Pancreatology 19 (2019) 10–16

Contents lists available at ScienceDirect

Pancreatology

journal homepage: www.elsevier.com/locate/pan

Epidermoid cyst in intrapancreatic accessory spleen: A systematic review

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ARTICLE INFO

Article history:
Received 15 September 2018
Received in revised form
16 October 2018
Accepted 21 October 2018
Available online 22 October 2018

Keywords:
Epidermoid cyst
Intrapancreatic accessory spleen
Epidemiology
Diagnosis
Treatment

ABSTRACT

Background/Objectives: Due to its rarity, epidermoid cyst in intrapancreatic accessory spleen (ECIPAS) is still a diagnostic dilemma during clinical practice. The aim of this review was to summarize the epidemiologic features and management of ECIPAS.
Methods: MEDLINE and EMBASE were searched for English articles reporting on ECIPAS up to April 30th, 2018 following the methodology suggested by the PRISMA guidelines. Categorical variables were reported as frequency and percentage. Continuous variables were reported as median (range).
Results: A total of 56 patients from 47 full articles were included for the final data synthesis. More than half of the ECIPASs (59%) were found incidentally. The female/male ratio was 1.33. ECIPAS is typically a single mono-/multi-lobular cystic lesions in the pancreatic tail with thickened cystic wall or various amount of solid component which had identical density/signal to the spleen on imaging examinations. The cyst is filled with serous or non-serous fluid. Recognition of the surrounding ectopic splenic tissue is the key point to diagnose ECIPAS. However, no preoperative examination was able to make a definite diagnosis. Almost all the patients (96%) received surgical treatment, due to the suspicion of pancreatic malignant or potentially malignant cystic tumor, especially mucinous cystic neoplasm (MCN).
Conclusions: Although seldom encountered, ECIPAS should be considered as a differential diagnosis for pancreatic cystic lesions, especially when solid component was detected. As a benign disease, unnecessary surgery should be avoided. Because it is difficult to make a definite diagnosis preoperatively by one single examination, multiple modalities may be required.

Introduction

Accessory spleen (AS), a congenital abnormality, develops through fusion failure of multiple splenic anlages [1]. Intrapancreatic accessory spleen (IPAS) is the second most common type with 11–17% of AS, and are generally located in the pancreatic tail [2,3]. Microscopically, IPAS is structurally identical to several other conditions, including; epidermoid cysts, lymphoma and leukemia, and can involve AS to the same extent as the spleen [4]. Splenic cysts are uncommon with incidence rate of 0.5% across the splenectomized patient population [5] and a further 0.08% diagnosed at autopsy [6]. Epidermoid cysts in the intrapancreatic accessory spleen (ECIPAS) is exceedingly rare and seldom encountered in clinical practice as most are relatively small and do not cause clinical symptoms. Unsurprisingly, articles reporting ECIPAS findings are limited to case reports or case series. This limited evidence-base is therefore unable to support practitioners with a diagnostic consensus.

Abbreviations: AS, accessory spleen; ADC, apparent diffusion coefficient; CA19-9, carbohydrate antigen 19–9; CEA, carcinoembryonic antigen; CT, computed tomography; CTA, computed tomographic arteriography; CE-CT, contrast-enhanced CT; CE-MRI, contrast-enhanced MRI; CE-US, contrast-enhanced ultrasonography; DWI, diffusion-weighted MRI; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasonography; ECIPAS, epidermoid cysts in IPAS; FNA, fine needle aspiration; IPMN, intraductal papillary mucinous neoplasm; ITP, idiopathic thrombocytopenic purpura; IPAS, intrapancreatic accessory spleen; MCN, mucinous cystic neoplasm; MRI, magnetic resonance imaging; nCLE, needle-based probe confocal laser endomicroscopy; p-net, pancreatic neuroendocrine tumor; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RES, reticuloendothelial system; SI, signal intensity; SPT, solid pseudopapillary tumor; SPIO, superparamagnetic iron-oxide; US, ultrasonography; USPSTF, United States Preventive Services Task Force; 99mTc-HDRBC, 99mTechnetium heat-damaged red blood cells; 99mTc-colloid, 99mTechnetium colloid.

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https://doi.org/10.1016/j.pan.2018.10.008
1424-3903/

ECIPAS is a non-neoplastic entity and does not pose a threat to life, and generally does not even require therapeutic intervention. Exceptionally, treatment may be required where ECIPAS combines with idiopathic thrombocytopenic purpura (ITP) or when symptoms manifest due to compression [7,8], torsion, spontaneous rupture or hemorrhage. However, almost all ECIPASs are diagnosed through postoperative pathology due to the misdiagnosis of potentially malignant cystic neoplasms of the pancreas such as mucinous cystic neoplasm (MCN), intraductal papillary mucinous neoplasm (IPMN), solid pseudopapillary tumor (SPT) or cystic pancreatic neuroendocrine tumor (p-net) [9,10]. Therefore, an accurate preoperative diagnosis is extremely important to avoid unnecessary surgery and the negative impact on individuals whom have received unnecessary invasive treatments. The aim of this systematic review is to synthesize best-evidence around epidemiologic features, the clinical manifestations, tumor biomarker abnormalities, as well as imaging characteristics of ECIPAS in order to develop both policy and to determine best clinical practice.

Materials and methods

Literature search

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines was followed when performing and reporting this systematic review [11]. Two researchers (BQL and JL) independently performed an online literature search of MEDLINE (via Pubmed) and EMBASE (via Embase.com) up until April 30th, 2018. No filters regarding study type, language, or time period was applied. The "related article" function was used to expand the search. The search terms are shown below.

MEDLINE (via Pubmed):

#1 "accessory spleen" OR splenu*; #2 pancrea* OR intrapancrea*; #3 1# AND 2#

EMBASE (via Embase.com):

#1 'accessory spleen'/exp OR 'accessory spleen'; 2# splenu*; 3# pancrea* OR intrapancrea*; #4 (#1 OR #2) AND 3#

Studies selection

All ECIPAS studies were collected, without stipulating study type. Only English articles reporting demographic and clinical data, including; age, gender, symptoms, serological anomalies, imaging, treatment and pathology diagnosis, were included. Articles reporting IPAS as well as IPAS with other combined lesions, were excluded. Only ECIPAS studies were eligible for inclusion. Where dual (or multiple) studies were reported by the same institution/authors, repeat patients were excluded and primary data from individual patients were combined. Conference abstracts, letters, editorials, retrospective studies, expert opinions and reviews without original data for further synthesis were excluded. Two reviewers (BQL and JL) screened titles and abstracts. All articles deemed eligible for inclusion were read in full by both reviewers. Additional studies were sought through references included within eligible articles, as recommended by the Cochrane Handbook for Systematic Reviews [12]. Any discrepancies between reviewers were resolved through discussion with a third reviewer (JCG).

Data extraction and study quality assessment

Two reviewers (BQL and JL) extracted data independently, using a standardized form. The following information was extracted when available for each ECIPAS patient: author/s, year of publication, study design, age, gender, symptoms, lesion size, lesion location, serum carbohydrate antigen 19–9 (CA19-9), carcinoembryonic antigen (CEA), imaging examination e.g. ultrasonography (US), contrast-enhanced ultrasonography (CE-US), contrast-enhanced CT (CE-CT), magnetic resonance imaging (MRI), nuclear medicine examination, endoscopic retrograde cholangiopancreatography (ERCP), endoscopic ultrasonography (EUS), computed tomographic arteriography (CTA), fine needle aspiration (FNA) pathology, postoperative pathology, preoperative diagnosis and treatment. All pertinent texts, tables, and figures were also reviewed for data extraction. Disagreement was addressed by a third author (JCG) in order to reach a consensus. Primary data are summarized in Supplementary file 1. The United States Preventive Services Task Force (USPSTF) rating criteria [13] was used to assess study quality.

Statistical analysis

Categorical variables were reported using frequency and percentage. Continuous variables were reported with a median and corresponding range.

Results

A total of 47 full articles containing 56 patients were included for synthesis (Fig. 1). Most ECIPASs were detected as incidental findings and presented as solitary mono-/multi-lobular cystic lesions in the pancreatic tail with a thickened cystic wall or with varying amounts solid components which had identical density/signalling according to spleen imaging. Almost all (96%) patients underwent unnecessary surgical treatment because of the suspicion of malignancies or potentially malignant pancreatic cystic neoplasm, and specifically MCN and IPMN. Preoperative data and cyst features are shown in Tables 1 and 2. Preoperative diagnosis, diagnostic modality and treatment are summarized in Table 3.

Discussion

Splenic epidermoid cysts, lined with epithelial cells, are classified as true splenic cysts and account for approximately 20% of all splenic cysts [14]. Both epidermoid cyst of spleen accounting for 10% of true nonparasitic splenic cysts [6] and IPAS comprehensively reviewed previously [15] are rare, while ECIPASs are considered exceedingly rare [10]. Since the first ECIPAS case was diagnosed by Davidson et al., in 1980 [7], only 56 cases have been reported within the English language evidence-base and almost all extra-splenic epidermoid cysts are exclusively found in the IPAS [16].

ECIPAS is typically a solitary uni-/multi-lobular cyst in the pancreatic tail lined with keratinized/non-keratinized stratified squamous epithelium or cuboidal epithelium surrounded by normal splenic tissues [17,18]. A cyst contains either serous or non-serous fluids and the absence of skin appendages and mature lymphoid tissues are key factors used to differentiate epidermoid cyst from dermoid cysts and lymphoepithelial cysts [17,19].

As the surrounding splenic tissue is structurally and morphologically identical to normal spleen, it is estimated that ECIPAS has the same histogenesis as splenic epidermoid cysts [20]. Several hypotheses have been proposed about the origin of splenic epidermoid cysts, among which two are widely accepted. The first hypothesis is that a cyst may originate from invagination of capsular mesothelium with subsequent squamous metaplasia [21,22]. The second of which is based on the presence of a keratokine profile of splenic cyst, and stipulates that an epidermoid cyst is of teratomatous derivation or from inclusion in fetal squamous epithelium [23]. Evidence is beginning to emerge and suggests that an epidermoid cysts are likely to originate from aberrant embryonic inclusion of the pancreatic duct epithelium [24] or from a

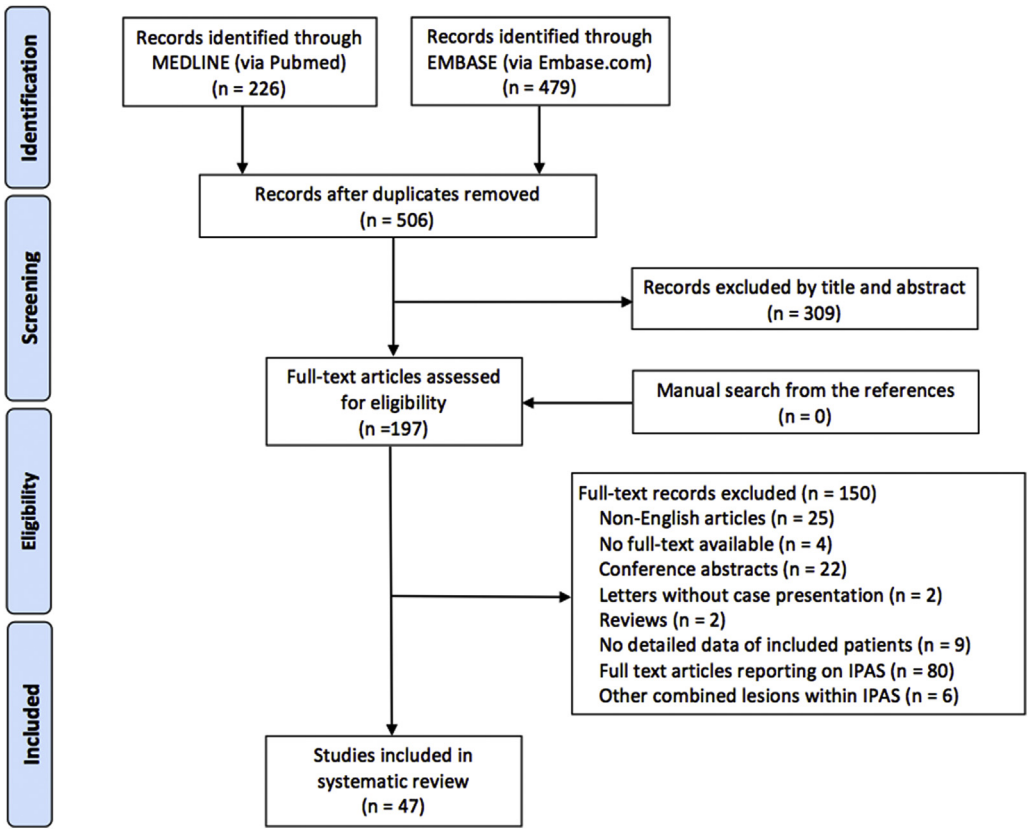

Fig. 1. The PRISMA flow chart for literature search.

Table 1
Patients' epidemiologic data, symptoms and cyst features.

Items		median (range), n/d (%)
Age (year)		47 (10–70)
	<40	20/56 (36)
	40 ≤ ≤ 65	33/56 (59)
	>65	3/56 (5)
Gender	female/male	1.33 (32/24)
Location	tail	56/56 (100)
	body	0/56 (0)
	head	0/56 (0)
Size (cm)		3.4 (1.3–15)
	<3 cm	23/56 (41)
	≥3 cm	33/56 (59)
Symptoms	incidental	33/56 (59)
	abdominal pain	12/56 (21)
	nonspecific gastrointestinal symptoms	11/56 (20)
	weight loss	4/56 (7)
	abdominal palpable mass	1/56 (2)
Cyst features	single cyst	49/55 (89)
	multiple cysts	6/55 (11)
	mono-lobular	28/47
	multi-lobular	19/47
	serous fluid	18/32
	non-serous fluid	14/32
	normal CA19-9	1/6
	elevated CA19-9	5/6
	normal CEA	2/9
	elevated CEA	7/9

CA 19–9: carbohydrate antigen 19–9; CEA: carcinoembryonic antigen.

protrusion of a pancreatic duct [25]. Firstly, normal pancreatic tissue was found intermingled with splenic tissue or located in the center of the IPAS [26]. Secondly, mono-layer cubical epithelium has been found to resemble the pancreatic duct in ECIPAS [20]. Thirdly, the epithelium in an ECIPAS demonstrates a distinct superficial CK20 immunostaining, which is a characteristic of the transitional epithelium [26], and the similarity between squamous epithelium and cuboidal epithelium suggests a transitional appearance from one to another [20]. Moreover, the epithelium in an ECIPAS is also immunohistochemically positive for CA19-9, sialylTn [27], CEA [28], PDX1 and cytokeratins [26] which are also positive within the pancreatic duct. However, some would argue that the ECIPAS is unconnected with pancreatic duct on MRCP [29] or ERCP [30] although this remains controversial.

CA19-9 and CEA are widely used tumor biomarkers for the evaluation of pancreatic masses. In the current study, a majority of patients were reported as having elevated levels of these tumor biomarkers which were suspected to be produced by the cyst epithelium based on positive immunohistochemical staining [27,28,31] and the postoperative normalization of these two tumor biomarkers [26,31,32]. However, the denominators were too small to generate conclusions about the degree of elevation.

ECIPAS usually presents as a single well-demarcated, uni-/multilobular cystic lesion with thickened cystic walls or with varying degrees of solid component in the pancreatic tail according to CE-CT. In the current study, thickened cystic walls and solid components were detected using CT scans in 62% patients. Hwang et al. reported that the cyst wall of ECIPAS is irregularly thickened, and their thickness is generally greater than that of typical pancreatic MCN or IPMN with a mean maximal thickness 5.2 mm and ranging from 1.0 to 11 mm [26]. Recognition surrounding ectopic splenic tissue is therefore a key factor in diagnosing ECIPAS [33]. Two specific features can help to identify ectopic splenic tissue on CE-CT. The first of which is that ectopic splenic tissue tend to have a similar density on both non-contrast and post-contrast scans [34]. The

Table 2
Preoperative examinations.

Examinations	Presentations	n/d (%)
Serum CA19-9	normal	17/37
	elevated	20/37
Serum CEA	normal	26/27
	elevated	1/27
Abdominal US	cystic lesion	23/23
CE-CT	consisting of only CC	20/52 (38)
	consisting of SC or TCW	32/52 (62)
	SC or TCW with enhancement	22/32
	SC or TCW with similar density or enhancement to spleen	9/32
	SC or TCW with calcification	3/32
MRI	CC with hypointensity on T1-WI	11/24
	CC with iso/hyperintensity on T1-WI	13/24
	CC with hyperintensity on T2-WI	22/24
	CC with hypointensity on T2-WI	2/24
	consisting of only CC	14/28
	consisting of SC or TCW	14/28
	SC or TCW with enhancement	5/12
	SC or TCW with similar SI to spleen	8/12
	SC or TCW with signal drop after SPIO on T2-WI	2/2
	SC or TCW with similar SI to spleen on DWI	2/2
EUS	consisting of only CC	9/22
	consisting of SC or mural nodule	13/22
FNA pathology	only cystic fluid	5/13
	cellular component	8/13
	consistent with spleen	2/8
	p-net	1/8
	non-diagnosis	5/8

CA 19–9: carbohydrate antigen 19–9; CEA: carcinoembryonic antigen; US: ultrasound; CE-CT: contrast enhanced computed tomography; CC: cystic component; SC: solid component; TCW: thickened cystic wall; MRI: magnetic resonance imaging; T1-WI: T1-weighted images; T2-WI: T2-weighted images; SI: signal intensity; SPIO: superparamagnetic iron-oxide; DWI: diffusion-weighted imaging; EUS: endoscopic ultrasound; FNA: fine needle aspiration; p-net: pancreatic neuroendocrine tumor.

Table 3
Preoperative diagnosis, diagnostic modality, and treatment.

Items		n/d (%)
Preoperative diagnosis	MCN/MCC	23/46
	IPMN	11/46
	SCN	7/46
	SPT	4/46
	cystic p-net	3/46
	pancreatic cystic neoplasm	8/46
	ECIPAS	5/46
	others	14/46
Diagnostic modality	postoperative pathology	53/56 (95)
	FNA pathology	1/56 (2)
	SPIO-enhanced MRI	1/56 (2)
	FNA pathology and SPIO-enhanced MRI	1/56 (2)
Treatment	non-surgical treatment	2/56 (4)
	surgical treatment	54/56 (96)
	open surgery	28/48
	minimal invasive surgery	20/48
	distal pancreatectomy	22/48
	distal splenopancreatectomy	24/48
	pancreatic tail cyst resection	2/48

MCN: mucinous cystic neoplasm; MCC: mucinous cystadenocarcinoma; IPMN: intraductal papillary mucinous neoplasm; SCN: serous cystic neoplasm; SPT: solid pseudo-papillary tumor; p-net: pancreatic neuroendocrine tumor; ECIPAS: epidermoid cyst in intrapancreatic accessory spleen; FNA: fine needle aspiration; SPIO: superparamagnetic iron-oxide; MRI: magnetic resonance imaging.

second is heterogeneous enhancement patterns during the arterial phase [35] which is caused by a different flow rate through red pulp and white cords [36]. However, this study found that no ECIPAS exhibited typical heterogeneous enhancement during the arterial phase and only 28% (9/32) ECIPASs had solid components or a thickened cystic wall with similar density or enhancement to a normal spleen. Several factors may increase the degree of difficulty in identifying surrounding splenic tissues, including the relatively small volume of splenic tissue [37] and the partial volume effect [38]. The additional CTA to routine CE-CT may be useful by demonstrating inhomogeneous enhancements in small lesions, due to exact time control and excellent spatial and contrast resolution

[35]. However, CTA technique has not been reported as an application in the work-up of ECIPASs.

Similar to CE-CT, ECIPAS is typically a cystic-solid mass or a cystic mass with/without thickened cystic wall on MRI. Cystic components usually have a high signal intensity (SI) on T2-WI and varying SI on T1-WI, ranging from low to high, based around cystic fluid characteristics. This review found that cystic components of approximately 92% (22/24) of all ECIPASs had a high SI on T2-WI and around 46% (11/24) had low SI on T1-WI. Corresponding findings show that 56% (18/32) of all ECIPASs contain serous fluid, the remaining 44% (14/32) contain non-serous fluid. The key factor for differentiating ECIPAS from other cystic neoplasms using MRI is the identification the accessory splenic tissue [32], which shows identical SI to the spleen and the inhomogeneous enhancement on arterial phase [39], around the cystic lesion. This systematic review found that only half (14/28) ECIPAS had thickened cystic walls or solid components and two thirds (8/12) ECIPAS showed similar SI to the spleen. However, as the ratio of red pulp to white pulp differs between individuals, not all the surrounding ectopic splenic tissue necessarily shows the same SI as the spleen [39]. The relatively small amount of AS tissue within ECIPAS makes it difficult to identify inhomogeneous enhancements in the arterial phase or to confirm whether the SI is similar with that of a normal spleen [40]. Adopting advanced scanning technologies will enhance diagnostic precision and therefore reduce the number of unnecessary surgeries. Diffusion-weighted imaging (DWI) and superparamagnetic iron-oxide (SPIO)-enhanced MRI can uncover important clues beyond the capabilities of conventional CE-MRI. Ectopic splenic tissue has low apparent diffusion coefficient (ADC) value and a high signal intensity under DWI [41]. Adding DWI to conventional MRI may therefore improve detection rates and the characterization of heterotopic splenic tissue within ECIPAS [42]. SPIO on the other hand is a reticuloendothelial system (RES)-specific contrast media, which can be phagocytosed by the RES, in the liver, spleen, lymph nodes, and bone marrow [43]. SPIO is exclusively absorbed by RES macrophages, resulting in a significant drop on T2-WI in the surrounding splenic tissue [44]. Motosugi et al. suggested SPIO-enhanced MRI is a promising diagnostic method for ECIPAS [45]. Moreover, as MRI offers superior spatial resolution to scintigraphy, SPIO-enhanced MRI may be more sensitive than scintigraphy [46]. Further research into diagnostic sensitivity would certainly be advocated in this area as the evidence-base develops.

ECIPAS is cystic mass on abdominal US, and no solid component was observed based on the population included in this review. CE-US is a useful tool in identifying IPAS [47,48], however, the diagnostic value remains undetermined for ECIPAS. Without interference caused by abdominal organs, EUS has a higher resolution and sensitivity to detect the ectopic splenic tissue around a cyst. Despite the similar features observed through both enhanced and non-enhanced US in ectopic splenic tissues [49], EUS combined with other techniques may provide additional information. EUS-guided needle-based probe confocal laser endomicroscopy (nCLE), allows direct dynamic tissue architecture evaluation [50], and has been used to analyze red pulp in the surrounding splenic tissue as cellular cords with red blood cells [51]. EUS-elastography is a useful tool for the diagnosis of pancreatic malignancy [52]. Differing from IPAS, displaying a homogeneous green elastographic pattern on EUS-elastography, ECIPAS showed inhomogeneous hardness [53].

Tc-99 m HDRBCs or colloid scintigraphy can be used to identify ectopic splenic tissue because of the prominent physiological uptake in functioning splenic tissue [54]. In order to overcome inferior spatial resolution, scintigraphy and SPECT is frequently used in conjunction with other cross-sectional imaging modalities. However, based on the current study, Tc-99 m HDRBCs or colloid scintigraphy has not been applied in the diagnosis of ECIPAS and the diagnostic value remains unexplored.

On FNA pathology, the red pulp is represented by numerous red blood cells, large platelet aggregates, endothelial cells, and stromal fragments, whereas, white pulp is represented by polymorphous lymphoid cells, lymphoglandular bodies, and three-dimensional lymphoid aggregates [55]. Another important feature is CD8 positive endothelial cells [56]. Due the relative small splenic tissue within ECIPAS, it is challenging to obtain diagnostic cellular components through FNA. The current study found cellular components obtained from approximately 61.5% (8/13) ECIPAS samples, among which only a quarter (2/8) had received a definitive diagnosis of splenic tissue. In addition, as a traumatic diagnostic method, FNA harbors the risk for severe complications such as intra-abdominal bleeding and pancreatic fistula, making it a second-line modality compared with other non-traumatic techniques.

Being a cystic or cystic-solid mass in the pancreatic tail, ECIPAS should be carefully differentiated from premalignant pancreatic cystic tumors, including; MCN, IPMN, SPT and cystic p-net. The typical and key preoperative findings of ECIPAS are summarized in Table 4. This study found that more than 90% patients with ECIPAS had been diagnosed through postoperative pathology and underwent an unnecessary surgical procedure. As most ECIPASs are asymptomatic and do not harbor malignant potential, the majority

Table 4
Typical and key preoperative findings of ECIPAS.

Items	Typical and key findings
Age	*40–65*
Gender	*M ≈ F*
Symptom	*incidentally detected/nonspecific alimentary symptom*
Median size	*3.4 cm*
Location	*tail*
CE-CT	*cystic-solid lesion or cystic lesion with TCW, the SC or TCW has similar attenuation to the spleen on all phases and heterogeneous enhancement on arterial phase*
CE-MRI	*cystic-solid lesion or cystic lesion with TCW, the SC or TCW has similar attenuation to the spleen on all phases and heterogeneous enhancement on arterial phase*
CE-EUS	*cystic-solid lesion or cystic lesion with TCW, the SC or TCW has similar enhancement pattern to the spleen on vascular and post vascular phases*
MRI-DWI	*the SC or TCW has similar attenuation to the spleen*
SPIO-enhanced MRI	*the SC or TCW shows SI drop on T2-WI*
99mTc-HDRBC scintigraphy	tracer uptake by SC or TCW
99mTc-colloid scintigraphy	tracer uptake by SC or TCW
FNA pathology	*polymorphous population of lymphocytes admixed with inflammatory cells, $CD8^+$ endothelial cells of the thin-walled vessels*

ECIPAS: epidermoid cyst in intrapancreatic accessory spleen; CE-CT: contrast enhanced computed tomography; CE-MRI: contrast enhanced magnetic resonance imaging; CE-EUS: (Levovist/Sonazoid) contrast enhanced endoscopic ultrasonography; DWI:; SPIO: superparamagnetic iron-oxide; 99mTc-HDRBC: 99mTechnetium heat-damaged red blood cell; 99mTc-colloid: 99mTechnetium colloid; FNA: fine needle aspiration; M: male; F: female; SI: signal intensity; SC: solid component; TCW: thickened cystic wall.

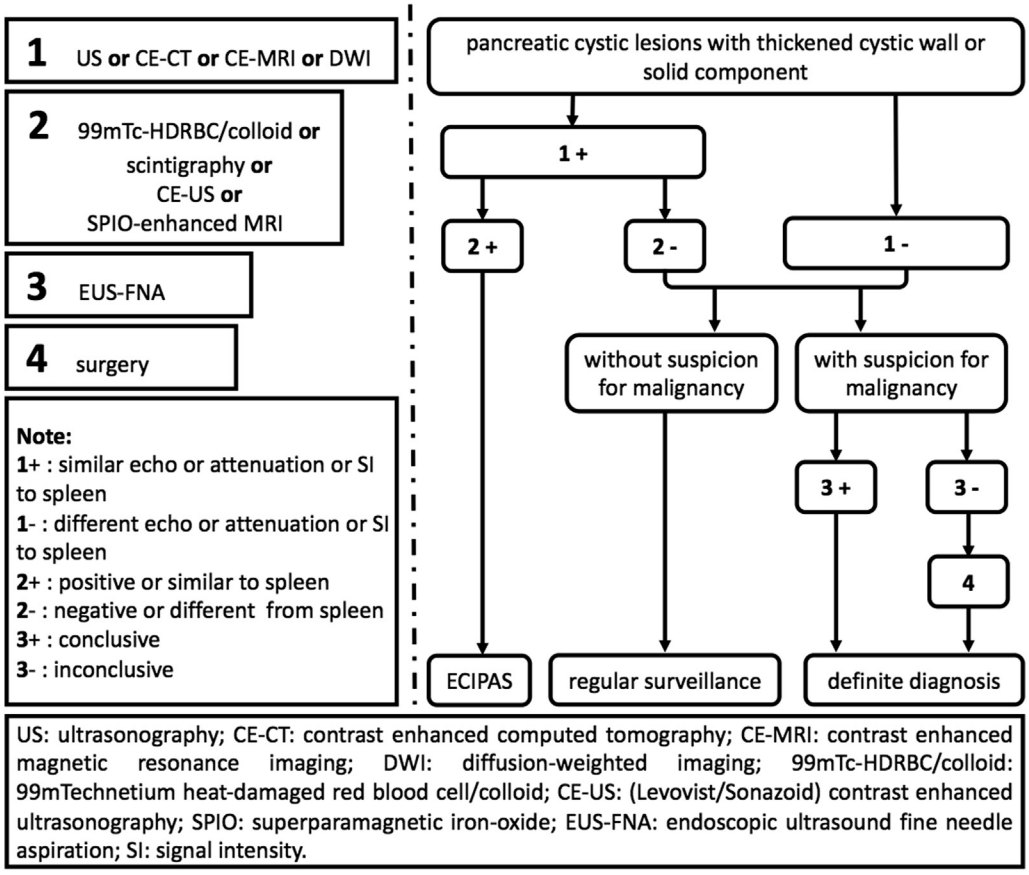

Fig. 2. Diagnostic algorithm recommended for ECIPAS.

of ECIPASs do not require any medical treatment. The indication for surgery is only limited to the ECIPASs combined with malignancy [57], ECIPASs causing compression [7,8] and ECIPASs with torsion or rupture. In order to avoid unnecessary surgical treatment, it is of great importance to include ECIPAS in the differentiation of pancreatic cystic lesions.

The key factor in the diagnose ECIPAS is to focus on the ectopic splenic tissue within ECIPAS. A potential diagnostic algorithm is further recommended for ECIPAS in Fig. 2. However, several issues should be considered. Firstly, as the splenic tissue within ECIPAS is usually vary small, the similar density/SI to the normal spleen or heterogeneous enhancement on arterial phase might not be easily detected with CE-CT, CE-MRI or even EUS technologies. DWI may be more sensitive to surrounding splenic tissue. Secondly, Tc-99 m HDRBCs or colloid scintigraphy is a useful tool to diagnose IPAS, even though the diagnostic value is yet undetermined for ECIPAS. Last but not least, it is too difficult to obtain enough cellular component to make a definite diagnosis using FNA.

Conclusions

ECIPAS comprises an extremely small fraction of pancreatic cysts and its prevalence is very low. Due to the fact that ECIPASs seldom cause symptoms or pose significant clinical threat, they do not require medical treatment. However, ECIPAS is usually misdiagnosed as MCN or IPMN, which leads to unnecessary surgical treatment. It would therefore be prudent to consider ECIPAS in a differential diagnosis for pancreatic cystic tumors. Whenever clinicians suspect the existence of ECIPAS, multiple examinations may be required to improve diagnosis and therapeutic decision making.

Disclosure statement

The authors declare that they have no conflict of interest.

Financial support

None.

Author contributions

Study design: Study design: Bing-Qi Li and Jun Lu; Data search, analysis and interpretation: Bing-Qi Li and Jun Lu; Initial draft: Bing-Qi Li; Critical revision for important intellectual content: Samuel Seery and Jun-Chao Guo. All authors approved the final version of the manuscript and are accountable for all aspects of the work. Jun-Chao Guo had full responsibility for the conduct of the study and access to the data, and controlled the decision to publish.

Manuscript category: review.

The paper is not based on a previous communication to a society or meeting.

Acknowledgments

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pan.2018.10.008.

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