such as azathioprine could be used for

Furthermore, immunosuppressive agents

who did not achieve complete remission.

and remission maintenance was needed to

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et al3 including 215 patients, the mean

patient is extreme hyperglobulinemia,

followed up.

ened bile duct normalized (Figs. 1F , G), as

that the enlarged pancreatic head and thick-

appeared. The following imaging showed

the albumin level increased, and edema dis-

91.13 g/L to 17.79 g/L. In the meantime,

IgG4 decreased from 31.5 g/L to 6.25 g/L,

of the glucocorticoid response, the level of

as empirical therapy and tapered down to

opsy or pancreatic fine-needle aspiration to

as having possible IgG4-related AIP . Be-

Therefore, the patient was suspected

as having possible IgG4-related AIP. Be-

cause he refused to undergo lymph node bi-

opsy or pancreatic fine-needle aspiration to

exclude malignancy, he was prescribed as

prednisone 0.6 mg/kg per day for 1 month

as empirical therapy and tapered down to

5 mg/d as maintenance therapy. As a result of

the glucocorticoid response, the level of

IgG4 decreased from 31.5 g/L to 6.25 g/L,

the globulin decreased from 111 g/L to

31 g/L, and the IgG decreased from

91.13 g/L to 17.79 g/L. In the meantime,

the albumin level increased, and edema dis-

appeared. The following imaging showed

that the enlarged pancreatic head and thick-

ened bile duct normalized (Figs. 1F, G), as

well as the enlarged lymph nodes. The patient

was, and is still currently, being followed up.

The specific characteristic of our AIP

patient is extreme hyperglobulinemia,

which is uncommon. In the study by Wang

et al12 including 215 patients, the mean

levels of IgG and IgG4 were 23.0 and

15.2 g/L, respectively. Based on the previ-

ous research,3,5 high level of serum

IgG4 might be related to hematologic mani-

festations, good response to glucocorti-

coid, and a high rate of relapse. According to

the study from Kim et al9 in 2010, the

glucocorticoid dosage for inducing remis-

sion was 30 to 40 mg/d for 1 to 2 months, and

remission maintenance was needed to

prevent relapse with a dosage of 5 to

10 mg/d for at least 6 months in patients

who did not achieve complete remission.

Furthermore, immunosuppressive agents

such as azathioprine could be used for

relapsed patients with AIP. Our patient with

high level of serum IgG and IgG4 had good

response to glucocorticoid and no evidence of

relapse with 5 mg/d prednisone for

maintenance of remission.

Another special characteristic is long-
time course of disease. Autoimmune pan-

creatitis is one type of chronic pancreatitis,

but it is unknown how long the natural course is. Our patient was 78 years old and was found to have a swollen pancreatic head nearly 10 years before being diagnosed and treated with glucocorticoid. In the study by Lin et al with 118 Chinese AIP patients, the mean age at diagnosis was 53.1 years, and the mean disease duration was 26.8 months.7 Therefore, our pa-

tient with a 108-month disease course is truly unusual.

From this AIP case, we illustrated that a high level of serum IgG4 might indicate good sensitivity to glucocorticoid, and el-
derly patients might endure a long course of disease without symptoms. Although this patient had a good condition at present, we still should be aware of the relapse of disease and the risk of hematologic malign-
ancy in the follow-up.

The authors declare no conflict of interest.

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Letters to the Editor

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Surgical Treatment of Pancreaticoduodenal Artery Aneurysm Due to Median Arcuate Ligament Syndrome for Which Intraoperative Doppler Ultrasonography Was Beneficial

A Case Report

To the Editor:

A lthough the first case of a pancreatic-

oduodenal artery aneurysm (PDAA) was reported by Ferguson1 in 1895, most of the publications since then have been case reports. Pancreaticoduodenal artery aneurysms are rare and account for 2% of all visceral aneurysms.2 Almost half of all PDAAs are associated with celiac axis stenosis (CAS)3 and median arcuate

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Pancreaticoduodenal artery aneurysms are usually asymptomatic, and a ruptured aneurysm is often fatal if untreated. The aneurysmal size is unrelated to the risk of rupture, so all PDAAs should be treated, regardless of size.3

Two treatment approaches, surgical resection or embolization, are currently followed. Embolization is less invasive but may cause intraoperative aneurysmal rupture or ischemic injury due to the absence of major collateral vessels.4 In addition, without CAS repair, new aneurysms or recurrence may occur. At present, no consensus exists in the literature on the management of PDAAs with MALS. Importantly, although surgical resection of PDAAs is curative, they involve the risk of life-threatening ischemic complications.5,6

Doppler ultrasonography can be used to assess the blood flow qualitatively and quantitatively during liver transplantation.7,8 The normal Doppler waveform of a hepatic artery shows a rapid systolic upstroke after continuous diastolic flow. Acceleration time and RI can serve as indicators of hepatic arterial blood flow. Acceleration time, the time from the end of diastole to the first systolic peak, should be less than 80 ms; RI, calculated as (peak systolic velocity – end diastolic velocity)/peak systolic velocity, should be between 0.5 and 0.7.7 A tardus-parvus waveform pattern, with an acceleration time greater than 80 ms and a RI less than 0.5, indicates insufficient arterial flow due to hepatic artery stenosis during liver transplantation.8 In our case, although the acceleration time was not measured during the clamping test, the peak and mean velocities and RI were decreased reproducibly in comparison with the baseline levels.

A reproducible decrease in hepatic arterial blood flow during the GDA clamping test necessitates MAL release. Moreover, recovery to baseline blood flow levels after MAL release eliminates the need for additional hepatic artery reconstruction. Because PDAAs with MALS are rare, the criteria may appropriately be determined using liver transplant surgery data. Large studies on hepatic artery assessment using Doppler ultrasonography are needed to define the threshold for MAL release or hepatic artery reconstruction during the resection of PDAAs with MALS.

CONCLUSIONS

The intraoperative quantitative evaluation of hepatic arterial blood flow using Doppler ultrasonography enabled successful resection of the PDAAs because of MALS.

The authors declare no conflict of interest.

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Validation of the Novel Eighth Edition of American Joint Committee on Cancer Staging Manual: An In-depth Analysis for Nonfunctional Pancreatic Neuroendocrine Neoplasms

Pancreatic neuroendocrine neoplasms (pNENs) are a group of tumors with a varied behavior, course, prognosis, and increasing prevalence, which consist of functional tumors (F-pNENs) and non-functional ones (NF-pNENs).1 Because of the rarity and heterogeneity, the ability to stage pNENs into prognostic groups has always been challenging. In 2010, the World Health Organization classified pNENs into well-differentiated pancreatic neuroendocrine tumors (G1/G2 pNETs) and poorly differentiated pancreatic neuroendocrine carcinoma (G3 pNECs).2 Also in 2010, the American Joint Committee on Cancer (AJCC) started to introduce a tumor-node-metastasis (TNM) system for pNENs (ie, seventh edition),3 which derived from the staging algorithm for pancreatic exocrine adenocarcinomas (pEACs) and was proven to be convenient but oversimplified.4–7

In 2017, AJCC incorporated some major changes in its eighth staging manual for both pEACs and pNENs, in which the new staging system for pNENs should only be applied to G1/G2 pNETs, whereas G3 pNECs should be classified according to the new one for pEACs.8 We have evaluated the applications of the AJCC eighth staging manual for G3 pNECs9 and G1/G2 pNETs.10 However, both studies enrolled a large portion of F-pNENs, especially insulinoma, which inevitably increased the heterogeneity of pNENs and influenced the accuracy of related analysis. Moreover, we have also demonstrated that F-pNENs and NF-pNENs should better be staged according to a different TNM system.11 In order to more accurately validate the AJCC eighth staging manual, we comprehensively analyzed the distribution characteristics and survival differences of AJCC eighth and seventh staging systems for both G1/G2 NF-pNETs and G3 NF-pNECs.

Our analysis enrolled 230 consecutive patients with NF-pNENs, including 152 cases with G1/G2 NF-pNETs, and 78 with G3 NF-pNECs (Fig. 1). For G1/G2 NF-pNETs, according to the definitions of different staging systems, 52 patients were grouped in AJCC eighth stage I, 40 in stage II, 41 in stage III, and 19 in stage IV, with an estimated 5-year overall survival (OS) of 81.9%, 76.9%, 34.9%, and 19.2%, respectively. Survival comparisons between AJCC eighth edition stage I and stage II (P = 0.017), or stage III (P < 0.001), or stage IV (P < 0.001), between stage II and stage III (P = 0.008), or stage IV (P < 0.001), between stage III and stage IV (P = 0.044) were all statistically significant. What’s more, there were, respectively, 71, 42, 20, and 19 classified from AJCC seventh edition stage I to stage IV, with an estimated 5-year OS of 79.7%, 61.6%, 39.3%, and 19.2%, respectively. Survival of patients in AJCC seventh stage I was notably better than that of patients in stage II (P = 0.016), or stage III (P < 0.001), or stage IV (P < 0.001), as well as those in stage II compared with stage IV (P = 0.001), while comparisons between stage III and stage II or stage IV were not significant (P = 0.111, P = 0.133, respectively). For G3 NF-pNECs, there were 17 patients defined in the AJCC eighth edition as stage I, 19 in stage II, 24 in stage III, and 18 in stage IV, with an estimated 5-year OS of 66.6%, 34.6%, not applicable (NA), and NA, respectively. Survival comparisons between AJCC eighth edition stage I and stage II (P = 0.035), or stage III (P < 0.001), or stage IV (P < 0.001), between stage II and stage III (P = 0.044), or stage IV (P < 0.001), between stage III and stage IV (P = 0.027) were significant as well. Moreover, 23, 21, 16, and 18 patients were, respectively, defined from AJCC seventh edition stage I to stage IV, with an estimated 5-year OS of 57.2%, 44.2%, NA, and NA. Patients in AJCC seventh stage I present a notably longer survival than those in stage II (P = 0.021), or stage III (P < 0.001), or stage IV (P < 0.001), as well as those in stage II compared with stage IV (P = 0.001), whereas comparisons between stage III and stage II or stage IV were not significant (P = 0.079, P = 0.126, respectively).

For both G1/G2 NF-pNETs and G3 NF-pNECs, the AJCC seventh edition system failed to discriminate the survival differences when comparing stage III with stage II or stage IV using Cox proportional hazards model, the AJCC eighth and seventh staging system was demonstrated to be independent predictors for the OS of NF-pNENs. The Harrell’s C-index of AJCC eighth system for G1/G2 NF-pNETs and system for G3 NF-pNECs was both statistically larger than that of AJCC seventh system, indicating a more informative ability about prognostic accuracy.

In conclusion, based on the results of previous studies,9,10 our analysis revealed the 2 AJCC eighth staging systems were also

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