Αυτοάνοση παγκρεατίτιδα/IgG4-σχετιζόμενη νόσος

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Επίκουρος καθηγητής γαστρεντερολογίας
Πανεπιστήμιο Κρήτης

Ασθενής άνδρας 60 ετών

Αιτία εισόδου:

Από εβδομάδος

- ικτερική χροιά δέρματος και επιπεφυκότων
- υπέρχρωση ούρων
- αποχρωματισμός κοπράνων
- απώλεια βάρους ~8κιλά σε 2 μήνες
- Διαρροϊκό σύνδρομο (6-7/ημέρα)

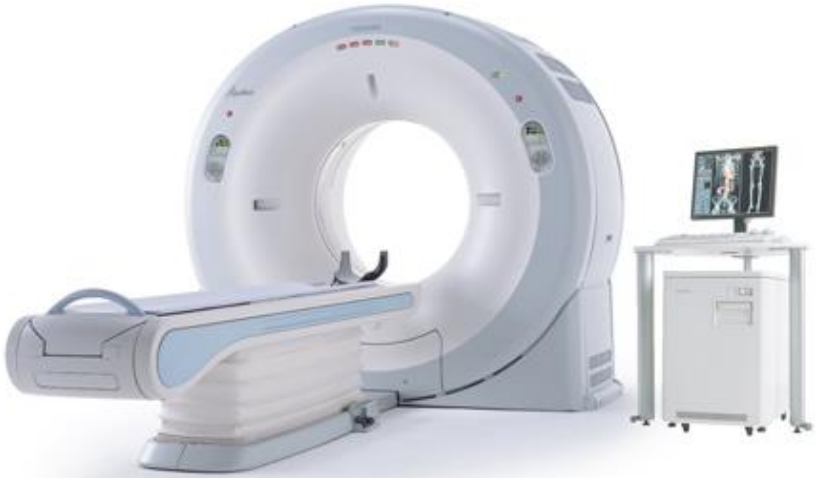
Ατομικό αναμνηστικό: ελεύθερο

Εργαστηριακός έλεγχος:

Hgb/Hct	**12,7**g/dl **/38,2**%	γGT	**769** U/l
WBC	7200 K/μl	ALP	**368** U/l
PLT	186 K/μl	BilTot/BilDir	**17/9,6** mg/dl
INR	1,14	Amylase	34 U/l
SGOT	**160** U/l	Alb	3,8 g/dl
SGPT	**239** U/l	Urea/ Creat	22/0,5 mg/dl

Ca19-9	**49,27** U/ml
CEA	2,47 ng/ml
IgG4	140 mg/dl (4-230)

Απεικονιστικός έλεγχος



U/S άνω κοιλίας:

•Ήπια διάταση χοληδόχου πόρου (8χιλ)

•Υποηχογενής ανομοιογενής, καλά περιγεγραμμένη βλάβη 4εκ (ενδ στην κεφαλή του παγκρέατος)

•Ήπαρ, χοληδόχος κύστη, σπλην κφ

CT άνω κοιλίας:

•Διόγκωση και ανομοιογένεια της κεφαλής του παγκρέατος

•Αρχόμενες διατάσεις χοληφόρων

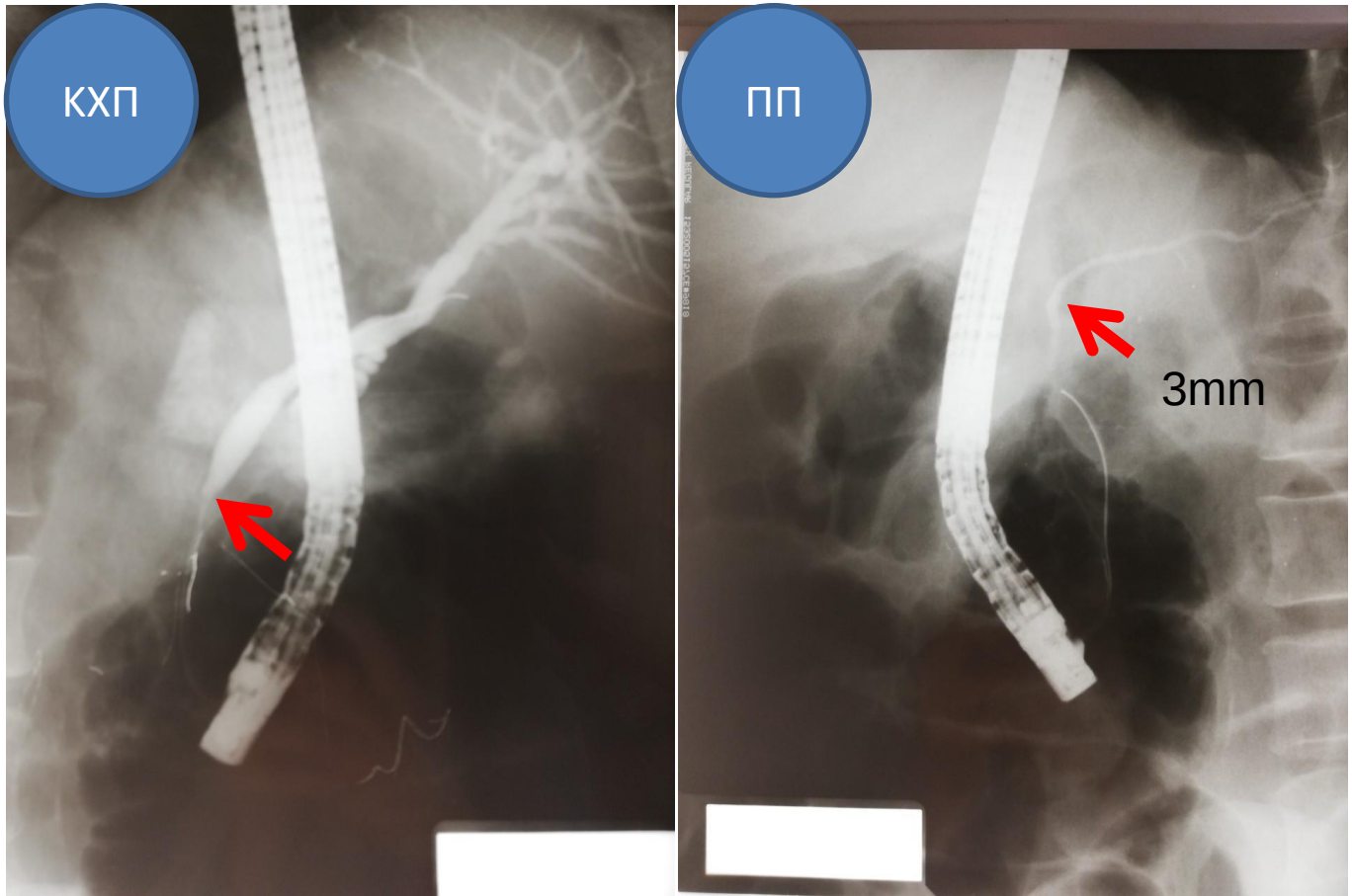
•Σημεία επινέμεσης της συμβολής της σπληνικής με την άνω μεσεντέριο φλέβα

•Αρχόμενη επινέμεση του λίπους γύρω από την πάσχουσα παγκρεατική κεφαλή

Σημεία ύποπτα νεοεξεργασίας παγκρέατος

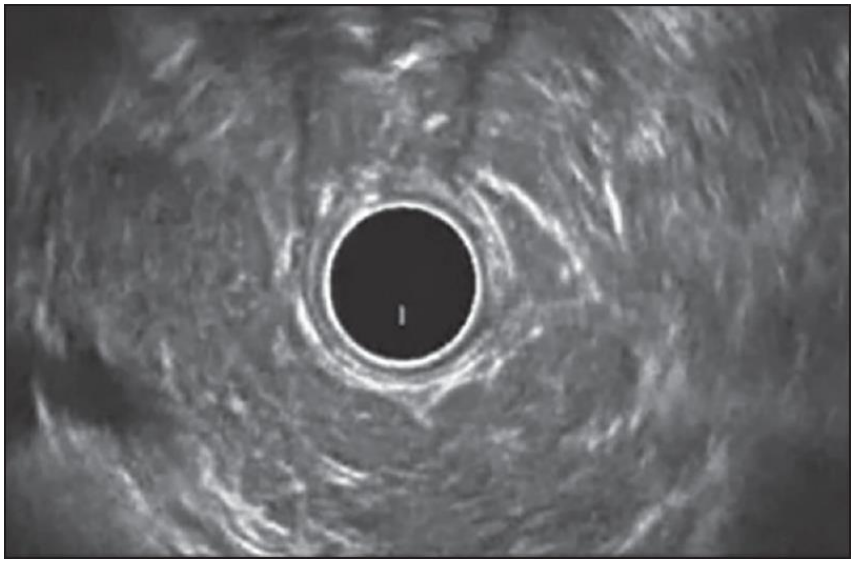
ERCP:

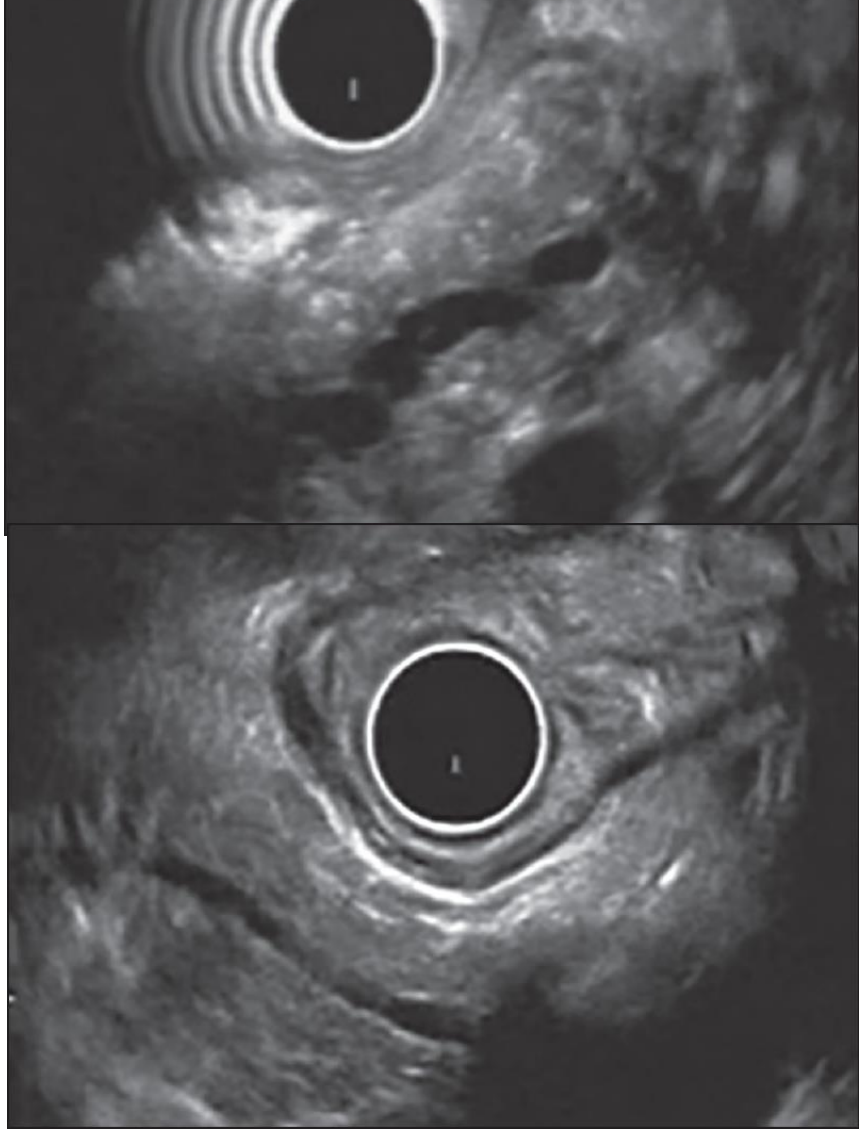
- Ομαλή στένωση κατώτερου χοληδόχου πόρου μήκους 2-3 εκ
- Οριακή διάταση εξω- και ενδο-ηπατικών χοληφόρων
- Ελαφρά διάταση παγκρεατικού πόρου
- Σφιγκτηροτομή-Τοποθέτηση πλαστικού stent με καλή ροή χολής



EUS (ενδοσκοπικός υπέρηχος)

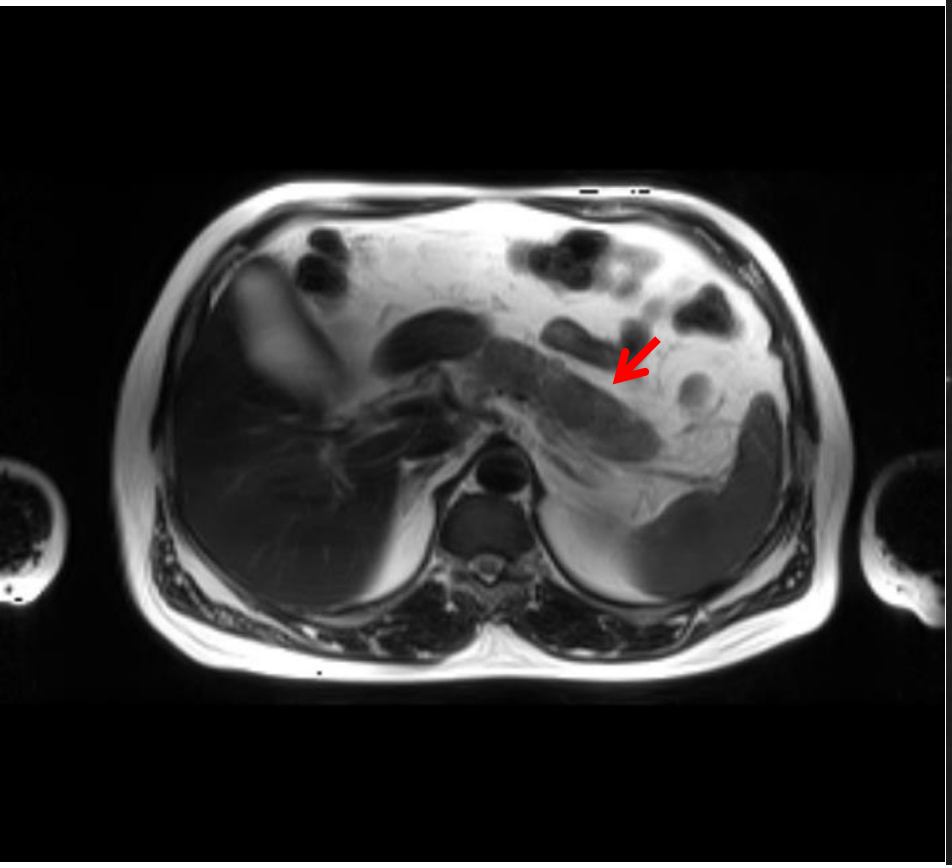
- Διάχυτη έντονη ανομοιογένεια όλου του παρεγχύματος του παγκρέατος (ιδίως κεφαλής)
- Υπερηχογενείς εστίες (δ>2χιλ)
- Υπερηχογενείς ταινίες (ίνωση)
- Λοβίωση παρεγχύματος
- Παγκρεατικός πόρος με υπερηχογενές τοίχωμα

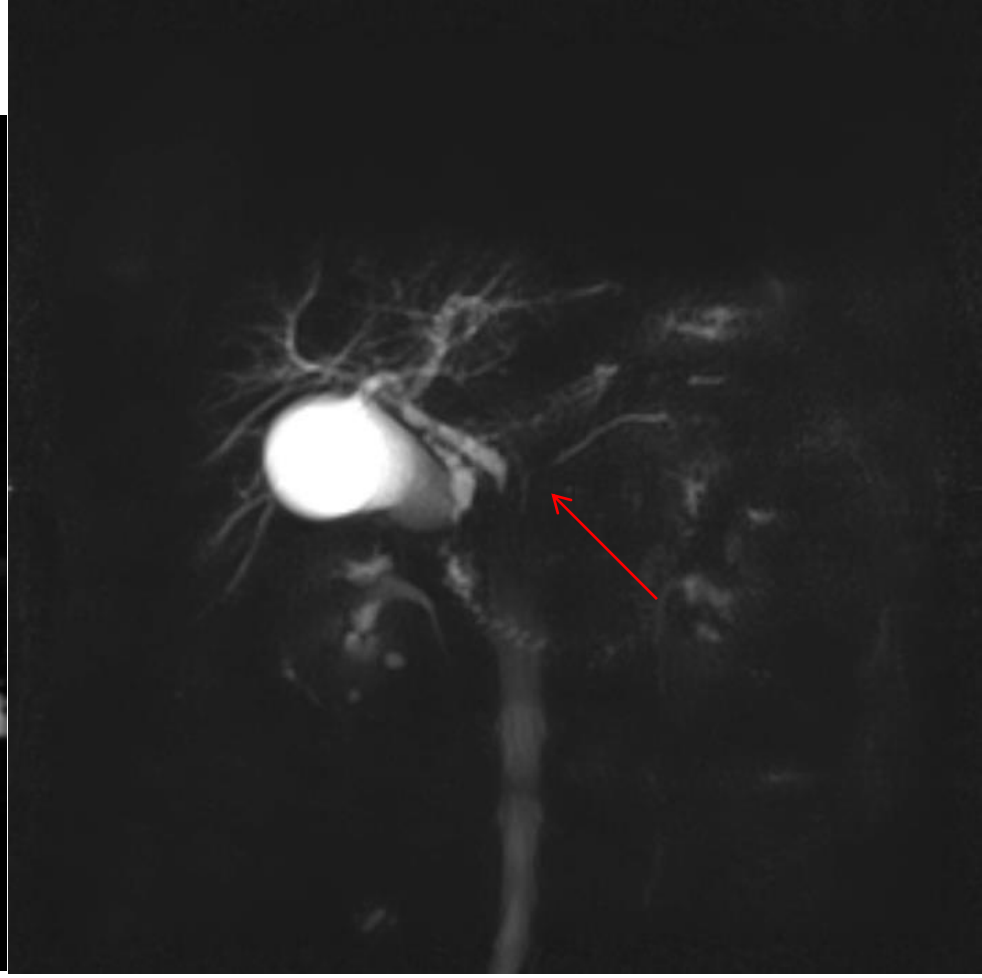




Αναρρόφηση με λεπτή βελόνη (υπό EUS)
Στοιχεία δεσμοπλαστικής και φλεγμονώδους αντίδρασης και αδενικά κύτταρα εκ των πόρων του παγκρέατος

MRI άνω κοιλίας/MRCP





…το ενδεχόμενο διάχυτης φλεγμονής του τύπου της ***αυτοάνοσης παγκρεατίτιδας*** δεν μπορει να αποκλειστεί πλήρως...

Autoimmune pancreatitis

	Type 1 AIP	Type 2 AIP
Mean age at diagnosis	7th decade	5th decade
Male sex	75%	50%
Serum IgG4 elevation	66%	25%
Other organ involvement	Common – up to 60%	No
IBD	2-6%	30%
Histologic findings	Lymphoplasmacytic infiltration Storiform fibrosis Obliterative phlebitis Abundant IgG4 positive plasma cells (≥10/hpf)	Granulocytic epithelial lesions Scant IgG4 positive plasma cells (<10/hpf)
Risk for relapse	Moderate-high (up to 60%)	Low (<10%)
IgG4-related disease	Yes	No

Dig Dis Sci 2017; 62: 1762-1769
Gastrointest Endosc Clin N Am 2017; 27: 643-655

IgG4 νόσος

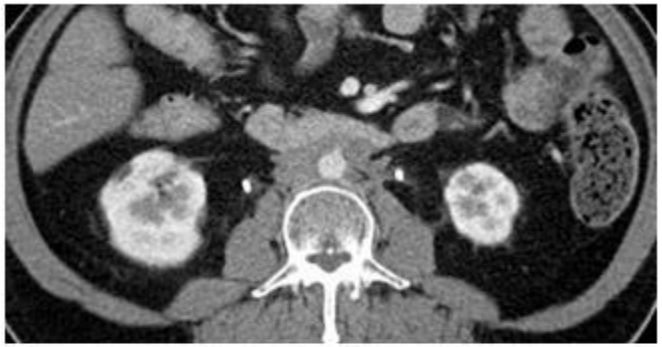


Figure 6. Retroperitoneal fibrosis. Computed tomographic scan of the abdomen reveals an inflammatory mass surrounding the abdominal aorta.

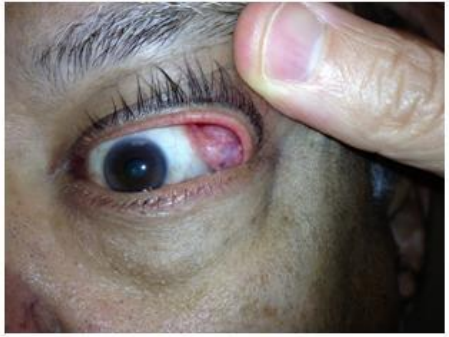


Figure 3. Dacryoadenitis. Lacrimal gland swelling in a patient with IgG4-related disease.

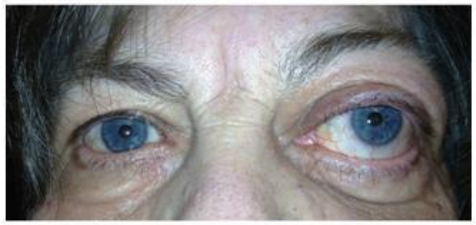
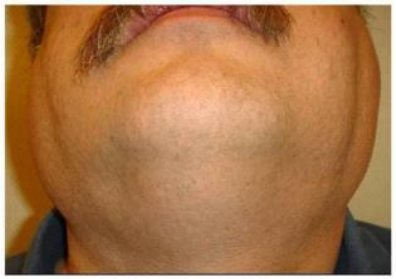


Figure 4. Orbital pseudotumor. Left eye proptosis caused by an orbital pseudotumor that spared the lacrimal gland.

Patient 1: Receiving Prednisone



Serum IgG4 = 1560 mg/dL
(nl < 135 mg/dL)

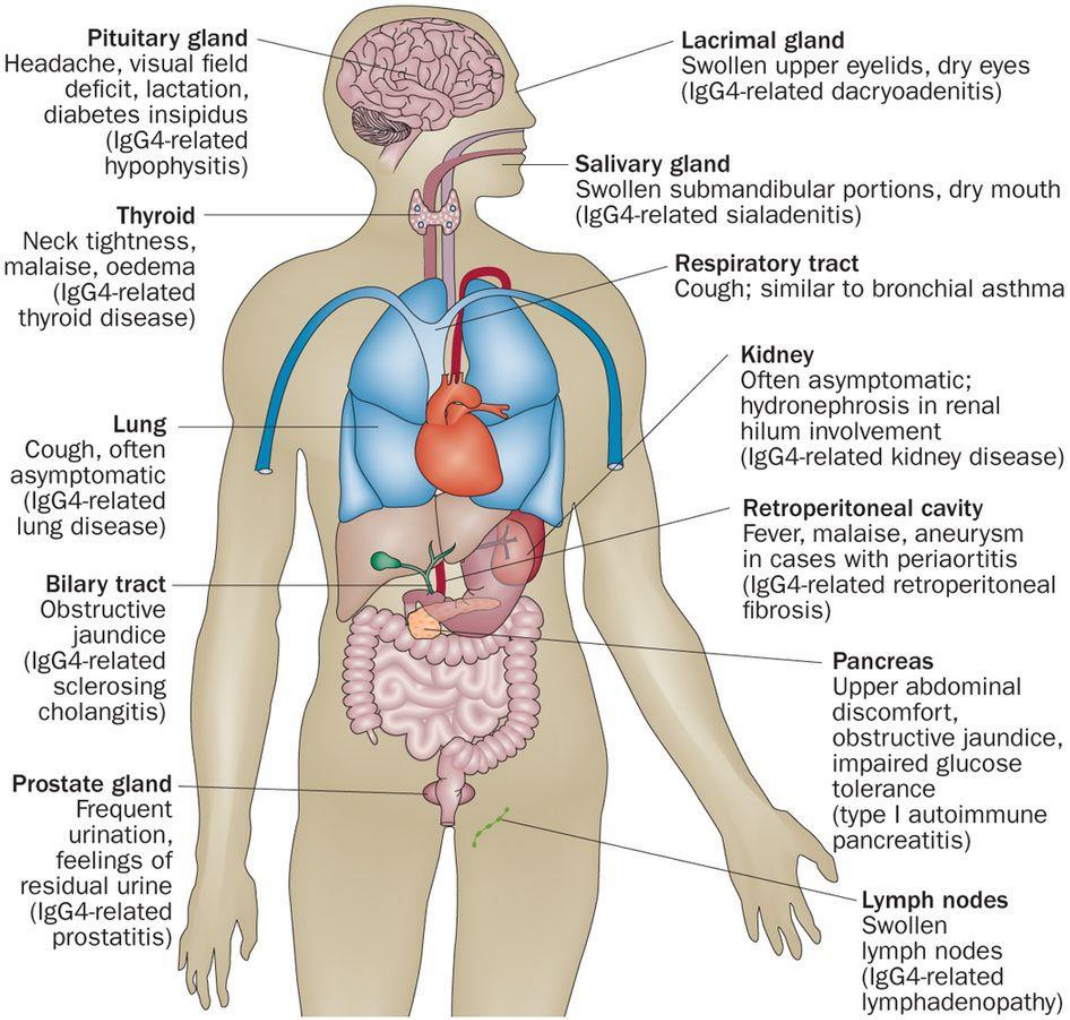


Table 1
Prevalence of extrapancreatic lesions complicating AIP

Organ	No. of Cases	Frequency, %
Total extrapancreatic lesions	83/90	92.2
Lacrimal or salivary gland	38/80	47.5
Hilar lymph node (CT)	54/69	78.3
Hilar lymph node (Ga-67 scintigraphy)	60/80	75.0
Lung	25/46	54.3
Bile duct	63/81	77.8
Peripancreatic or para-aortic lymph node	51/90	57.0
Kidney	13/90	14.4
Retroperitoneum	17/86	19.8
Ligamentum teres	2/90	2.2
Prostate	8/80	10.0

From Fujinaga Y, Kadoya M, Kawa S, et al. Characteristic findings in images of extra-pancreatic lesions associated with autoimmune pancreatitis. Eur J Radiol 2010;76(2):229; with permission.

Gastrointest Endoscopy Clin N Am 28 (2018) 493–519

<u>Έλεγχος για εξωπαγκρεατική εντόπιση IgG4 νόσου στον ασθενή μας</u>

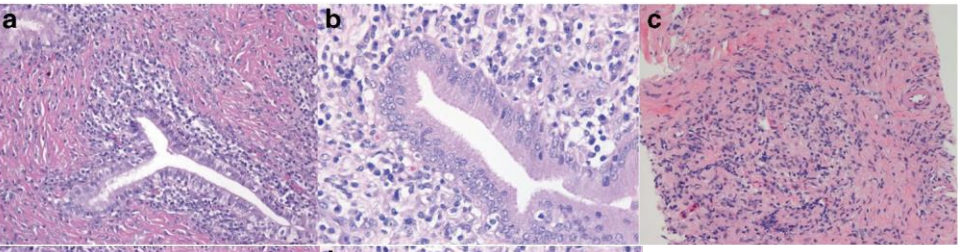
U/S παρωτίδων

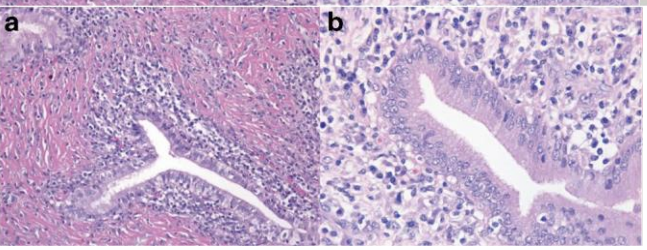
MRI σπλαχνικού κρανίου

CT θώρακος

TABLE 2. Level 1 and Level 2 Criteria for Type 1 AIP

	Criterion	Level 1	Level 2
P	Parenchymal imaging	Typical: Diffuse enlargement with delayed enhancement (sometimes associated with rim-like enhancement)	Indeterminate (including atypical†): Segmental/focal enlargement with delayed enhancement
D	Ductal imaging (ERP)	Long (>1/3 length of the main pancreatic duct) or multiple strictures without marked upstream dilatation	Segmental/focal narrowing without marked upstream dilatation (duct size, <5 mm)
S	Serology	IgG4, >2× upper limit of normal value	IgG4, 1–2× upper limit of normal value
OOI	Other organ involvement	a or b	a or b
		a. Histology of extrapancreatic organs Any three of the following: (1) Marked lymphoplasmacytic infiltration with fibrosis and without granulocytic infiltration (2) Storiform fibrosis (3) Obliterative phlebitis (4) Abundant (>10 cells/HPF) IgG4-positive cells	a. Histology of extrapancreatic organs including endoscopic biopsies of bile duct‡: Both of the following: (1) Marked lymphoplasmacytic infiltration without granulocytic infiltration (2) Abundant (>10 cells/HPF) IgG4-positive cells
		b. Typical radiological evidence At least one of the following: (1) Segmental/multiple proximal (hilar/intrahepatic) or proximal and distal bile duct stricture (2) Retroperitoneal fibrosis	b. Physical or radiological evidence At least one of the following: (1) Symmetrically enlarged salivary/lachrymal glands (2) Radiological evidence of renal involvement described in association with AIP
H	Histology of the pancreas	LPSP (core biopsy/resection) At least 3 of the following: (1) Periductal lymphoplasmacytic infiltrate without granulocytic infiltration (2) Obliterative phlebitis (3) Storiform fibrosis (4) Abundant (>10 cells/HPF) IgG4-positive cells	LPSP (core biopsy) Any 2 of the following: (1) Periductal lymphoplasmacytic infiltrate without granulocytic infiltration (2) Obliterative phlebitis (3) Storiform fibrosis (4) Abundant (>10 cells/HPF) IgG4-positive cells
	Response to steroid (Rt)*	Diagnostic steroid trial Rapid (≤2 wk) radiologically demonstrable resolution or marked improvement in pancreatic/extrapancreatic manifestations	





HISORt criteria

A	B	C
• Histology: diagnostic histology on resection specimen or pancreatic core biopsy • LPSP, OR • >10 IgG4 cells/hpf +2/3 out of: • Periductal lymphoplasmacytic infiltrate • Obliterative phlebitis • Storiform fibrosis • IDCP, OR • GEL with minimal IgG4 positive cells.	• Imaging: diffusely enlarged gland with featureless borders and delayed enhancement with/without capsule-like rim AND any one of the following: • Elevated IgG4 • Other organ involvement* • Storiform fibrosis with lymphoplasmacytic infiltration (but not meeting all criteria in A)	• Response to steroids** (resolution/marked improvement in pancreatic/extrapancreatic manifestations in patients meeting criteria for steroid use: • Groups A or B • Patients without typical imaging features¶ and negative cancer workup who have • One highly suggestive feature for AIP#, OR • Two supportive features of AIP&

Am J Gastroenterol (2018) 113:1301–1309

Histopathologic diagnosis of AIP

ORIGINAL ARTICLE

International Consensus Diagnostic Criteria for Autoimmune Pancreatitis

Guidelines of the International Association of Pancreatology

Tooru Shimosegawa, MD, Suresh T. Chari, MD,† Luca Frulloni, MD,‡ Terumi Kamisawa, MD,§ Shigeyuki Kawa, MD,|| Mari Mino-Kenudson, MD,¶ Myung-Hwan Kim, MD,# Günter Klöppel, MD,** Markus M. Lerch, MD,†† Matthias Löhr, MD,‡‡ Kenji Notohara, MD,§§ Kazuichi Okazaki, MD,|||| Alexander Schneider, MD,¶¶ and Lizhi Zhang, MD##*

Pancreas 2011; 40:352-358

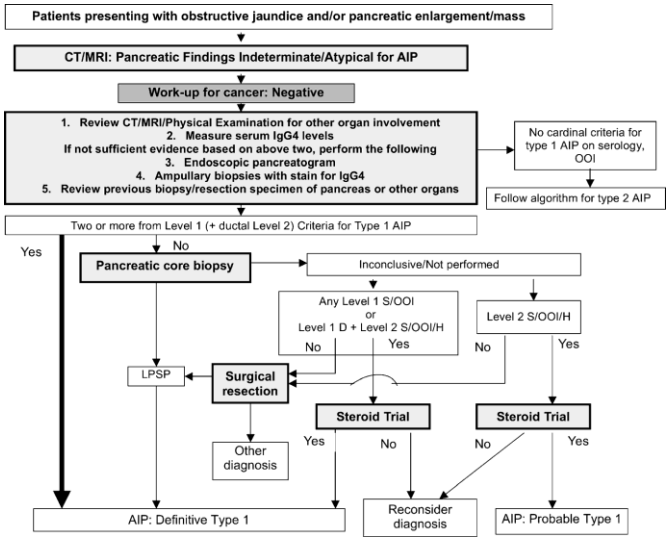


FIGURE 2. Algorithm to diagnose type 1 AIP in subjects presenting with obstructive jaundice and/or pancreatic mass. This schematic drawing shows a flow to diagnose type 1 AIP with indeterminate or atypical findings of the pancreas on CT/MRI (level 2 parenchymal findings).

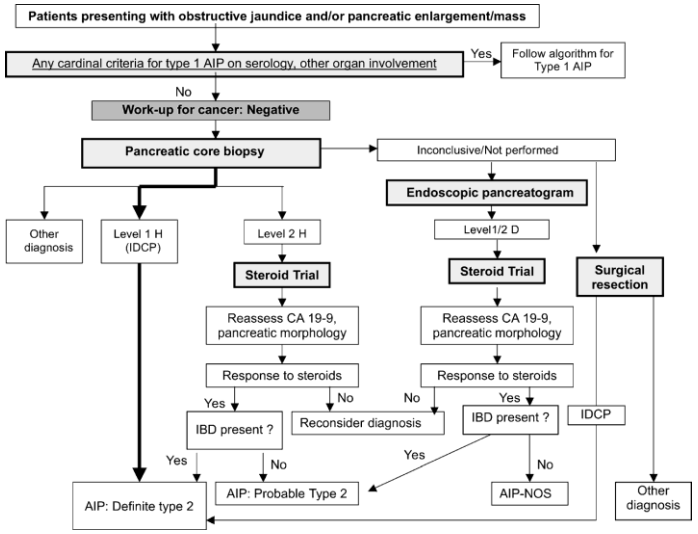
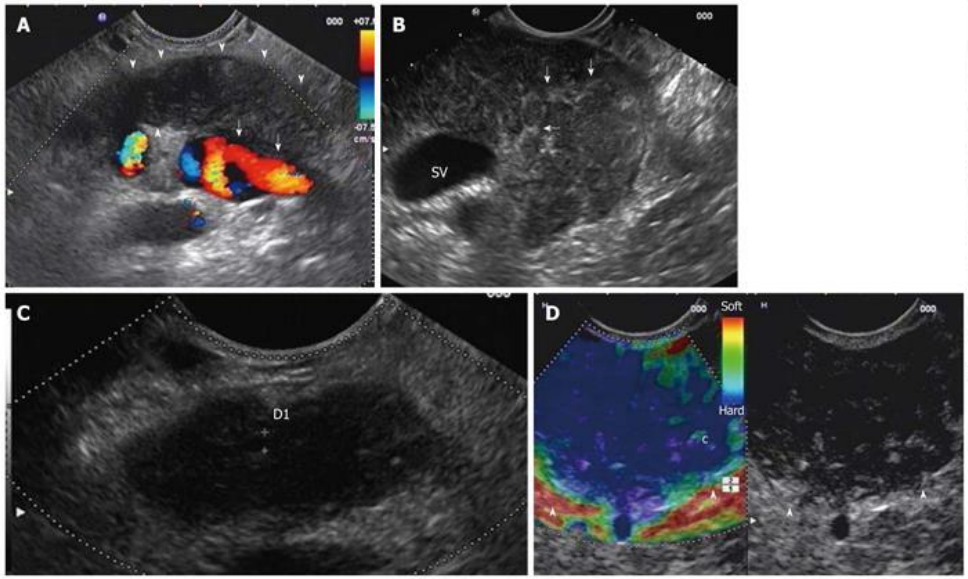


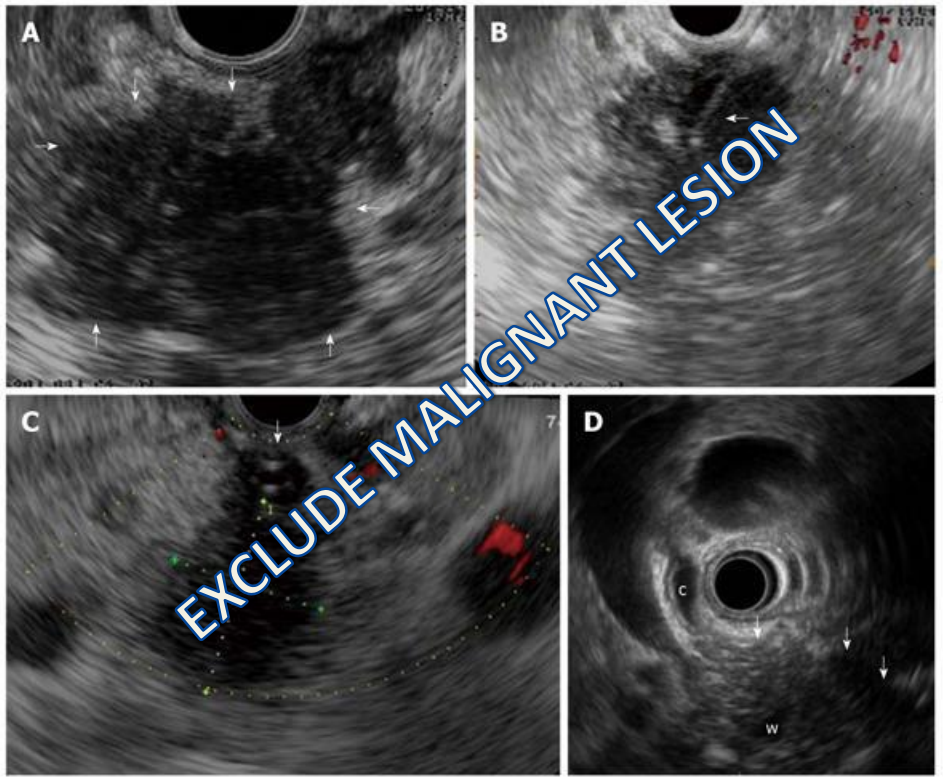
FIGURE 3. Algorithm to diagnose type 2 AIP in subjects presenting with obstructive jaundice and/or pancreatic mass. This schematic drawing shows a flow to diagnose type 2 AIP with typical/indeterminate (atypical) findings of the pancreas on CT/MRI (level 1 and 2 parenchymal findings).

Δεν υπάρχουν ΠΑΘΟΓΝΩΜΟΝΙΚΑ απεικονιστικά χαρακτηριστικά στον EUS για την AIP



Διάχυτη διόγκωση του παγκρέατος
Υπόηχογενές ετερογενές παρέγχυμα
Υπόηχα περιπαγκρεατικά όρια
Ανώμαλος μειζ. ΠΠ

AIP μπορεί να μιμηθεί χρόνια παγκρεατίτιδα
✓ Λοβίωση
✓Υπερηχογενείς ταινίες/εστίες



Εστιακή υπόηχη μάζα
συνήθως στην παγκρεατική κεφαλή
Στένωση κύριου ΠΠ με προστενωτική διάταση

World J Gastroenterol 2011;17:2080-2085
Gastrointest Endosc Clin N Am 2017; 27: 643-655

EUS-FNA for histopathologic diagnosis of AIP

ORIGINAL ARTICLE: Clinical Endoscopy

Prospective multicenter study on the usefulness of EUS-guided FNA biopsy for the diagnosis of autoimmune pancreatitis (CME)

Tomomasa Morishima, MD,[1] Hiroki Kawashima, MD, PhD,[1] Eizaburo Ohno, MD, PhD,[1] Takeshi Yamamura, MD, PhD,[2] Kohei Funasaka, MD, PhD,[2] Masanao Nakamura, MD, PhD,[1] Ryoji Miyahara, MD, PhD,[1] Osamu Watanabe, MD, PhD,[1] Masatoshi Ishigami, MD, PhD,[1] Yoshie Shimoyama, MD, PhD,[3] Shigeo Nakamura, MD, PhD,[3] Senju Hashimoto, MD, PhD,[4] Hidemi Goto, MD, PhD,[1] Yoshiki Hirooka, MD, PhD[2]

Nagoya, Japan

n=50 patients, 45/50 with final diagnosis of AIP
Standard 22G needle

Operating characteristics for level 1 histology features

Sensitivity	7.9%
Specificity	100%
Positive predictive value	100%
Negative predictive value	25.5%

Gastrointest Endosc 2016;84:241-8

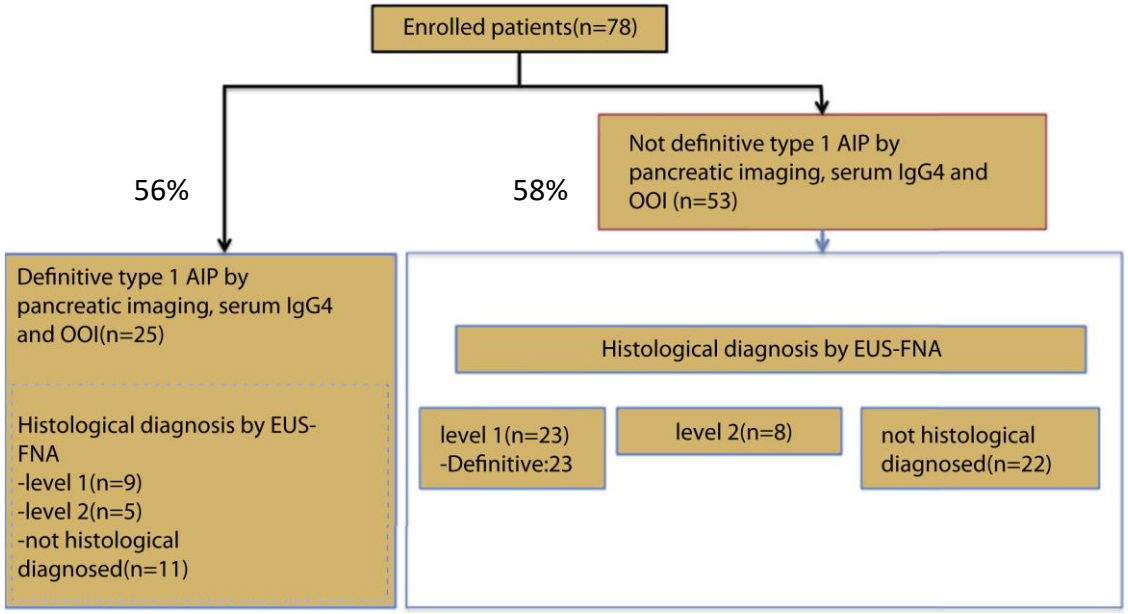
EUS-FNA for histopathologic diagnosis of AIP

ORIGINAL ARTICLE: Clinical Endoscopy

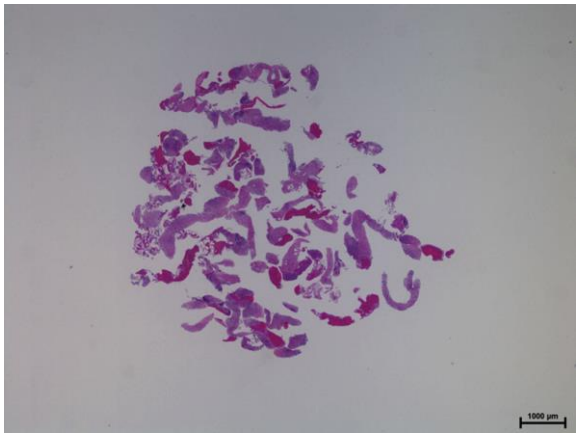
Diagnosis of autoimmune pancreatitis by EUS-guided FNA using a 22-gauge needle: a prospective multicenter study CME

Atsushi Kanno, MD, PhD,[1] Atsushi Masamune, MD, PhD,[1] Fumiyoshi Fujishima, MD, PhD,[2] Takuji Iwashita, MD, PhD,[3] Yuzo Kodama, MD, PhD,[4] Akio Katanuma, MD,[5] Hirotaka Ohara, MD, PhD,[6] Masayuki Kitano, MD, PhD,[7] Hiroyuki Inoue, MD, PhD,[8] Takao Itoi, MD, PhD,[9] Nobumasa Mizuno, MD, PhD,[10] Hiroyuki Miyakawa, MD, PhD,[11] Rintaro Mikata, MD, PhD,[12] Atsushi Irisawa, MD, PhD,[13] Satoko Sato, MD, PhD,[2] Kenji Notohara, MD, PhD,[14] Tooru Shimosegawa, MD, PhD[1]

Sendai, Gifu, Kyoto, Sapporo, Nagoya, Osaka, Tsu, Tokyo, Chiba, Aizu-wakamatsu, Kurashiki, Japan



No of HPFs in the specimen	n=78
>10	29 (37%)
5-10	18 (23%)
1-4	15 (19%)
0	16 (21%)



Gastrointest Endosc 2016;84:797-804

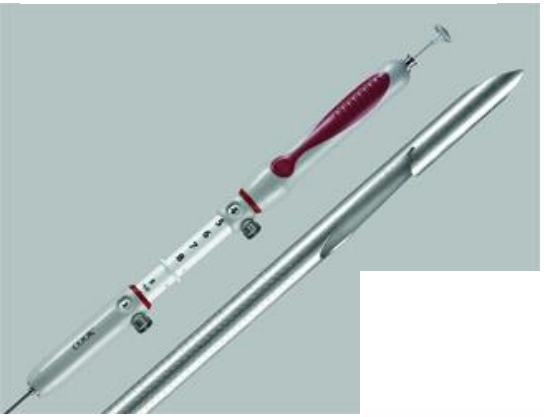
EUS-FNB for histopathologic diagnosis of AIP

Pathology International

Pathology International 2017; **67:** 514–520 doi:10.1111/pin.12563

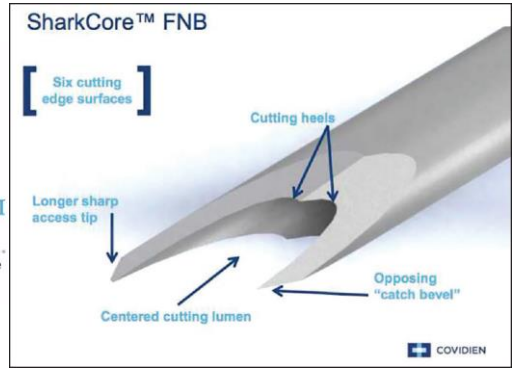
Case Report

Microscopic findings in EUS-guided fine needle (SharkCore) biopsies with type 1 and type 2 autoimmune pancreatitis



Sönke Detlefsen,[1] Maiken Thyregod Joergensen[2] and Michael Bau Mortensen[3]

[1]*Senior Consultant Pathologist, Department of Pathology, Odense University Hospital, Odense C, Denmark,* [2]*Senior Consultant Gastroenterologist, Department of Medical Gastroenterology, Odense University Hospital, Odense C, Denmark, and* [3]*Senior Consultant Surgeon, HPB Section, Department of Surgery, Odense University Hospital, Odense C, Denmark*



Διάγνωση

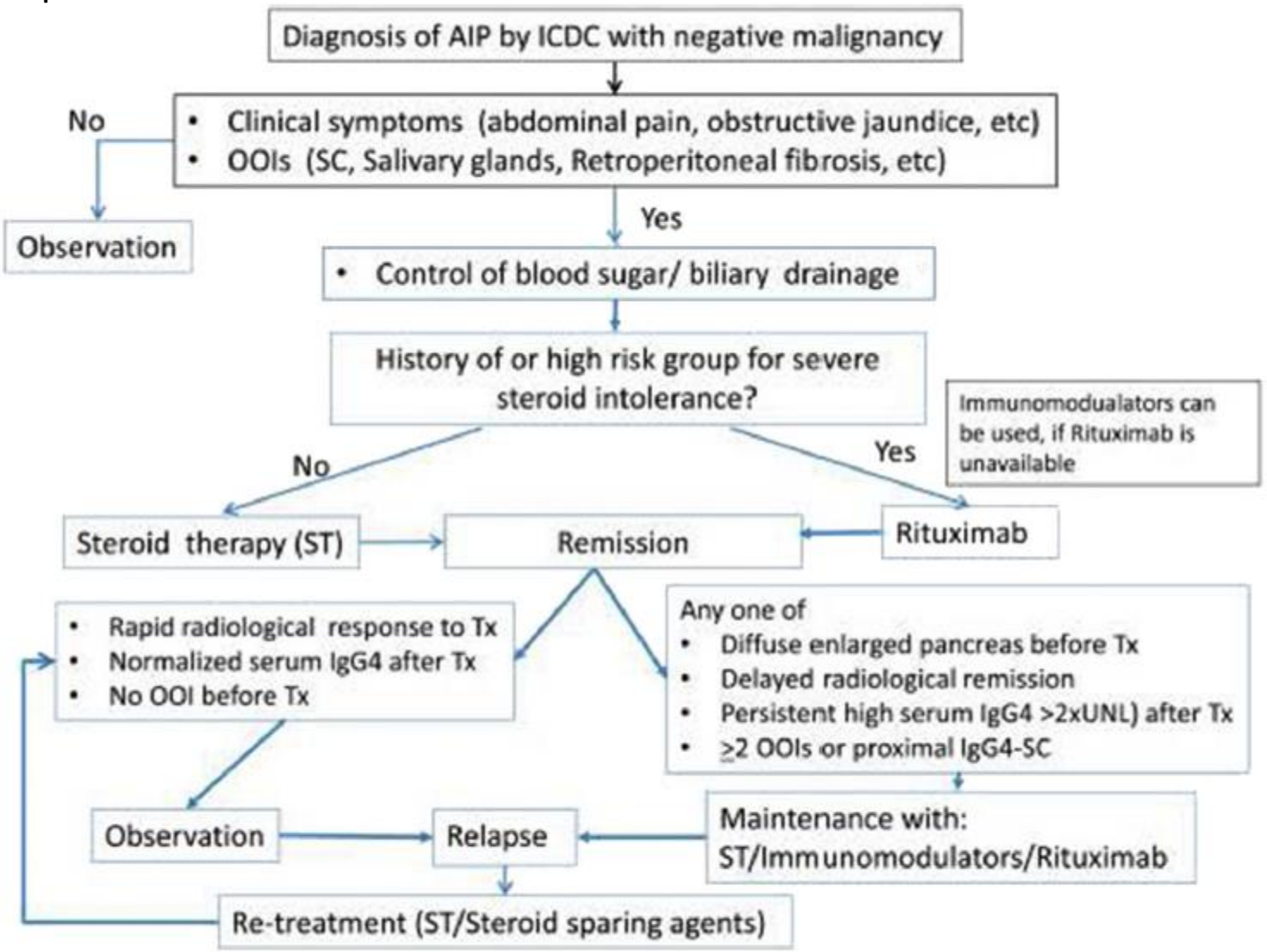
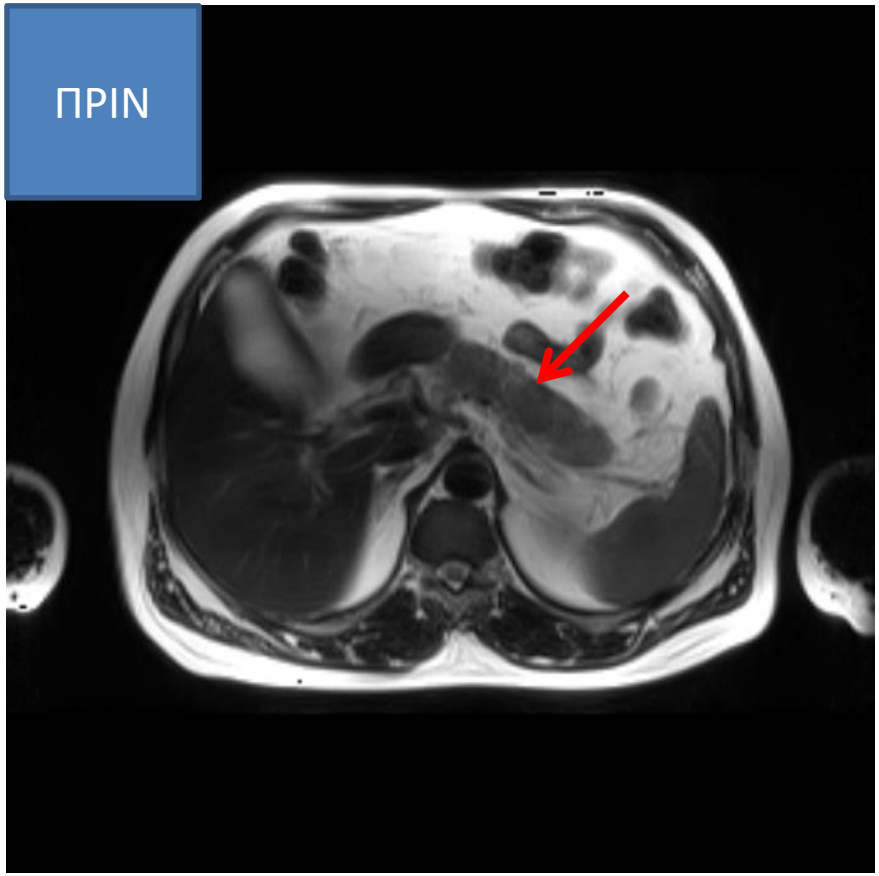


Fig. 7. Therapeutic algorithm for AIP. SC, sclerosing cholangitis; Tx, treatment. (*From* Okazaki K, Chari ST, Frulloni L, et al. International consensus for the treatment of autoimmune pancreatitis. Pancreatology 2017;17(1):5; with permission.)

ΘΕΡΑΠΕΙΑ

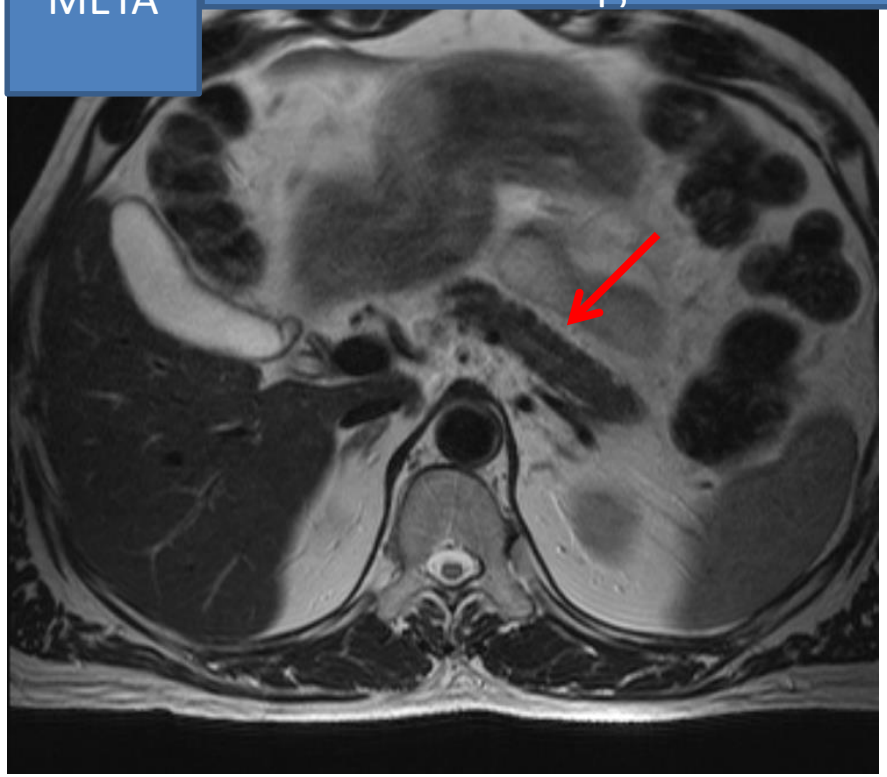
Πρεδνιζολόνη 40mg

ΠΡΙΝ



ΜΕΤΑ

Βελτίωση παγκρέατος-εμμονή στένωσης ΚΧΠ



•μείωση διαστάσεων κεφαλής και σώματος παγκρέατος
•Υποχώρηση πυλαίων λεμφαδένων
•Διάχυτη πάχυνση ΚΧΠ

Ευχαριστώ για την προσοχή σας