search included the following search terms: VIPoma, vasoactive intestinal peptide producing tumor, multiple endocrine neoplasia-1(MEN1)-associated tumors. The author reviewed bibliographies of all selected articles to identify the additional relevant studies.

Study selection and eligibility criteria

Collectively, 8349 8355 records were identified since inception to February 2019 based on titles or abstract. After deduplication full-text of 163 169 articles were reviewed and screened and 93 99 articles excluded due to unrelated subjects and abstract. After screening of studies, 70 articles were eligible

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and 41 articles were excluded due to non-originality and non-pancreatic NETs. The author reviewed bibliographies of all selected articles (case reports) to identify the additional relevant studies. In presence of non-English papers, they were translated and there were 3 non-English articles (2 case reports and one review article) in this study that were excluded due to unavailable electronic access. 29 published articles included 30 case reports and patients for qualitative and quantitative synthesis [Figure 1]. In this retrospective study, all experimental participants (patients) of pNETs were investigated since neonate to old-age. Prevalence of primary and metastatic sites in these patients assessed. Moreover, all symptoms and signs of patients at initial presentation were extracted from articles. Serum electrolytes, creatinine, glucose, hormones, arterial blood gas was were investigated in this study. Furthermore, diagnostic methods, treatment modalities and outcomes were examined.

Ethical states

This article does not contain examinations performed on human participants directly. Then, ethical approval was not necessary by author of this paper, but case reports' authors mentioned obtaining written consent from their patients in the mentioned case reports.

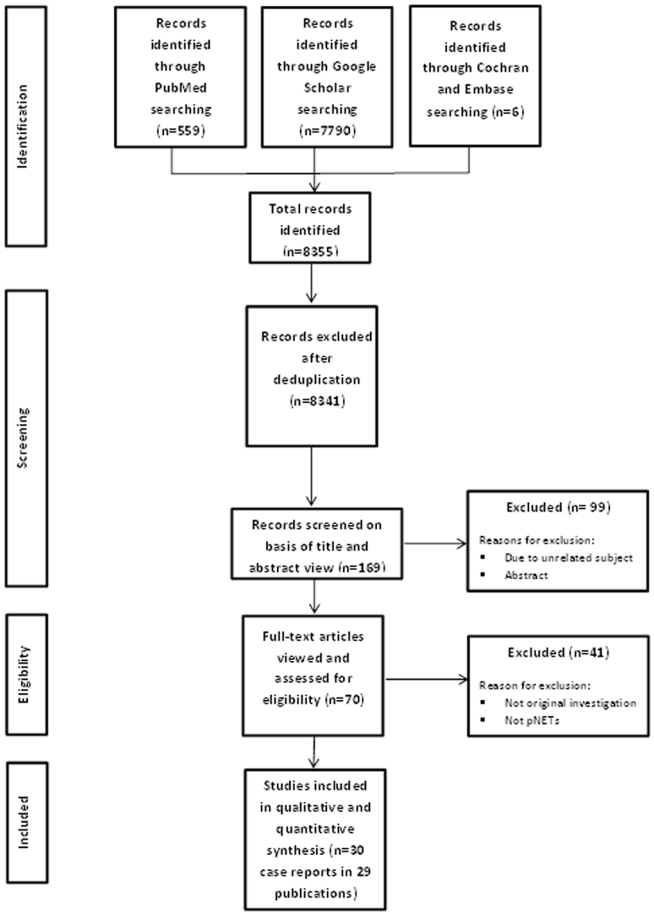

Figure 1: Workflow for identification of clinical studies. pNETs, pancreatic neuroendocrine tumors

Study design and settings

In this retrospective study, all patients of vipoma were investigated. Clinical features, laboratory data at initial presentation, management and outcomes were collected.

Definition

All patients of pNETs since neonate to old-age were investigated. Prevalence of primary and metastatic sites in these patients assessed. Moreover, all symptoms and signs of patients at initial presentation were extracted from articles. Serum electrolytes, creatinine, glucose, hormones, arterial blood gas was investigated in this study. Furthermore, diagnostic methods, treatment modalities and outcomes were examined.

Statistical analysis

Categorical variables are recorded as frequency (N) and percentage (%). Continuous variables are reported as mean ± standard deviation (SD). Comparisons between variables were assessed by F test and two-tailed *t* test analysis. Significance was assessed with *P* value of <0.05.

Results

Patient's characteristics

This study selected 30 patients and demographic characteristics of VIPoma are summarized in ' Table 1'. Mean (± SD) age of patients at time of diagnosis was 50 ± 17.85 years (ranging from 2 to 80 years). Of these, 15 patients (15/30, 50%) were male and 15 patients (15/30, 50%) were female [Figure 2].[2-30]

Anatomic involvement of tumor

Prevalence of primary and metastatic sites of tumors include pancreas (29/30, 96.6%), liver (14/30, 46.6%), parathyroid and lymph nodes (3/30, 10%), adrenal gland, pituitary and duodenum (2/30, 6.6%), stomach, kidney, ovary and sigmoid colon (1/30, 3.3%).

Patient's complaints

Patient's history and physical examination are of paramount importance, especially in the setting of functional pNETs. It classically presents with severe secretory diarrhea with hypokalemia, dehydration and hypochlorhydria. In this

Table 1: Distribution of age, gender and mean age of vipoma patients

	Frequency (percent)	Mean±SD
Age (years)		
0-19	2/30 (66.6%)	7.5±5.5
20-39	5/30 (16.6%)	31.6±4.22
40-59	13/30 (43.3%)	50.7±4.35
60-79	8/30 (26.6%)	68.25±4.91
≥80	1/30 (3.3%)	
Gender		
Male	15/30 (50%)	
Female	15/30 (50%)	

study, all patients presented with watery diarrhea (30/30, 100%), 10 patients with dehydration (10/30, 33.3%), 9 patients with weight loss (9/30, 30%), 6 patients with generalized weakness (6/30, 20%), 5 patients with nausea and vomiting (5/30, 16.6%), 3 patients with increased bowel sounds, anorexia, fatique or tiredness, acute renal failure, skin lesions (3/30, 10%), 2 patients with muscle weakness, abdominal pain, epigastric pain (2/30, 6.6%), one patient with left-sided weakness, acute flaccid bilateral lower limb weakness, liver mass, asthenia or weakness or loss of energy and strength, malaise or a vague feeling of being unwell, erb's palsy, rectal pain, melena, epigastric mass, and chronic kidney disease (1/30, 3.3%) [Figure 3].

Laboratory measurements

Hypokalemia has been detected in 25 case reports (25/30, 83.3%), and it has been characterized as quantification in 21/30 patients (70%) that serum K levels were ranging from 1.5 mmol/l to 3.5 mmol/l with mean values of 2.23 ± 0.57 mmol/l. There was hypokalemia without mentioning quantification and missing data in 4 patients (4/30, 13.3%) and normal plasma potassium level in one patient (1/30, 3.3%). Elevated vasoactive intestinal peptide (VIP) levels have been seen in 23 (23/30, 76.6%) case reports that quantification has been reported in 22 (22/30, 73.3%) patients and amount in one patient (1/30, 3.3%) hasn't been reported. Mean values of VIP levels in these patients were 882.85 ± 1134.87 pg/ml. There were metabolic acidosis in 9 patients (9/30, 33.6%), hypercreatinemia in 7 patients (7/30, 23.3%), hypercalcemia in 6 patients (6/30, 20%), leukocytosis in 4 patients (4/30, 13.3%), hyperglycemia, hyperchloremia in 3 patients (3/30, 10%), achlorhydria, hypochloremia, elevated pancreatic polypeptide in two patients (2/30,6.6%%), and metabolic alkalosis in one patient (1/30, 3.3%). There were elevated intact parathyroid hormone (iPTH) with primary hyperparathyroidism in 2 patients (2/30, 6.6%) that were attributed to heterozygous mutation of MEN1 gene in genetic testing. This finding was infavor of MEN1-associated vipoma [Figure 4].

Diagnostic methods

There are different methods for diagnosis of vipoma such as ultrasonography, computed tomography (CT) scan, contrast-enhanced computed tomography (CECT) scan, magnetic resonance imaging (MRI), radiolabeled positron emission tomography-computed tomography (Radiolabeled PET-CT scan), gastrointestinal (GI) endoscopy, ultrasonography-guided needle biopsy, CT-guided needle biopsy, 99technetium-methoxyisobutylisonitrile parathyroid (99TC-MIBI) scintigraphy and somatostatin receptor scintigraphy (SRS) with radiocompound. In this study, diagnostic methods were used for vipoma in 28 patients (28/30, 93.3%), except 2 patients with pre-existing disease (2/30, 6.6%). CT scan was diagnostic modality in 19 patients (19/30, 63.3%), ultrasonography (US) in 15 patients (15/30, 50%), SRS in 8 patients (8/30, 26.6%), CECT in 7 patients (7/30, 23.3%), MRI, colonoscopy and upper GI endoscopy in 6 patients (6/30, 20%), US-guided biopsy in 3 patients (3/30, 10%), CT-guided biopsy, 99Tc-MIBI scintigraphy, contrast-enhanced MRI, MRI scan, endoscopic ultrasonography (EUS), selective angiography and lower GI endoscopy in 2 patients (2/30, 6.6%), triple-phase CT scan and contrast enhanced-multidetector computerized tomography (CE-MDCT) in one patient (1/30, 3.3%). Radio-labeled PET-CT scan and fine needle biopsy (FNB) through radio-labeled PET CT scan were diagnostic method in one patient (1/30, 3.3%). Other radiologic imaging modalities have been described completely in Figures 5 and 6].

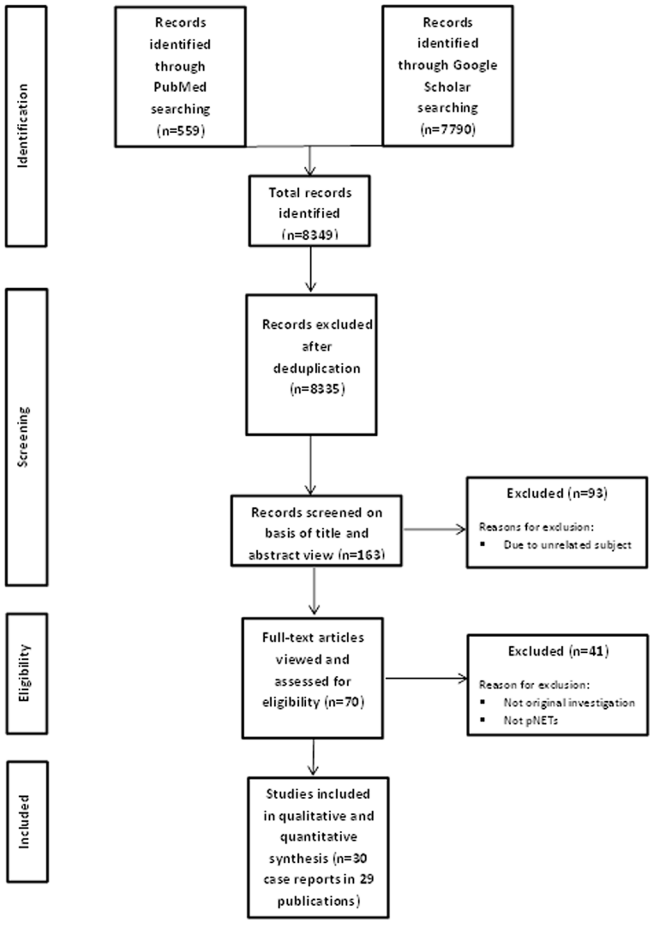

Figure 2: Distribution of vipoma in different ages in clinical studies

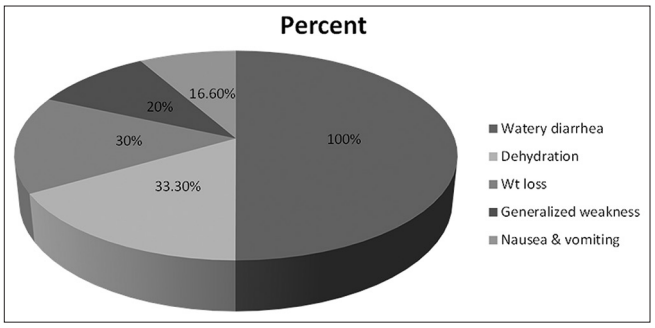

Figure 3: Distribution of symptoms in all patients of the study

Treatment

Medical treatments include somatostatin and its analogues in 18 patients (18/30,60%), potassium supplementation in 10 patients (10/30, 33.3%), symptomatic therapy e.g., oral rehydration and intravenous (IV) fluid therapy in seven patients (7/30, 23.3%), IV antibiotic therapy in 3 patients (3/30,10%), antispasmodic agents including diosmectite, diphenoxylate and loperamide, chemotherapy including capecitabine, capecitabine/temozolomide, sunitinib and mammalian target of inhibitors (TOR) inhibitors (everolimus) and steroids in 2 patients (2/30, 6.6%), radiolabeled somatostatin analogues, rituximab, roferon (interferon alpha), IV zoledronic acid therapy, chemotherapy with temozolomide, cetuximab, 5-flourouracil, streptozocin, STZ/5-FU, chemoablation with mitomycin, cisplatin, doxorubicin and blood transfusion in one patient (1/30, 3.3%). Liver-directed therapies including hepatic artery embolization and thermoablation of hepatic metastasis in one patient (1/30, 3.3%) [Figure 7]. Surgical treatments include simple enucleation, distal pancreasectomy with or without splenectomy, central pancreasectomy, whipple's pancreatico-duodenectomy, total pancreasectomy, Roux-en-Y procedure, partial and total hepatectomy. In this paper, surgical treatment include distal or caudal pancreasectomy, pylorus-preserving pancreatoduodenectomy plus resection of two tumor and exploratory laparotomy in 2 patients (2/30, 6.6%), Roux-en-Y, whipple procedure, caudal pancreasectomy plus splenectomy, caudal pancreasectomy plus splenectomy plus total hepatectomy, pancreatectomy plus splenectomy plus radiofrequency ablation (RFA) of liver metastasis plus hepatic artery embolization (HAE) plus salpingoophorectomy, pancreaticoduodenectomy plus wedge resection of liver metastasis, body-caudal pancreasectomy plus splenectomy plus left hepatic trisegmentectomy, surgical resection of pancreatic vipoma with gastrointestinal stromal tumor (GIST), head and body resection of pancreas in laparotomy plus left nephrectomy and resection of metastatic nodules of liver and pylorus-preserving pancreaticoduodenectomy plus regional lymphadenectomy plus hepatic resection plus wirsung-jejunostomy in one patient (1/30, 6.6%).

Outcome

Outcome of patients include time lapsed after onset of symptoms (initial time of asymptomatic period) or symptomatic improvement especially diarrhea, recurrence of laboratory findings [hypokalemia, elevated VIP and chromogranin A (CgA)], recurrence of radiological imagings (US, CT scan, MRI), nuclear scintigraphy (octreoscan, VIP scintigraphy)

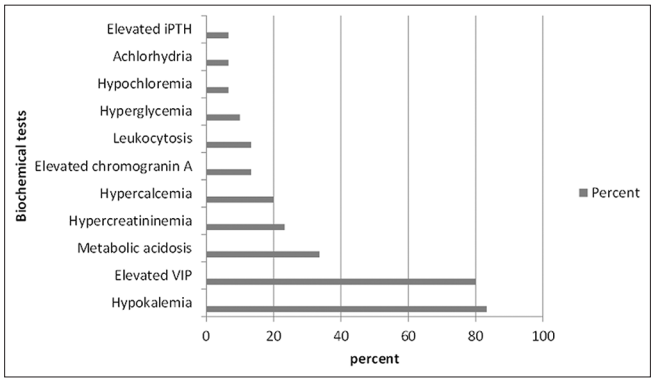

Figure 4: Distribution of laboratory data in all patients of this study

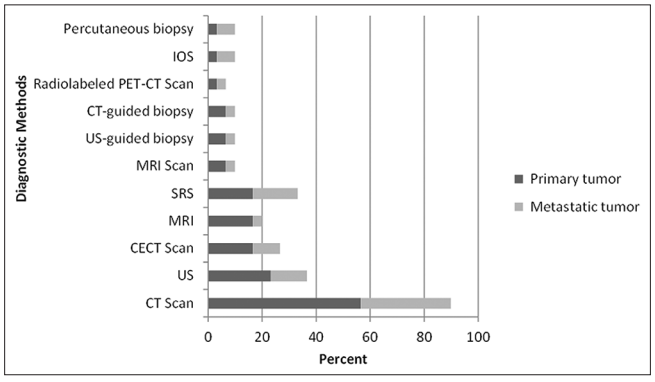

Figure 6: Distribution of used diagnostic methods in diagnosis of primary and metastatic tumors. CECT, contrast-enhanced computerized tomography; IOS, intraoperative sonography; SRS, somatostatin receptor scintigraphy; US, ultrasonography

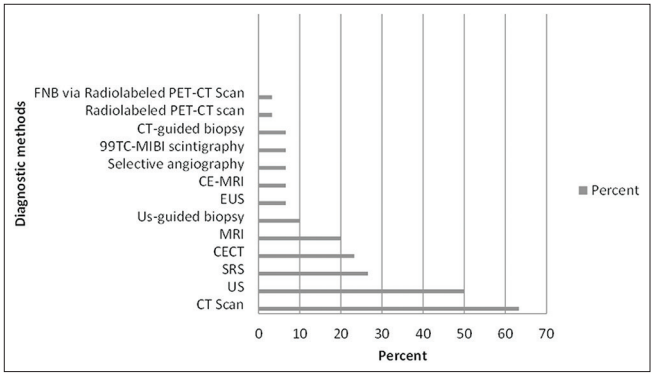

Figure 5: Distribution of diagnostic methods in all patients of this study. CECT, contrast-enhanced computerized tomography; EU, ultrasonography; EUS, endoscopic ultrasonography; MRI, magnetic resonance imaging; PET-CT Scan, positron emission tomography-computerized tomography; SRS, somatostatin receptor scintigraphy

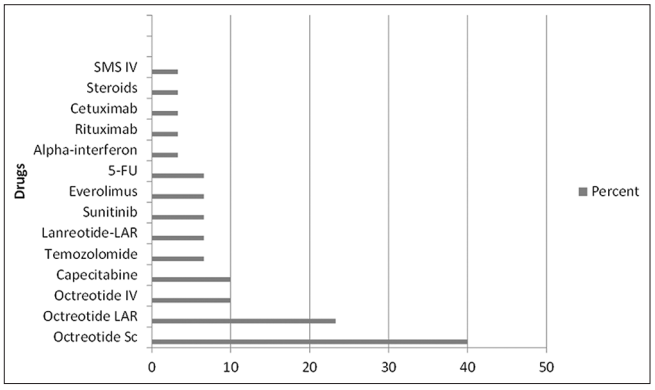

Figure 7: Distribution of used drugs in all patients of this study. 5-FU, 5-fluorouracil; Octreotide LAR, octreotide long-acting repeatable; Sc, subcutaneous; SMS, somatostatin intravenous

and death. There were symptomatic improvement of diarrhea after surgery or starting drug in 29 patients (29/30, 96.6%) and missing data in one patient (1/30, 3.3%). Lapsed time after onset of symptoms (asymptomatic time) has been characterized in 24 patients (24/30, 80%). There was unrecognized time of disappeared symptoms in 6 patients (6/30, 20%). Lapsed time after onset of symptoms (disappeared time of symptoms after initial presentation) have been estimated with mean ± SD of 2.41 ± 5.46 months. In reported lapsed time after onset of symptom (initial time of asymptomatic period), two groups of age between male and female were compared that mean ± SD of ages in 14 male patients (n = 14/24, 58.3%) has been reported 54.14 ± 14.33 years. Mean ± SD of ages in 10 female patients (n = 10/24, 41.6%) has been reported 47.1 ± 19.57 years. Mean difference between 2 variables (two age groups in males and females) was assessed with *P* value of 0.37. There was recurrence of diarrhea in 4 patients (4/30, 13.3%) during follow-up that symptoms disappeared in one patient (1/30, 3.3%) after 3 years. Potassium normalization has been occurred after surgery or drug treatment in 5 patients (5/30, 16.6%) and there was persistent hypokalemia in one patient (1/30, 3.3%). There were elevated CgA in 2 patients (2/30, 6.6%) during follow-up. Decreased VIP levels to normal (< 75 pg/ml) have been seen in 15 (15/30, 50%) of case reports that these levels have been reported as quantitative amount after surgery or drug treatment in 10 patients (10/30, 33.3%). There were elevated VIP levels after surgery, drug treatment or during follow-up in two patients (2/30, 50%) with mean ± SD of 24.58 ± 14.57 in males and 25.82 ± 14.93 in females (*P* = 0.93) [Table 2]. There were elevated CgA in two patients (2/30, 6.6%) during follow-up. Ultrasound in follow-up has been performed in one patient (1/30, 3.3%) that was detected no recurrence. There were recurrence in CT scan in 4 patients (4/30, 13.3%) and prevalence of recurrence in liver was reported in 3 patients (3/30, 10%) during follow-up. There were lymph node and ovary recurrence in one patient with equal rate (1/30, 3.3%). MRI has been performed in 5 patients (5/30, 16.6%) that liver metastasis was detected in one patient (1/30, 3.3%). Nuclear scintigraphy has been performed in 3 patients (3/30, 10%): one VIP scintigraphy and 2 SRS scintigraphy. There were no tumor recurrence on VIP scintigraphy and OctreoScan during 14 and 6 weeks follow-up, but there was recurrence in one patient (1/30, 3.3%) at 6 and 15 months surveillance. There were regular follow-up in 14 patients (14/30, 46.6%) with mean ± SD duration of 12.06 ± 10.38 months. 3 patients (3/30, 10%) died due to complications such as pancreatic abscess, pulmonary sepsis and sepsis/denutrition. 8 patients (8/30, 26.6%) were alive and symptom-free during the mentioned follow-up duration [Figure 8].

Table 2: Comparison of mean age of asymptomatic patients, mean age of succumbed patients and mean of vasoactive intestinal peptide (VIP) levels between two groups of sex in outcomes

Characteristics	Variable 1 (Male) Mean±SD	Variable 2 (Female) Mean±SD	*P*
Age (years)	47.1±19.57	54.14±14.33	0.37
VIP level	24.58±14.57	25.82±14.93	0.93
Mortality age (years)	-	46.66±16.21	-

VIP levels <75 pg/ml is considered as normal

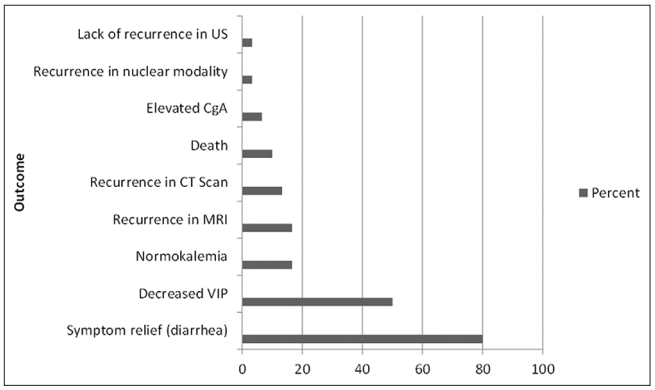

Figure 8: Distribution of outcomes of all patients of this study. Outcomes of vipoma patients include symptomatic improvement, recurrent tumor or lack of tumor recurrence in laboratory findings, imaging studies and survival or death. CgA, chromogranin A; CT Scan, computerized tomography; MRI, magnetic resonance imaging; VIP, vasoactive intestinal peptide; US, ultrasonography

Discussion

Pathogenesis

The pathogenesis of pNETs is largely unknown but is growing as a research topic. Approximately 10% of all pNETs are component of familial endocrine tumor syndromes such as MEN-1, von hippel-lindau disease, neurofibromatosis type 1 and tuberous sclerosis. The etiology of pNETs within the context of these familial syndromes is the inherited germline loss of the respective tumor suppressor gene. Several studies have been performed on the pathogenesis of sporadic pNETs, which comprise 90% of all pNETs. Loss of chromosome 1,3p, 6q, 11p or 22q and gains of chromosome 4 or 9q have been observed in pNETs. It is assumed that the loss of a tumor suppressor gene or the gain of an oncogene is the mechanism by which chromosomal alterations cause pNETs, but stochastic chromosomal number changes are also possible. Cyclin D1 oncogene has identified an important role in pathogenesis of human pancreatic endocrine tumors (PETs).[31] In this study, 6.6% of patients inherited vipoma as one of multiple endocrine neoplasia (MEN1) - associated tumors.

Clinical manifestations

VIPomas represent less than of ten percent of functional pNETs and secret vasoactive intestinal polypeptide leading to verner-morrison syndrome, also known as WDHA syndrome or pancreatic cholera, characterized by watery diarrhea, hypokalemia, hypochlorhydria, hyperglycemia, hypercalcemia and dehydration.[32] In this study, all patients presented with watery diarrhea (30/30, 100%), dehydration (10/30, 33.3%), weight loss (9/30, 30%), generalized weakness (6/30, 20%) and other symptoms and signs that above mentioned completely.

Diagnosis

American society concerns diagnostic pathway, imaging techniques [i.e., ultrasound or contrast-enhanced computed tomography or magnetic resonance] are necessary to detect both the primary tumor and metastases. Somatostatin receptor scintigraphy is suggested to detect metastases, including extrahepatic disease, although positron emission tomographic using 68 gallium (68 Ga) appears to be more sensitive, particularly in case of small lesions. Radiolabeled (with Tc-99m, In-111or Ga-68) somatostatin analogs have been used for imaging of NETs. Ultrasound endoscopy is recommended to small pancreatic tumors and to achieve a diagnosis by means of fine needle aspiration. The combination of endoscopic ultrasonography and somatostatin receptor scintigraphy may be able to provide most of the information required preoperatively and seems to be the optimal approach available to date.[33] Laboratory tests, including CgA, pancreatic polypeptide and specific hormones according to clinical presentation should be performed in all patients at the diagnosis and during follow-up. To date, the most widely accepted test for NETs has been CgA. An increased CgA level is 'generally considered' to be sensitive, ~60-90%, and accurate once an NET has been identified. It is however an ineffective first-line diagnostic marker.[34] Study by Zatelli *et al.* indicated that CgA serum levels can be helpful for the clinical management of NETs, but with low sensitivity and specifity for diagnostic purposes. On the other hand, the main utility of CgA measurement may be in patient monitoring.[35] CgA has been described to be the best marker in patients with NETs in both sporadic and MEN1-related forms, and the highest CgA values usually occur in patients with metastatic disease.[36] In this study, diagnosis of vipoma was established in accordance with clinical symptom of diarrhea (30/30, 100%), imaging studies (28/30, 93.3%), hypokalemia (25/30, 83.3%) and VIP levels (23/30, 76.6%) in patients. Moreover, Al-Risi *et al.* in a retrospective study evaluated diagnostic utility and limitations of chromogranin A as a biomarker for NETs in a tertiary care hospital in Oman. Authors concluded that serum CgA is a sensitive and effective noninvasive laboratory test for the clinical detection and management of NETs.[37]

Differential diagnosis

Causes of secretory diarrhea in adults of the developed countries include laxative abuse, carcinoid syndrome, microscopic colitis, and bile salt malabsorption due to ileal resection. Though more common in the developing countries, diarrhea due to infection from vibrio cholera, enterotoxigenic Escherichia coli may also need to be ruled out after careful assessment of the history. Secretory diarrhea may occasionally occur in association with gastrointestinal disorders like crohn´s disease and the short bowel syndrome. In rare cases, Munchausen syndrome by proxy may also need to be ruled out. In children, rarely inherited electrolyte transport defects, like congenital chloride diarrhea and congenital sodium diarrhea, may cause secretory diarrhea. These present in early infancy.[38]

Treatment

Because most pNETs are indolent, a wait-and-see approach has historically predominated. The treatment strategy for pNETs has undergone a paradigm shift in the last 10-20 years. An aggressive approach has become popular in academic centers throughout the world. The aggressive approach is based on the reasonable assumptions that patients benefit from reducing the tumor burden and that interventions are increasingly safer in academic centers. Therefore, the aggressive approach advocates removing as much of primary and metastatic tumors as possible. Although no prospective randomized trials have been performed to study the efficacy and safety of the aggressive method and experience confirming it. Surgery therefore remains the only curative approach for neuroendocrine tumors whenever possible; in case of poorly differentiated tumors; surgery as well as other liver-directed therapies such as embolization are almost never applicable, and these patients are mainly managed with chemotherapy. In case of functioning well-differentiated neuroendocrine tumors, it is important to control the hormone hypersecretion, which determines symptoms, usually by the administration of SSAs. Beside surgery, a variety of therapeutic options exist for metastatic neuroendocrine disease: i.e., locoregional therapies, medical therapy including chemotherapy, biotherapy with SSAs and IFN-alpha, and more recently the molecular targeted therapies and the systemic peptide receptor radionuclide therapy. Furthermore, in highly selected patients' orthotopic liver transplantation might be considered. In this study, medical treatments include somatostatin and analogues in 18 patients (18/30, 60%), potassium supplementation in 10 patients (10/30, 33.3%), symptomatic therapy e.g., oral rehydration and intravenous fluid therapy in 7 patients (7/30, 23.3%). Surgical treatment contained caudal pancreasectomy, pylorus-preserving pancreatoduodenectomy plus resection 2 tumor and exploratory laparotomy in 2 patients (2/30, 6.6%).

Other studies in different papers

In cohort study by Gunavathy *et al.*, they showed that patients with gasteroenteropancreatic-neuroendocrine tumors (GEP-NETs) in Malaysia commonly presented late in the disease with presence of distant metastases. Less than half had adequate hormonal and biochemical examinations performed for diagnostic as well as prognostic purposes, and only a third received systemic therapy.[39] Morover, study by Crona *et al.*, a retrospective analysis of 972 patients with GEP-NETs treated in hospital. They concluded diversity of pNET hormone secretion either at diagnosis or during the disease course occurred in a minority of patients (9.3%). These phenomena had a major impact on patient outcome both through increased morbidity and mortality. Their results support that patients with metastatic pNETs should be monitored for clinical symptoms of secondary hormone secretion during the disease course.[40] Bloom and Polak reported 1000 adult patients with various forms of diarrhea. 39 (3.9%) patients had greatly elevated levels of VIP, and in each case, a tumor was found. In

more than 50% of these patients, the tumor was successfully removed, the symptoms remitted, and the plasma levels of VIP returned to normal. Twelve patients had diarrhea secondary to thyrocalcitonin (TCT) - producing tumors of the thyroid, 13 had carcinoma of the lung, 4 had a villous adenoma of the rectum, and 24 had carcinoid tumors. All 53 of these patients had normal plasma VIP levels. Additional eleven patients had classic clinical features of the VIPoma syndrome in whom VIP levels were normal and no tumor was found. They probably were secreting an unidentified humoral substance with the biological properties of VIP.

Conclusion

The clinical symptoms that accompany VIPoma most commonly include watery diarrhea, hypokalemia and achlorhydria (or metabolic acidosis). This collection of symptoms is also known as WDHA syndrome. Timely diagnosis and appropriate treatment of vipoma prevent hazardous complications of this entity. Ongoing research is needed for more identification of disease and detection of newer tumor markers for early detection, adequate treatment and metastatic prevention.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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