Asociación Territorial de la SEAP de Madrid

Hospital Universitario de Getafe
27-Octubre-2007

"*IgG4-related sclerosing disease*" : Caracterización de una enfermedad multisistémica

Manuel Rodríguez-Justo

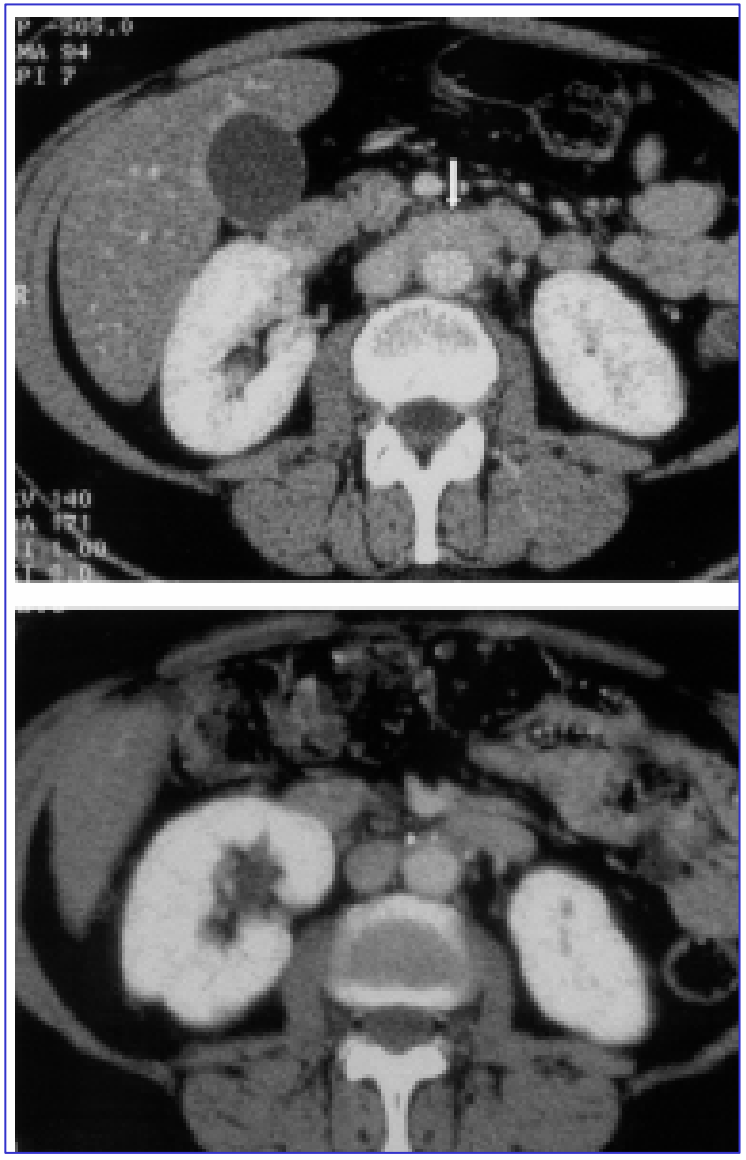
University College London Hospitals NHS
NHS Foundation Trust

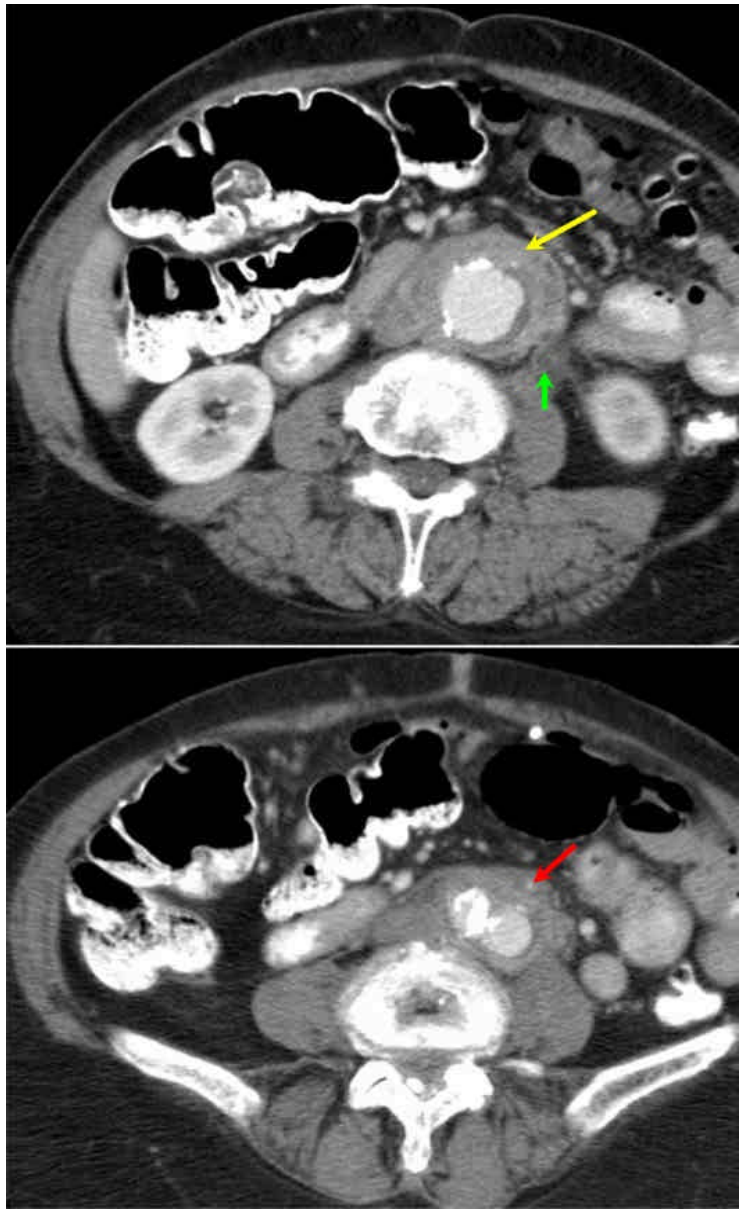
- Varón 39 años, origen magrebí, instalador de acero.
- Dolor abdominal, perdida peso, linfadenopatía generalizada, anemia y trombocitosis.
- Alb 35 g/l; IgG 21, IgA 2.9, IgM 0.6g/l
- VIH negativo, serología negativa.
- Mantoux: débilmente positivo. BAL negativo. Esputo: micobacteria atipica (isoniazida resistente)
- Radiología:
  - Engrosamiento pleural atípico, hidronefrosis izquierda.
  - Ecografía abdomen: Dilatación ducto pancreatico y biliar

1. Mayo 2003 – Cuádruple tratamiento anti-Tb

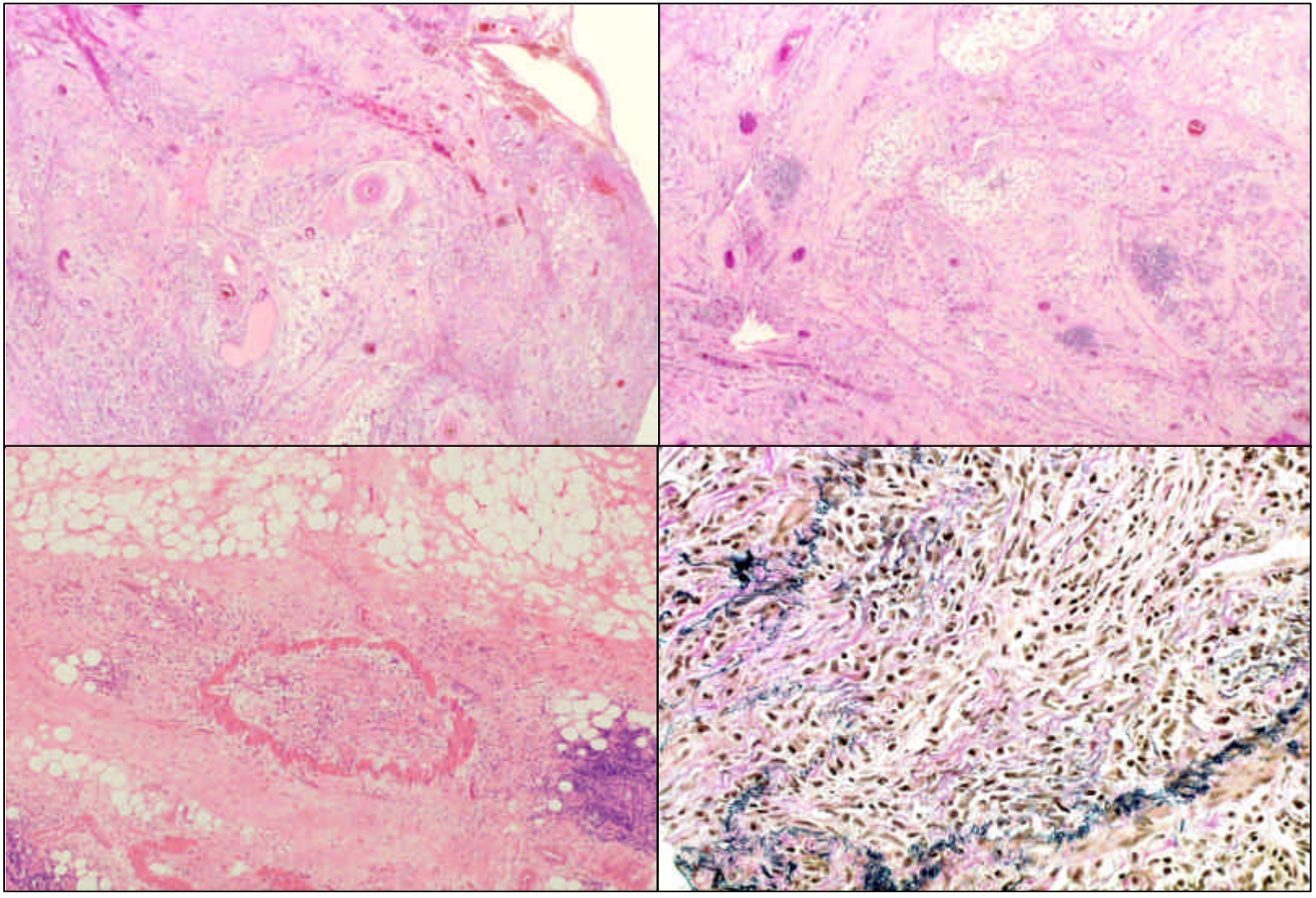
2. Julio 2003 – Cambio de tratamiento a: isoniazida, rifampicina, etambutol y pyrazinamida

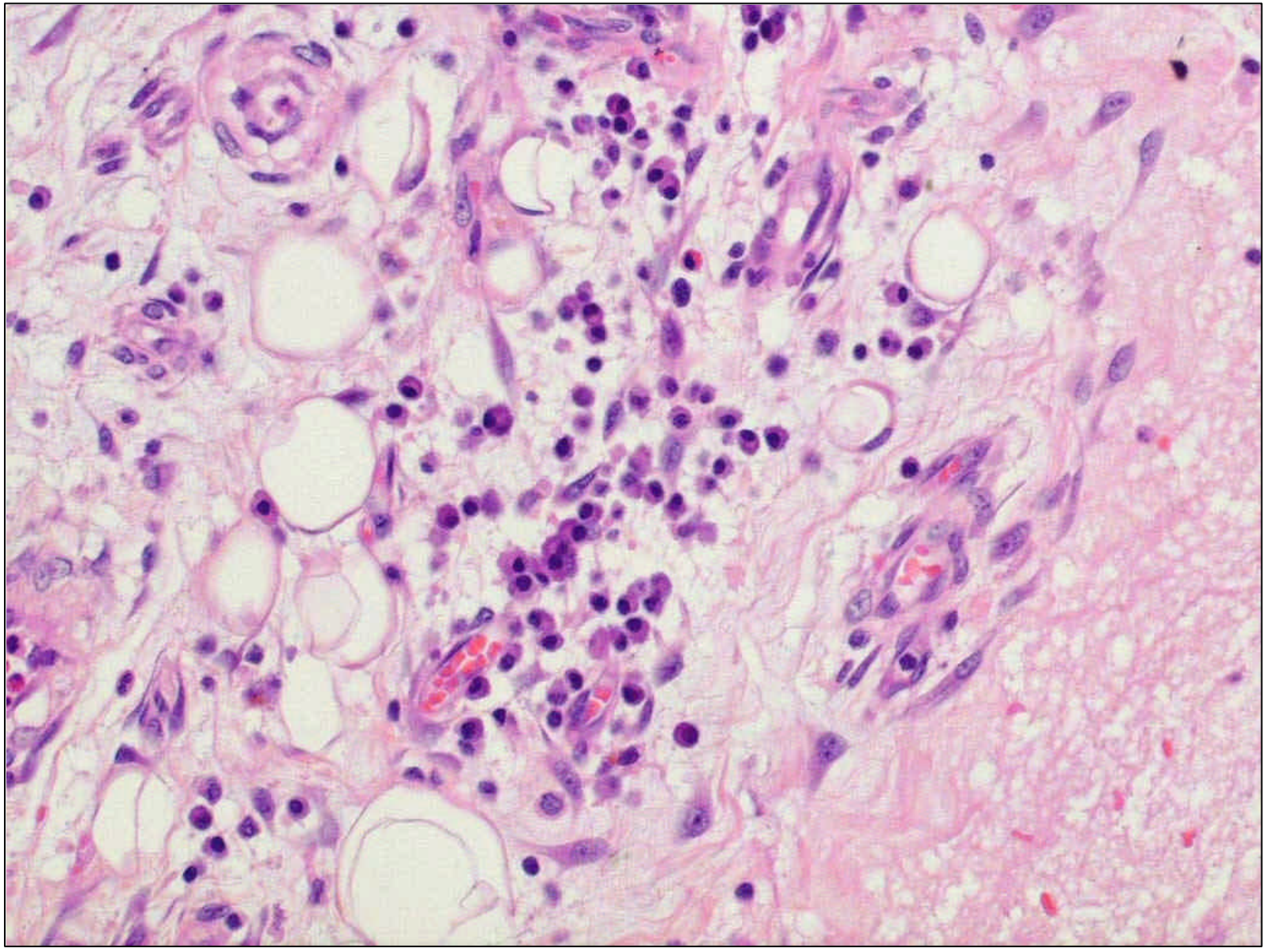
3. Noviembre 2003 Recaída clínica - predisolona 20mg ✍ “curado”

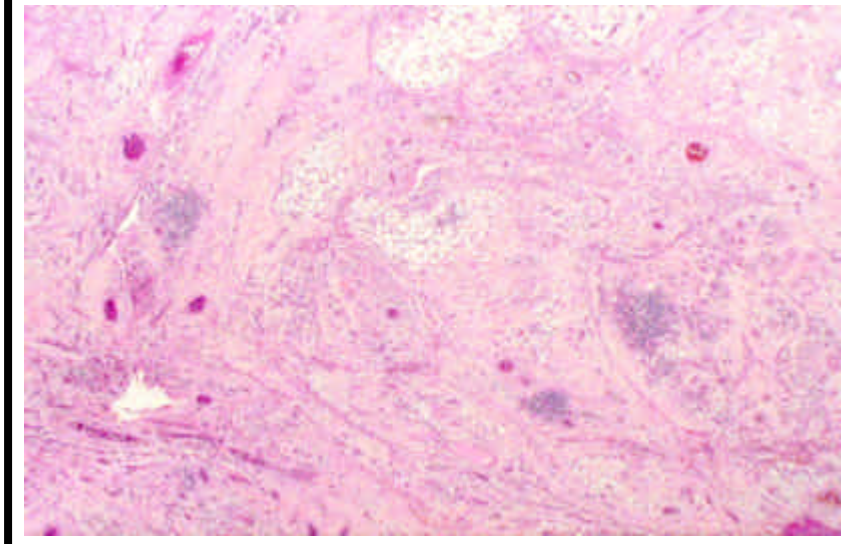


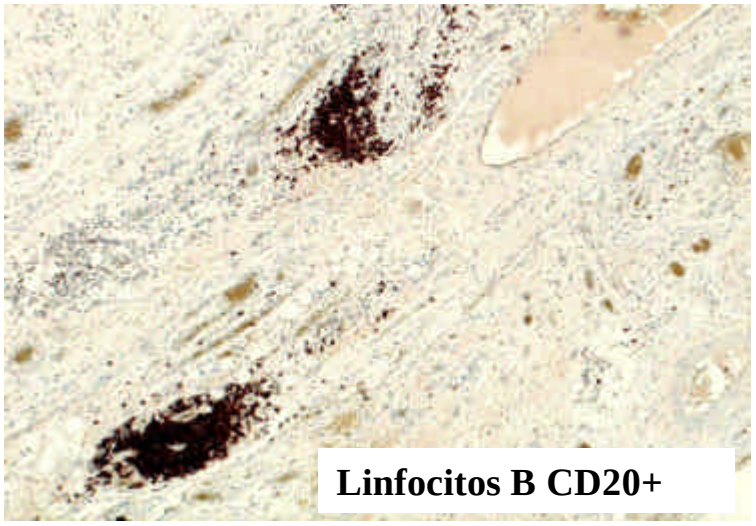


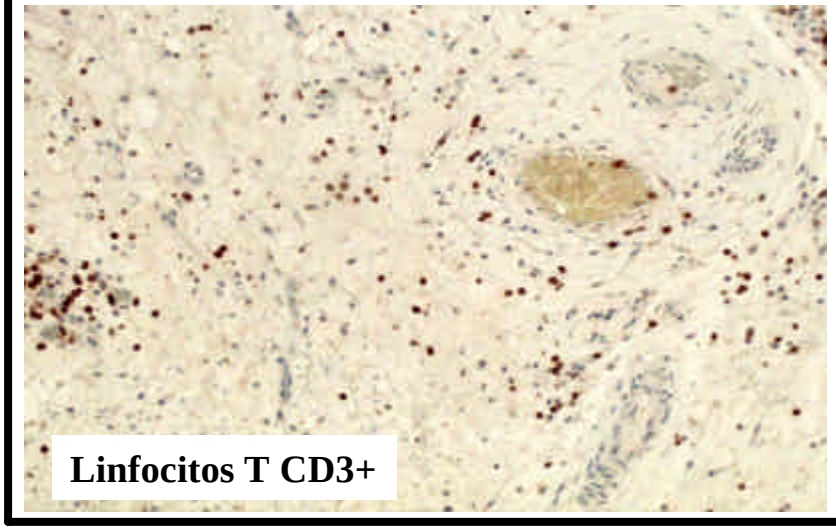
1. Marzo 2004 recaída con dolor torácico, hidronefrosis derecha. Tratamiento con quintuple terapia anti-Tb y predinoslona 60mg ✍ mejoría clínica.
2. Sept 2004 dolor abdominal, laparotomía para remover masa peritoneal ✍ tratamiento anti-Tb y esteroides
3. Marzo 2005 Nueva recaída ✍ Inicio con antibióticos y paciente derivado a UCLH

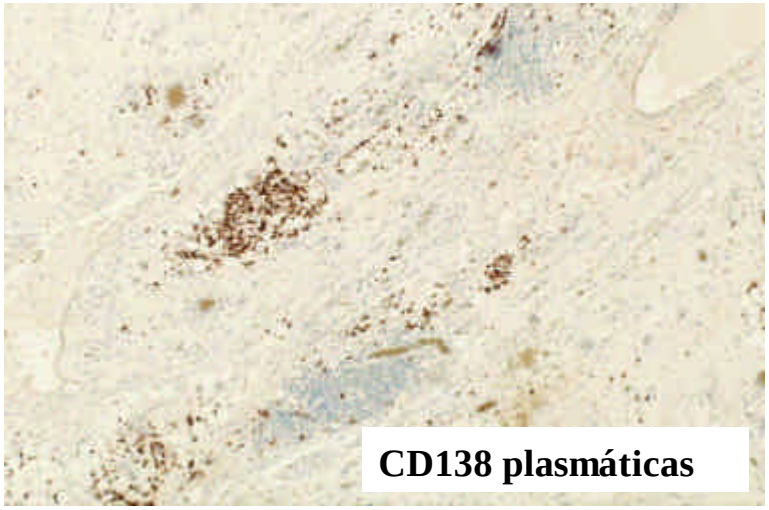


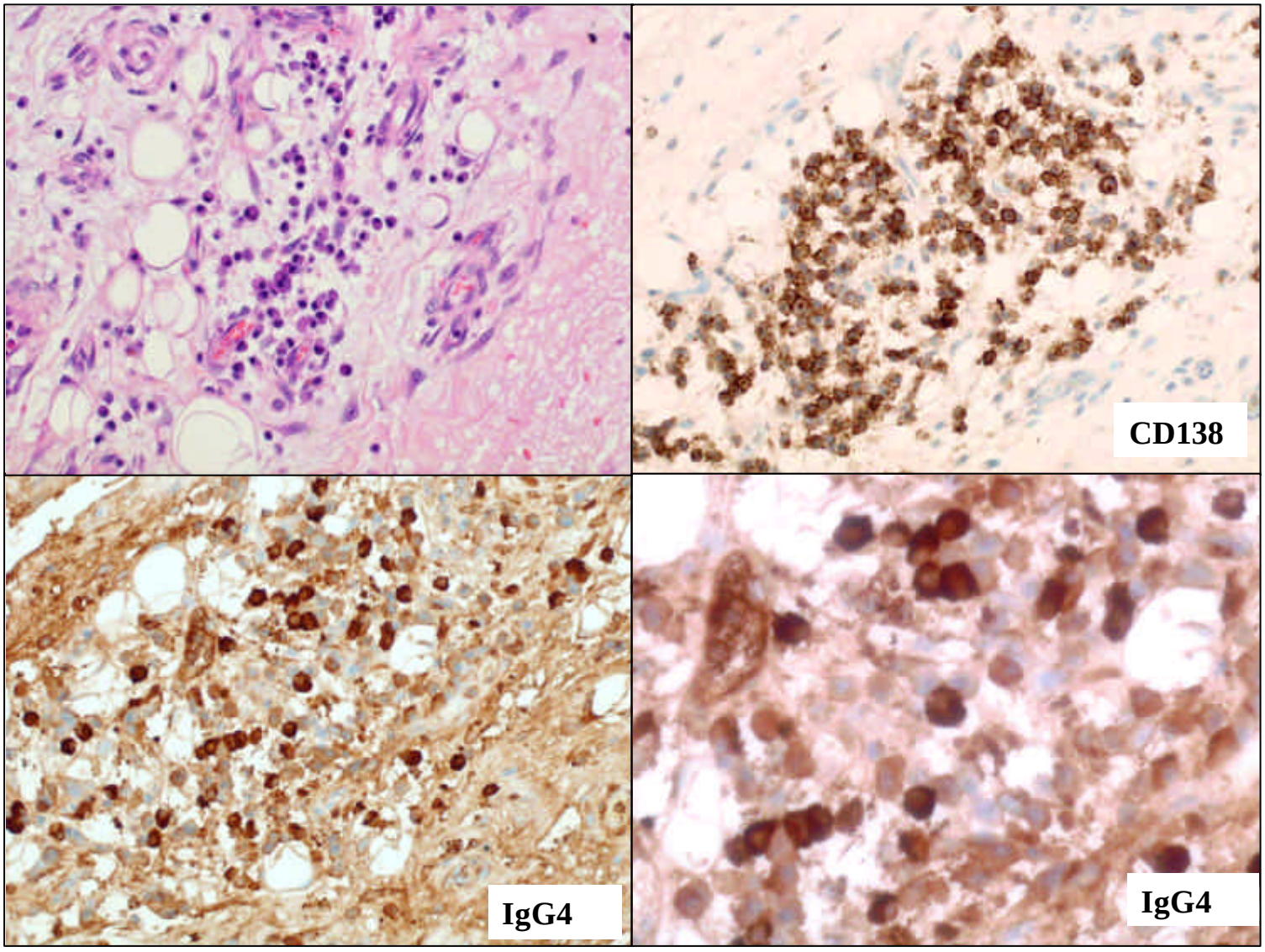


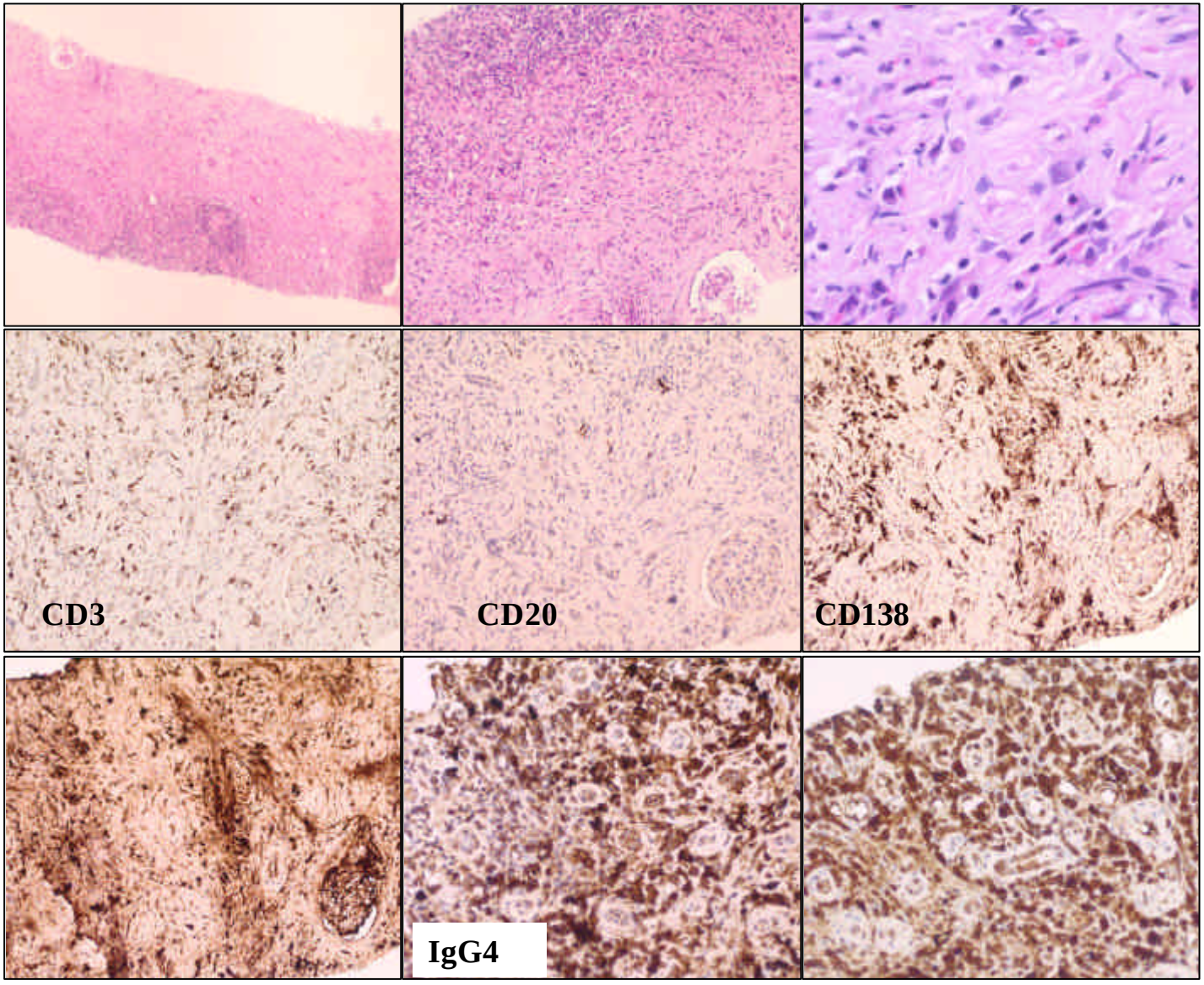



Linfocitos B CD20+


Linfocitos T CD3+


CD138 plasmáticas


CD138
IgG4
IgG4


CD3
CD20
CD138
IgG4

Hallazgos microscópicos

- Fibrosis
- Infiltrado inflamatorio denso: Linfocitos, plasmáticas, ocasionales neutrófilos y eosinófilos.
- Linfocitos: CD8+ y CD4+ T con menor proporción de células B [generalmente en forma de pequeños folículos]
- Vasculitis afectando pequeñas venas
- Arteritis obliterante
- Células plasmáticas: IgG4 +

Kloppel-G et al. J Pancreas 2005,6:97
Zamboni-G et al. Virchows Archiv 2004

The New England Journal of Medicine

HIGH SERUM IgG4 CONCENTRATIONS IN PATIENTS WITH SCLEROSING PANCREATITIS

HIDEAKI HAMANO, M.D., SHIGEYUKI KAWA, M.D., AKIRA HORIUCHI, M.D., HIROSHI UNNO, M.D., NAOYUKI FURUYA, M.D., TAIJI AKAMATSU, M.D., MANA FUKUSHIMA, M.D., TOSHIO NIKAIDO, PH.D., KOHZO NAKAYAMA, PH.D., NOBUTERU USUDA, M.D., AND KENDO KIYOSAWA, M.D.

N Engl J Med, Vol. 344, No. 10 · March 8, 2001 · www.nejm.org

¿Qué sabemos sobre IgG4?

- IgG4 la menos frecuente de los subtipos de IgG
- 3-6 % IgG en plasma de individuos sanos es IgG4
- Única IgG que es incapaz de unirse a C1q y por tanto no activa la vía clásica de activación del completemento
- Baja afinidad por antígenos
- IL-4 induce “upregulation” de IgE e IgG4
- Condiciones en las que hay ? IgG4:

  Dermatitis atópica, infecciones parasitarias (helmintos, filaria, estrongiloides), pénfigo foliaceo y pénfigo vulgar, GN membranosa con depósitos de IgG4

(*Arch Pathol Lab Med.* 2005;129:1148–1154)

Review Article

Autoimmune Pancreatitis

More Than Just a Pancreatic Disease? A Contemporary Review of Its Pathology

Vikram Deshpande, MD; Mari Mino-Kenudson, MD; William Brugge, MD; Gregory Y. Lauwers, MD

Table 1. Clinical Features of Autoimmune Pancreatitis

- Obstructive jaundice
- Vague abdominal pain, without acute pancreatitis-like pain
- Frequently associated with other autoimmune diseases
- On imaging, diffuse enlargement of pancreas (sausage sign) or focal enlargement (mass forming)
- On ERCP, diffusely irregular main pancreatic duct with strictures and strictures of the common bile duct*
- Clinical response to steroids

Virchows Arch (2004) 445:552–563
DOI 10.1007/s00428-004-1140-z

ORIGINAL ARTICLE

Giuseppe Zamboni · Jutta Lüttges · Paola Capelli · Luca Frulloni · Giorgio Cavallini · Paolo Pederzoli · Alexander Leins · Daniel Longnecker · Günter Klöppel

Histopathological features of diagnostic and clinical relevance in autoimmune pancreatitis: a study on 53 resection specimens and 9 biopsy specimens

Case no.	Age (years)	Sex	Site	Disorders	Follow-up	Recurrence (years)
AIP/GEL-neg						
1	29	Male	Head	Sjögren's syndrome	/	/
2	59	Male	Head	Crohn's disease, rheumatoid arthritis (before)	/	/
3	36	Male	Head	Sjögren's syndrome, thyroiditis (+1 yr)	1 year, CBD stenosis	1, CBD stenosis
4	69	Male	Head	Sjögren's syndrome, retroperitonal fibrosis (+3 yrs)	3 years, recurrence	3, recurrence
5	49	Male	Head	Sjögren's syndrome (+2 yrs)	8 years, recurrence	8, recurrence
6	50	Male	Head-body	Ulcerative colitis (simultaneously), sialadenitis (+1 yr)	6 years, recurrence	6, recurrence
7	60	Male	Head-body	Retroperitoneal fibrosis (simultaneously)	6 years, NED	No
AIP/GEL-pos						
1	59	Male	Head	Crohn's disease (before)	/	/
2	36	Male	Head	Crohn's disease (before)	8 years, NED	No
3	56	Male	Head	Ulcerative colitis (−12 years)	16 years, NED	No
4	62	Female	Head	Ulcerative colitis (−1 year)	1 year, NED	No
5	32	Male	Head	Ulcerative colitis (+2 years)	6 years, NED	No
6	47	Male	Head	Ulcerative colitis (−3 years)	10 years, NED	No
7	25	Female	Head	Ulcerative colitis (+1 week)	8 years, NED	No

“Pancreatitis Autoinmune” (AIP)

Sinónimos:

- Pancreatitis crónica no alcohólica, ducto-destructiva
- Pancreatitis linfoplasmocitaria esclerosante con colangitis
- Pancreatitis crónica esclerosante

Epidemiología:

- 5-6% de pacientes con pancreatitis crónica pero hasta en el 40% de pacientes con pancreatitis idiopática ✍ algún marcador autoinmune positivo
- 2.5% de pancreatectomías por cáncer ✍ AIP y hasta 21-23% de Whipple’s por pancreatopatía benigna.
- Ratio varón:mujer 1:1 ó 2:1
- Generalmente >50 años.

Clínica:

• Ictericia (63%), dolor abdominal (35%)

• Síntomas asociados con otros sistemas afectos: Enfermedad inflamatoria intestinal (17%, principalmente CU) y Diabetes tipo II (40% pacientes)

• Linfadenopatías (hasta 80% pacientes)

Analítica:

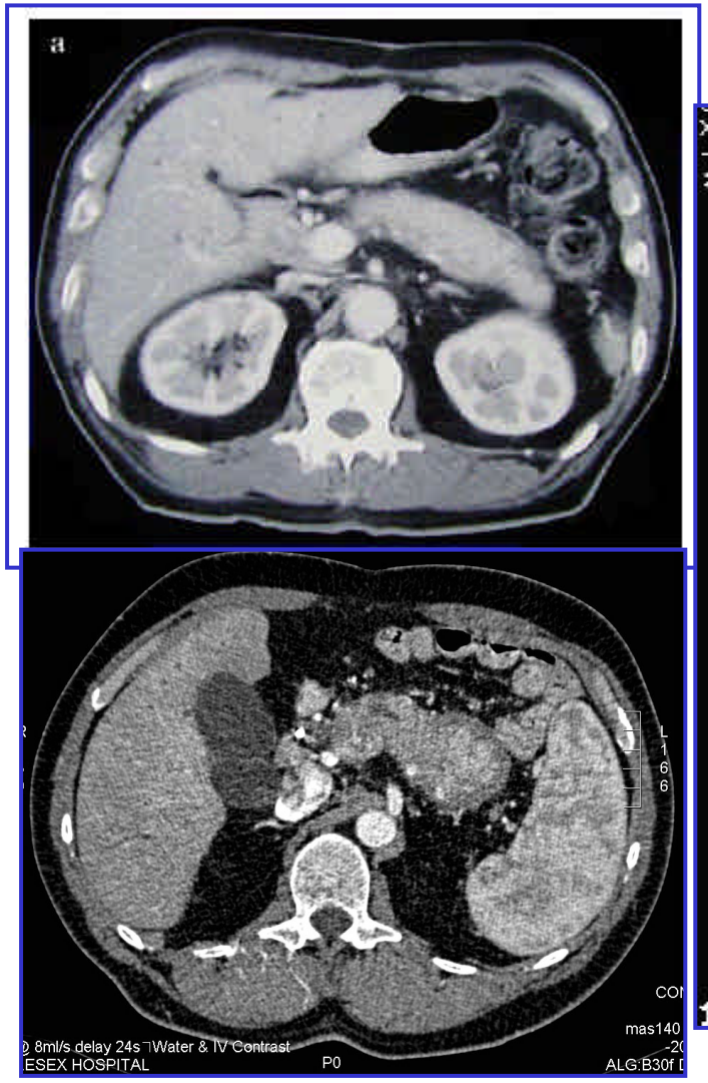
• Hiperbilirubinemia, eosinofiilia periferica, IgE, hiperglobulinemia,

• Anticuerpos (ANA en 43-75%, anti-factor reumatoide 13-30%)

• IgG4 elevada en plasma

Radiología:

- Páncreas difusamente aumentado de tamaño (pérdida de "lobularidad")
- Atrofia pancreática en enfermedad de larga evolución
- Linfadenopatía regional.
- Masa pancreática (cabeza) – difícil diagnóstico diferencial con adenocarcinoma ductal en CT
- "*Hallmark*" – Colangiopancreatografía endoscópica retrograda: estenosis focal o difusa de ducto pancreático principal + estenosis de porción intrapancreática de conducto biliar (CBD) + ductos biliares extra-pancreticos.
- Utilidad de resonancia magnetica: sin determinar.

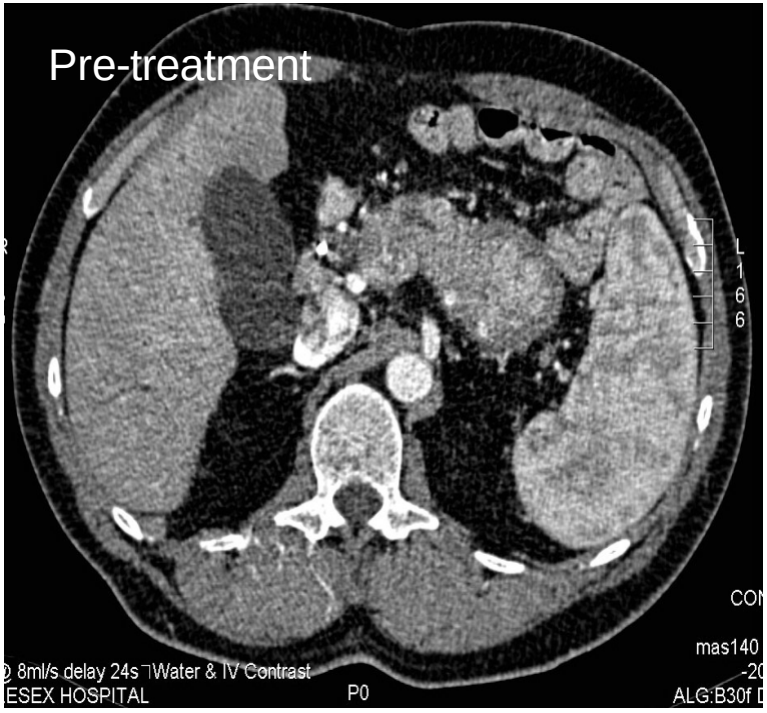

a
8ml/s delay 24s Water & IV Contrast
ESEX HOSPITAL
P0
mas140
ALG:B30f

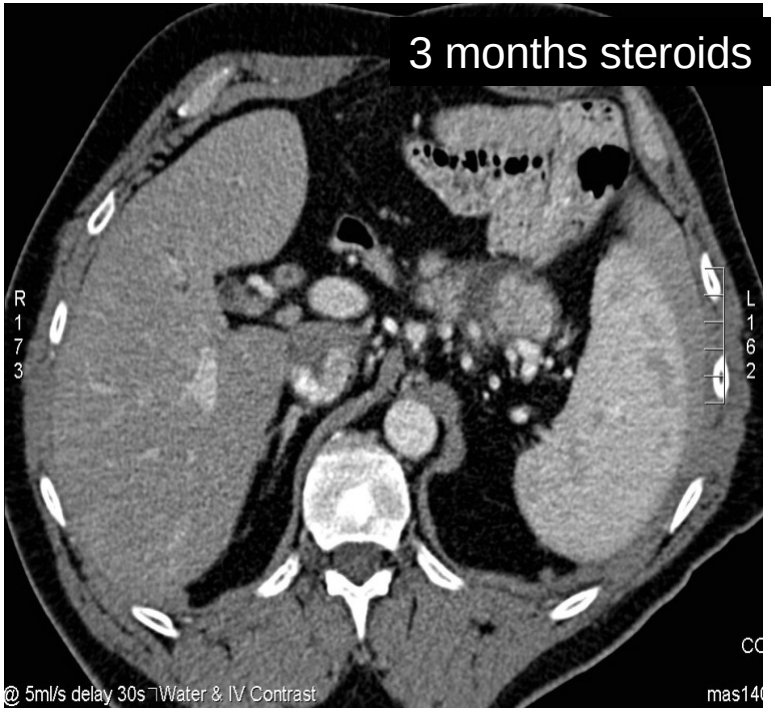
Tratamiento

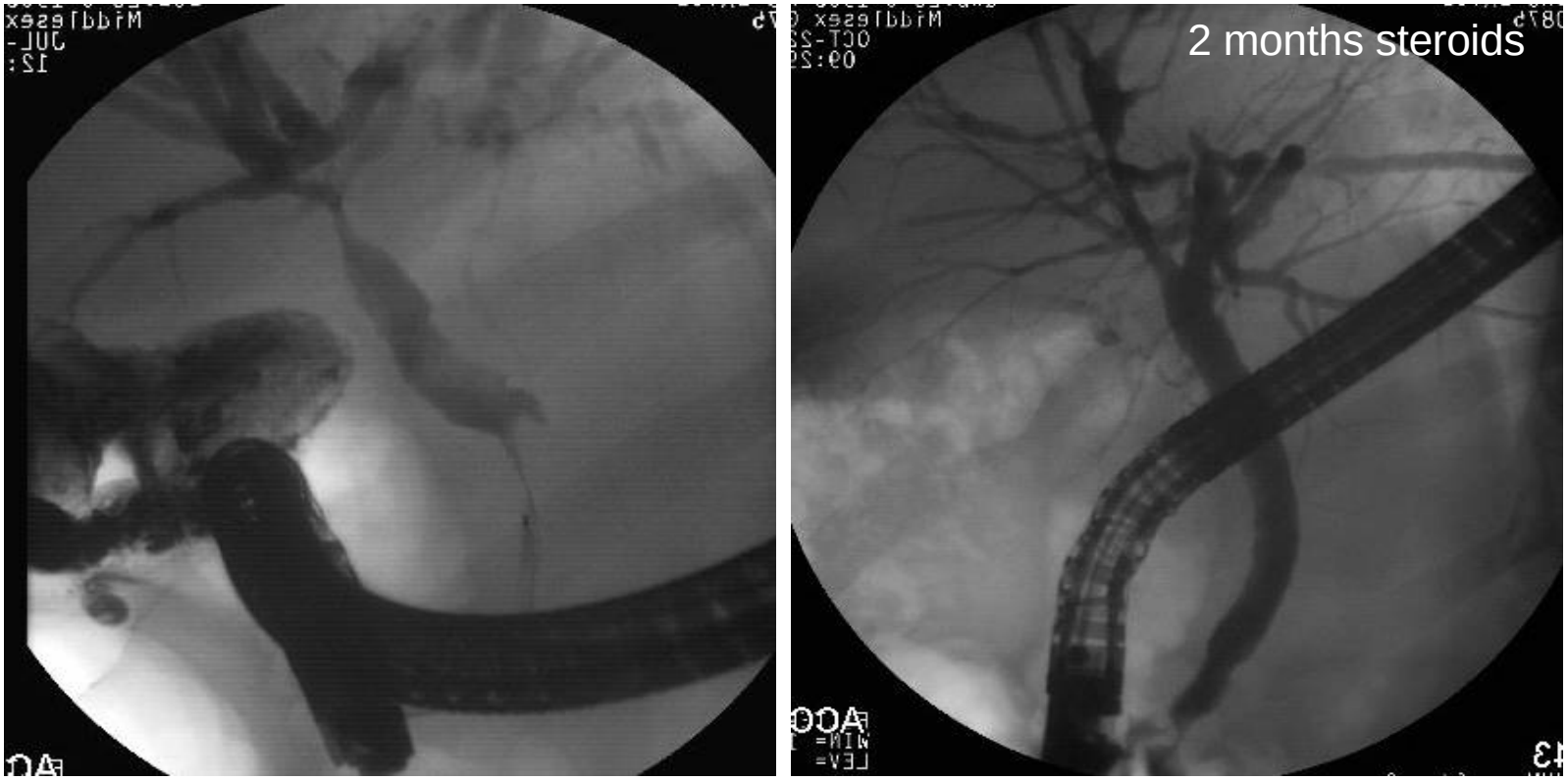
- Corticoides (pero casos de resolución espontánea sin esteroides también descritos)

- Respuesta inmediata – Seguimiento con CT 2-4 semanas tras inicio de tratamiento.

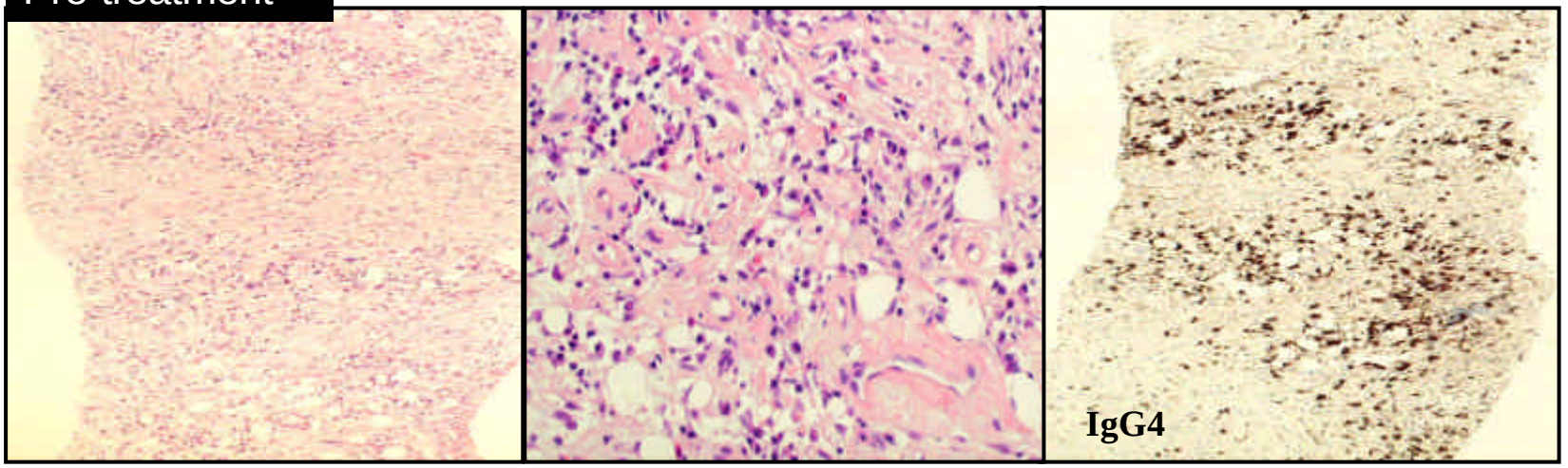
- Alteraciones analíticas, afectación biliar... también respuesta a esteroides


Pre-treatment
8ml/s delay 24s Water & IV Contrast
ESEX HOSPITAL
P0
mas140

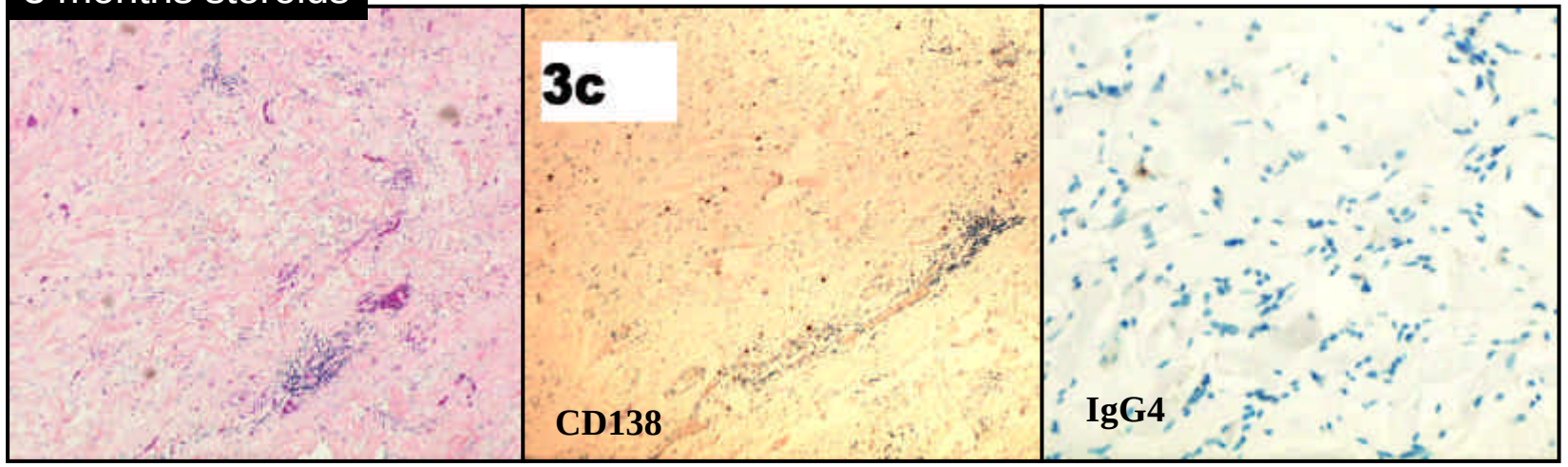

3 months steroids
@ 5ml/s delay 30s Water & IV Contrast


2 months steroids

Pre-treatment



3 months steroids



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Autoimmune Pancreatitis: Clinical and Radiological Features and Objective Response to Steroid Therapy in a UK Series

Nicholas I. Church, M.D., M.R.C.P.,[1] Stephen P. Pereira, B.Sc., Ph.D., F.R.C.P.,[1,4] Maesha G. Deheragoda, M.A., M.R.C.P.C.H.,[3] Neomal Sandanayake, F.R.A.C.P.,[1] Zahir Amin, M.R.C.P., M.D., F.R.C.R.,[2] William R. Lees, F.R.C.R., F.R.C.S.,[2] Alice Gillams, M.R.C.P., F.R.C.R.,[2] Manuel Rodriguez-Justo, M.Sc.,[3] Marco Novelli, M.Sc., Ph.D., F.R.CPath.,[3] Edward W. Seward, B.Sc., M.D., M.R.C.P.,[1] Adrian R.W. Hatfield, M.D., F.R.C.P.,[1] and George J.M. Webster, B.Sc., M.D., F.R.C.P.[1,4]
Departments of [1]Gastroenterology, [2]Radiology, and [3]Pathology, University College Hospital, London, United Kingdom; and [4]The Institute of Hepatology, University College London, London, United Kingdom

- Respuesta a esteroides rápida en 4 semanas.
- Hay progresión de enfermedad sin tratamiento esteroideo.
- Recidiva en hasta 55% pacientes con dosis pequeñas de esteroides o cuando esteroides son retirados.
- Generalmente buena respuesta con incremento de esteroides +/- azaiotropina.
- Pacientes con no respuesta / recidiva no consiguieron niveles normales séricos de IgG4 durante tratamiento.

Japan-Korea Symposium on Autoimmune Pancreatitis (KOKURA 2007)

Terumi Kamisawa, MD, PhD, Jae Bock Chung, MD, PhD,† Hiroyuki Irie, MD, PhD,‡ Tadayoshi Nishino, MD, PhD,§ Toshiharu Ueki, MD, PhD,|| Masaru Takase, MD, PhD,¶ Shigeyuki Kawa, MD, PhD,# Isao Nishimori, MD, PhD,** Kazuichi Okazaki, MD, PhD,†† Myung-Hwan Kim, MD, PhD,‡‡ and Makoto Otsuki, MD, PhD§§*

Table 1. Characteristic Features of Autoimmune Pancreatitis

i.	Increased levels of serum gammaglobulin or IgG4
ii.	Presence of autoantibodies
iii.	Diffuse enlargement of the pancreas or a pancreatic mass
iv.	Diffuse irregular narrowing of the main pancreatic duct
v.	Fibrotic changes with lymphocyte infiltration
vi.	No symptoms or only mild symptoms, usually without attacks of acute pancreatitis
vii.	Rare pancreatic calcification or cysts
viii.	Occasional association with other autoimmune diseases
ix.	Effective steroid therapy

Interstitial pneumonia associated with autoimmune pancreatitis

T Taniguchi, M Ko, S Seko, O Nishida, F Inoue, H Kobayashi, T Saiga, M Okamoto
Department of Internal Medicine, Radiology, and Pathology, Ohtsu Red Cross Hospital, Ohtsu, Japan

Gut 2004;53:770–774

Digestive Diseases and Sciences, Vol. 50, No. 6 (June 2005), pp. 1052–1057 (© 2005)
DOI: 10.1007/s10620-005-2703-9

High Prevalence of Hypothyroidism in Patients with Autoimmune Pancreatitis

KENICHI KOMATSU, MD,* HIDEAKI HAMANO, MD,* YASUHIDE OCHI, MD,* MARI TAKAYAMA, MD,* TAKASHI MURAKI, MD,* KANAME YOSHIZAWA, MD,* AKIHIRO SAKURAI, MD,† MASAO OTA, PhD,‡ and SHIGEYUKI KAWA, MD*

Nephrol Dial Transplant (2004) 19: 2397–2399
DOI: 10.1093/ndt/gfh050

Nephrology Dialysis Transplantation

Case Report

Retroperitoneal fibrosis, sclerosing pancreatitis and bronchiolitis obliterans with organizing pneumonia

Christian Duvic[1], Jérôme Desrame[2], Christophe Lévêque[3] and Georges Nedelec[1]

Human Pathology (2006) 37, 239–243

ELSEVIER

Human PATHOLOGY

www.elsevier.com/locate/humpath

A case of retroperitoneal and mediastinal fibrosis exhibiting elevated levels of IgG4 in the absence of sclerosing pancreatitis (autoimmune pancreatitis)

Yoh Zen MD[a,b,*], Aiko Sawazaki MD[c], Shiro Miyayama MD[d], Kazuo Notsumata MD[c], Nobuyoshi Tanaka MD[c], Yasuni Nakanuma MD[e]

Internal Medicine Journal **36** (2006) 58–61

BRIEF COMMUNICATION

High-rate pulmonary involvement in autoimmune pancreatitis

K. Hirano,[1,2] T. Kawabe,[2] Y. Komatsu,[2] S. Matsubara,[2] O. Togawa,[2] T. Arizumi,[2] N. Yamamoto,[2] Y. Nakai,[2] N. Sasahira,[2] T. Tsujino,[2] N. Toda,[2] H. Isayama,[2] M. Tada[2] and M. Omata[2]

[1]Department of Gastroenterology, Mitsui Memorial Hospital and [2]Department of Gastroenterology, University of Tokyo, Tokyo, Japan

BMC Medicine

BioMed Central

Research article

Open Access

Hyper-IgG4 disease: report and characterisation of a new disease

Guy H Neild*[1,2], Manuel Rodriguez-Justo[3], Catherine Wall[1] and John O Connolly[1,2]

Name	Synonyms
RPF	Ormond's disease
Retro-orbital tumour	Fibrous pseudotumour of the orbit, Graves' orbitopathy
Riedel's thyroiditis	
Chronic sclerosing sialadenitis[151]	Kuttner's tumour
Panniculitis	Weber-Christian syndrome steatonecrosis, necrosing panniculitis
Sclerosing pancreatitis[158]	Primary inflammatory pancreatitis (P)[159], lymphoplasmacytic sclerosing P[7,160,161], autoimmune P[162], sclerosing pancreaticocholangitis[163], pancreatic pseudo-tumour[95]
Sclerosing cholangitis	
Bronchiolitis obliterans with organizing pneumonia	Cryptogenic organizing pneumonia, pulmonary hyalinizing granuloma.
Benign pleural mesothelioma[180,181], calcifying pseudotumour[182,183]	Asbestos-related?

Systemic Extrapancreatic Lesions Associated With Autoimmune Pancreatitis

Hirotaka Ohara, MD, Takahiro Nakazawa, MD, Hitoshi Sano, MD, Tomoaki Ando, MD, Tetsu Okamoto, MD, Hiroki Takada, MD, Kazuki Hayashi, MD, Yasuhiro Kitajima, MD, Haruhisa Nakao, MD, and Takashi Joh, MD

TABLE 5. Review of AIP Cases With Systemic Extrapancreatic Lesions

	Western Countries (n = 172)	Japan (n = 132)	Total (n = 304)	
Sjögren syndrome	13 [2),11),18),19),20),22),23),24)]	24 [25),26),27),28),29),30),32),33),37)]	37	P < 0.01
IBD				
UC	14 [19),20),23),24)]	5 [33),35),36),45),49)]	19	NS
CD	4 [19),23)]	0	4	NS
Total	18	5	23	P < 0.05
Retroperitoneal fibrosis	9 [12),14),15),16),17),19),23),24)]	8 [34),39),40),42),our case]	17	NS
Sialadenitis	5 [3),20),21),23)]	4 [44),our case]	9	NS
Thyroid disease	4 [14),19),20),23)]	1 [38)]	5	NS
ITP	2 [23)]	3 [31),41),our case]	5	NS
RA	2 [20),23)]	1 [37)]	3	NS
Interstitial pneumonia	0	3 [32),47),our case]	3	NS
Tubulointerstitial nephritis	1 [20)]	2 [46),48)]	3	NS
SLE	0	2 [33)]	2	NS
AIH	0	2 [33)]	2	NS
Orbital pseudotumor	2 [3),4)]	0	2	NS
Malignant lymphoma	2 [19)]	0	2	NS

J Gastroenterol 2003; 38:982–984
DOI 10.1007/s00535-003-1175-y

Journal of Gastroenterology

Rapid communication

A new clinicopathological entity of IgG4-related autoimmune disease

Terumi Kamisawa[1], Nobuaki Funata[2], Yukiko Hayashi[2], Yoshinobu Eishi[3], Morio Koike[3], Kouji Tsuruta[4], Atsutake Okamoto[4], Naoto Egawa[1], and Hitoshi Nakajima[1]

[1]Department of Internal Medicine, Tokyo Metropolitan Komagome Hospital, 3-18-22 Honkomagome, Bunkyo-ku, Tokyo 113-8677, Japan
[2]Department of Pathology, Tokyo Metropolitan Komagome Hospital, Tokyo, Japan
[3]Department of Pathology, Tokyo Medical and Dental University School of Medicine, Tokyo, Japan
[4]Department of Surgery, Tokyo Metropolitan Komagome Hospital, Tokyo, Japan

J Gastroenterol 2006; 41:613–625
DOI 10.1007/s00535-006-1862-6

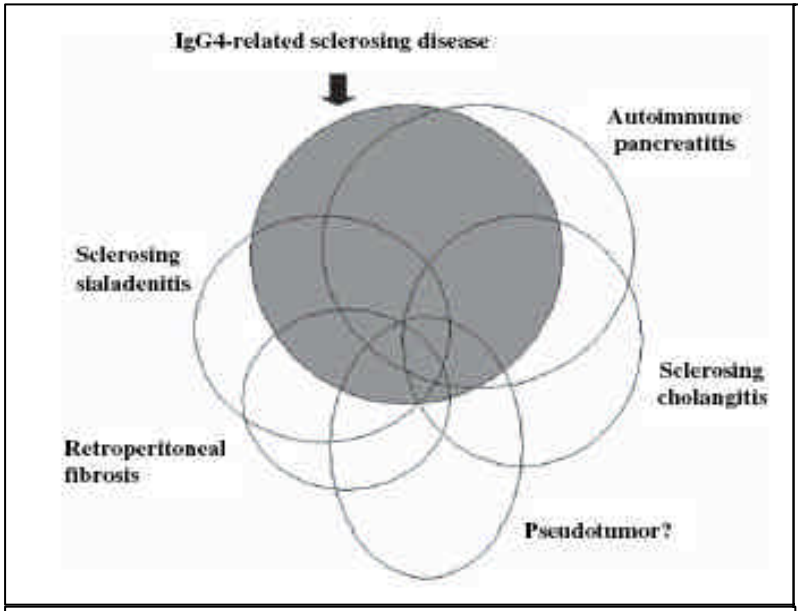
Journal of Gastroenterology

Review

Autoimmune pancreatitis: proposal of IgG4-related sclerosing disease

Terumi Kamisawa[1] and Atsutake Okamoto[2]

[1]Department of Internal Medicine, Tokyo Metropolitan Komagome Hospital, 3-18-22 Honkomagome, Bunkyo-ku, Tokyo 113-8677, Japan
[2]Department of Surgery, Tokyo Metropolitan Komagome Hospital, Tokyo, Japan



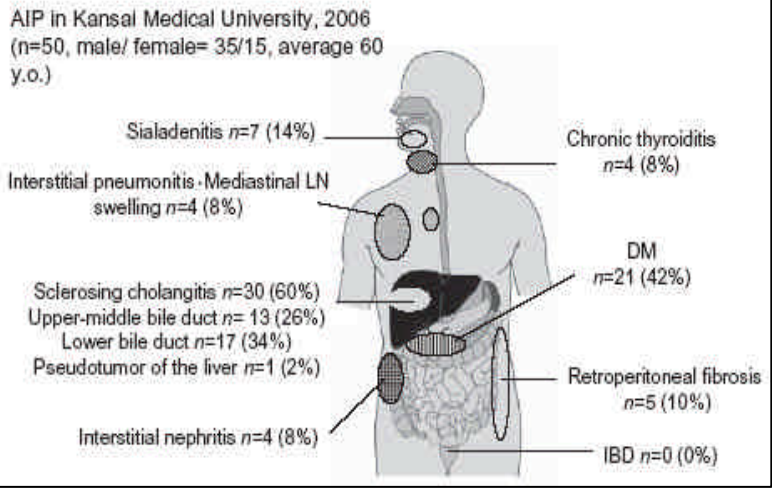


Table 1. Clinicopathological findings of IgG4-related sclerosing disease

- Systemic disease characterized histopathologically by extensive IgG4-positive plasma cell infiltration of various organs together with T lymphocytes
- Major clinical manifestations are apparent in the organs in which tissues fibrosis with obstructive phlebitis is pathologically induced

Pancreas	Autoimmune pancreatitis
Bile duct	Sclerosing cholangitis
Gallbladder	Sclerosing cholecystitis
Salivary gland	Sclerosing sialadenitis
Retroperitoneum	Retroperitoneal fibrosis

- Some pseudotumors may be involved in this disease
- Possibility of close relationship to multifocal fibrosclerosis
- Occasional association with lymphadenopathy
- Elderly male preponderance
- Frequent elevation of serum IgG4 levels
- Favorite response to steroid therapy
- Differentiation from malignant tumor is important.
- Precise pathogenesis and pathophysiology remain unclear

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

CURRENT CONCEPTS

Autoimmune Pancreatitis

Dmitry L. Finkelberg, M.D., Dushyant Sahani, M.D., Vikram Deshpande, M.D., and William R. Brugge, M.D.

N Engl J Med 2006;355:2670-6.

Table 1. Diagnostic Criteria for Autoimmune Pancreatitis.*

Findings on Imaging Radiography (One Required)		Serologic and Histologic Findings (One Required)		
Cross-Sectional Imaging	ERCP or MRCP	Serologic Analysis	Pancreatic–Biliary Histologic Analysis	Nongastrointestinal Histologic Analysis
Diffusely enlarged pancreas	Segmental pancreatic ductal narrowing	Elevated serum IgG4 level	Periductal lymphoplasmacytic infiltration or fibrosis	Tubulointerstitial nephritis with immune deposits within tubular basement membranes
Enhanced peripheral rim of hypoattenuation "halo"	Focal pancreatic ductal narrowing	Elevated serum IgG or gamma globulin level	Obliterative phlebitis	Pulmonary interstitial lymphoplasmacytic infiltration with IgG4-positive plasma cells†
Low-attenuation mass in head of pancreas	Diffuse pancreatic ductal narrowing	Presence of ALA, ACA II, ASMA, or ANA	IgG4-positive plasma cells in tissue†	Chronic sialadenitis with IgG4-positive plasma cells†

Algunas preguntas que necesitan respuesta

- ¿Es o no es una enfermedad autoinmune?

- Si es autoinmune, ¿cuáles son los antígenos implicados?

- ? IgG4: ¿respuesta secundaria a un factor iniciador de la enfermedad todavía desconocido? o ¿factor etiopatogénico de la enfermedad?

- ¿Sabemos algo de la etiopatogenia de la enfermedad?

ORIGINAL ARTICLE

Autoimmune Pancreatitis: A Systemic Immune Complex Mediated Disease

Vikram Deshpande, MD, Sonia Chicano, MD,* Dmitry Finkelberg, MD,† Martin K. Selig, BA,* Mari Mino-Kenudson, MD,* William R. Brugge, MD,† Robert B. Colvin, MD,* and Gregory Y. Lauwers, MD**

(*Am J Surg Pathol* 2006;30:1537–1545)

- Asociación con otras enfermedades autoinmunes: Sjögren, enfermedad inflamatoria intestinal, artritis reumatoide...

[Coexistencia con enfermedades autoinmune 35-56% Asia vs. 8-16% Europa/USA]

- Asociación con haplotipo DRB1*0405-DBR1*0401
- Hiperganmaglobulinemia, anticuerpos anti-anhidrasa carbonica II y lactoferrina ✍ ¿mecanismos primarios de la enfermedad?
- No todos los paciente tienen hiperganmaglobulinemia o ANA
- Antígenos primarios no identificados.

Th2 and Regulatory Immune Reactions Are Increased in Immunoglobin G4-Related Sclerosing Pancreatitis and Cholangitis

Yoh Zen,[1,2] Takahiko Fujii,[1] Kenichi Harada,[1] Mitsuhiro Kawano,[3] Kazunori Yamada,[3] Masayuki Takahira,[4] and Yasuni Nakanuma[1]

(HEPATOLOGY 2007;45:1538-1546.)

	Number
IgG4-related diseases	
Autoimmune pancreato-cholangitis	14*
Chronic sclerosing sialadenitis	9*
Chronic sclerosing dacryoadenitis	2
Pulmonary inflammatory pseudotumor	8
Disease controls	
Primary sclerosing cholangitis	12
Primary biliary cirrhosis	2
Sjögren's syndrome	5
Hepatolithiasis	5
Sialolithiasis	5

- *Treg* CD4+CD25+, que expresan factor de transcripción Forkhead box P3 (FoxP3). [Células generalmente "inhabilitadas" funcionalmente en algunos transtornos autoinmunes -PBC, hepatitis autoinmune-].
- Incremento de IL-4 y 10 en AIP frente a PBC y PSC
- IL-10 y TGF-Beta producido por Tregs inducen incremento de IgG4 in plasma y de plasmáticas IgG4+
- TGF-Beta es un factor fibrogénico
- Mecanismo Th2 y Tregs es más común de procesos alérgicos (tipo astma o dermatitis atópica) más que autoinmune.

(*Am J Surg Pathol* 2007;31:521–528)

Autoimmune Pancreatitis: Frequency, IgG4 Expression, and Clonality of T and B Cells

Motohiro Kojima, MD,† Bence Sipos, MD,* Wolfram Klapper, MD,* Olaf Frahm, MD,* Hans-Christian Knuth,* Akio Yanagisawa, MD,‡ Giuseppe Zamboni, MD,§ Toshio Morohoshi, MD,† and Günter Klöppel, MD**

TABLE 4. Clonality Analysis of the T-cell Receptor γ-chain (TCRγ) and the FR3 Region of the Immunoglobulin Heavy Chain Gene (IgH-FR3) in Patients With AIP and Non-AIP CP

Case No.	Age (y)	Sex	Diagnosis	TCRγ	IgH-FR3
1	24	Female	AIP	Polyclonal	Polyclonal
2	56	Male	AIP	Polyclonal	Polyclonal
3	70	Female	AIP	Polyclonal	Polyclonal
4	76	Female	AIP	Polyclonal	Polyclonal
5	28	Female	AIP	Polyclonal	Polyclonal
6	62	Female	AIP	Polyclonal	Polyclonal
7	66	Male	AIP	Polyclonal	Polyclonal
8	25	Male	AIP	Polyclonal	Polyclonal
9	66	Male	AIP	Polyclonal	Oligoclonal
10	56	Male	AIP	Polyclonal	Polyclonal
11	65	Female	AIP	Polyclonal	Polyclonal
12	49	Male	Non-AIP CP	Polyclonal	Polyclonal
13	62	Male	Non-AIP CP	Polyclonal	Polyclonal

Algunas preguntas que necesitan respuesta

- ¿Es o no es una enfermedad autoinmune?
  - ✍ **No está claro**
- Si es autoinmune, ¿cuáles son los antígenos implicados?
  - ✍ **Desconocidos por ahora**
- ? IgG4: ¿factor etiopatogénico de la enfermedad?
  - ✍ **Probablemente más un “marcador” de la enfermedad que un factor etiopatogénico**
- ¿Sabemos algo de la etiopatogenia de la enfermedad?
  - ✍ **Muy poco**

Más preguntas …

- ¿Es la determinación serológica de IgG4 específica de la enfermedad?

- ¿Cuál es la especificidad del incremento de células plasmáticas IgG4 en el diagnóstico de la enfermedad?

JOP. J Pancreas (Online) 2004; 5(6):531-533.

PANCREAS NEWS

IgG4 as a Serological Marker of Autoimmune Pancreatitis: The Latest News

Raffaele Pezzilli, Roberto Corinaldesi

Department of Internal Medicine, Sant'Orsola-Malpighi Hospital. Bologna, Italy

IgG4 “cut off value”: 135mg/dl

Sensibilidad del 100% en series Japón/Korea, pero en Europa-USA: 63-68%.

¿Utilidad como marcador de respuesta / seguimiento?

Experiencia UCLH: En 5/6 pacientes con IgG4 normal en suero ✍ incremento de plasmáticas en tejido biopsiado

Modern Pathology (2007) 20, 23–28

www.modernpathology.org

IgG4-positive plasma cell infiltration in the diagnosis of autoimmune pancreatitis

Lizhi Zhang[1], Kenji Notohara[2], Michael J Levy[3], Suresh T Chari[3] and Thomas C Smyrk[1]

Table 1 IgG4+ plasma cell infiltration in AIP, CAP and PA

IgG4+ plasma cell infiltration	*AIP (n = 29)*	*CAP (n = 9)*	*PA (n = 25)*
None	1	4	16
Mild	7	4	6
Moderate	8	1	2
Marked	13	0	1
Moderate-marked (total)	21/29 (72.4%)	1/9 (11.1%)	3/25 (12%)

AIP, autoimmune pancreatitis; CAP, chronic alcoholic pancreatitis; PA, pancreatic ductal adenocarcinoma.

Although there were three pancreatic ductal adenocarcinomas with moderate to marked IgG4-positive plasma cell infiltrates, the distribution of these positive cells was different from autoimmune pancreatitis. Two cases had scattered clusters of positive cells in stroma of infiltrating carcinoma, and one had moderate numbers of positive cells in extrapancreatic lymphoid aggregates, patterns different from the diffuse and dense periductal IgG4-positive plasma cell infiltrates in autoimmune pancreatitis. Some of theses cases with prominent obstructive chronic pancreatitis also showed absence of moderate or marked IgG4-positive plasma cell infiltration.

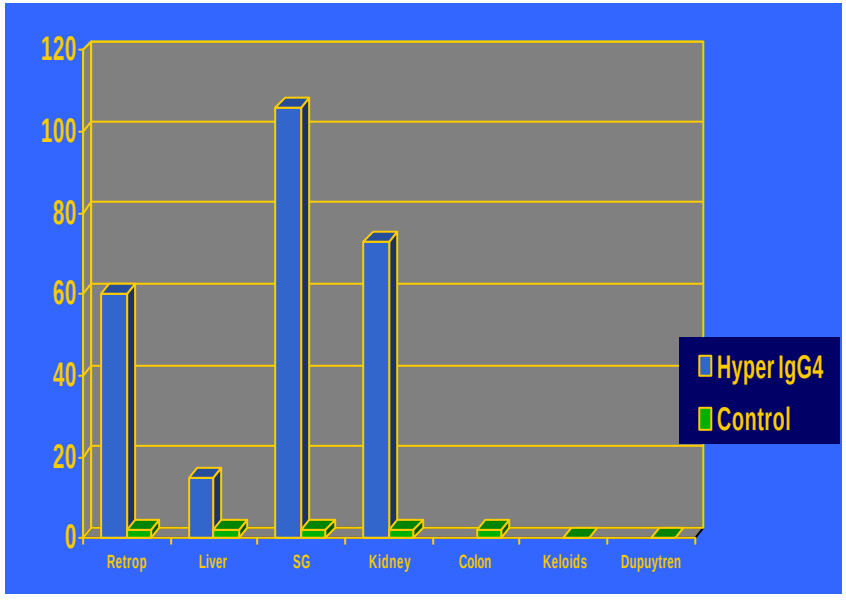
Clinical Gastroenterology and Hepatology
Official Clinical Practice Journal of the AGA Institute

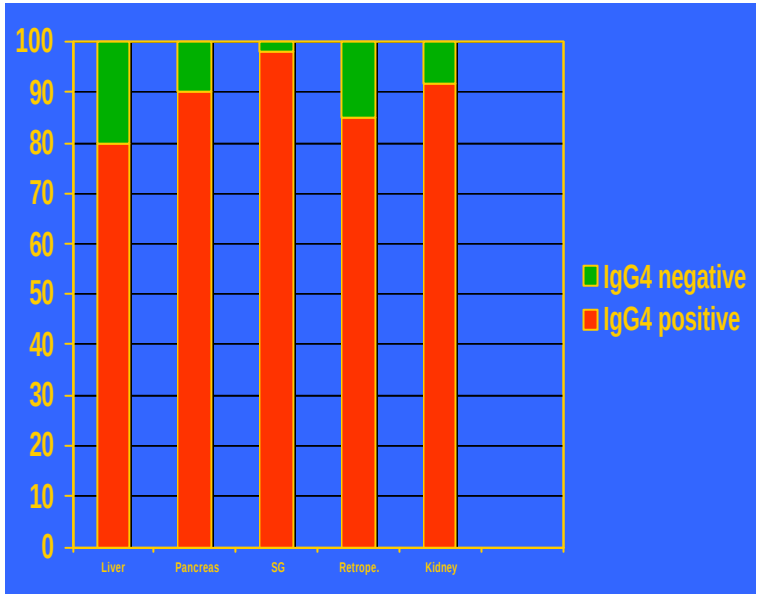
Volume 5, Issue 10, Pages 1229-1234 (October 2007)

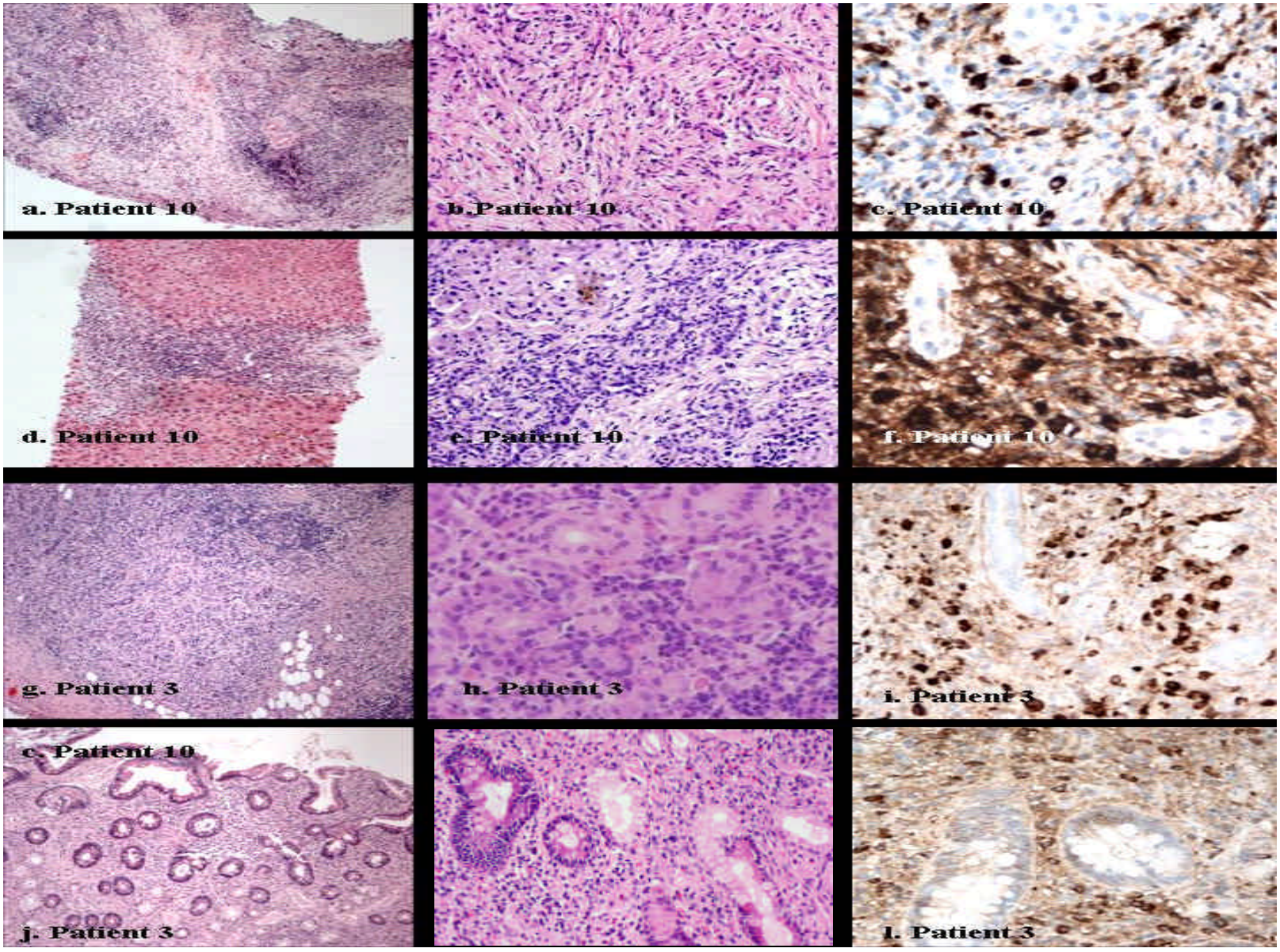
The Use of Immunoglobulin G4 Immunostaining in Diagnosing Pancreatic and Extrapancreatic Involvement in Autoimmune Pancreatitis

MAESHA G. DEHERAGODA,* NICHOLAS I. CHURCH,‡ MANUEL RODRIGUEZ-JUSTO,* PHILIPPA MUNSON,§ NEOMAL SANDANAYAKE,‡ EDWARD W. SEWARD,‡ KEITH MILLER,§ MARCO NOVELLI,* ADRIAN R. W. HATFIELD,‡ STEPHEN P. PEREIRA,‡,‖ and GEORGE J. M. WEBSTER‡,‖

*Department of Histopathology, and ‡Department of Gastroenterology, University College Hospital, London United Kingdom; the ‖UCL Institute of Hepatology, and §UCL Advanced Diagnostics, Department of Pathology, University College Hospital, London, United Kingdom






a. Patient 10
b.Patient 10
c. Patient 10
d. Patient 10
e. Patient 10
f. Patient 10
g. Patient 3
h. Patient 3
i. Patient 3
c. Patient 10
j. Patient 3
l. Patient 3

Más preguntas …

- ¿Es la determinación serológica de IgG4 específica de la enfermedad? **<70% casos**

- ¿Cuál es la especificidad del incremento de células plasmáticas IgG4 en el diagnóstico de la enfermedad? **Sólo en casos con alto número de plasmáticas IgG4+ o >80% plasmáticas expresan IgG4**

Otro caso clínico:

UCL HOSPITALS — University College London Hospitals NHS
NHS Foundation Trust

Consultant Gastroenterologists

G J M Webster BSc MD MRCP
A R W Hatfield MD FRCP
S P Pereira BSc PhD FRCP

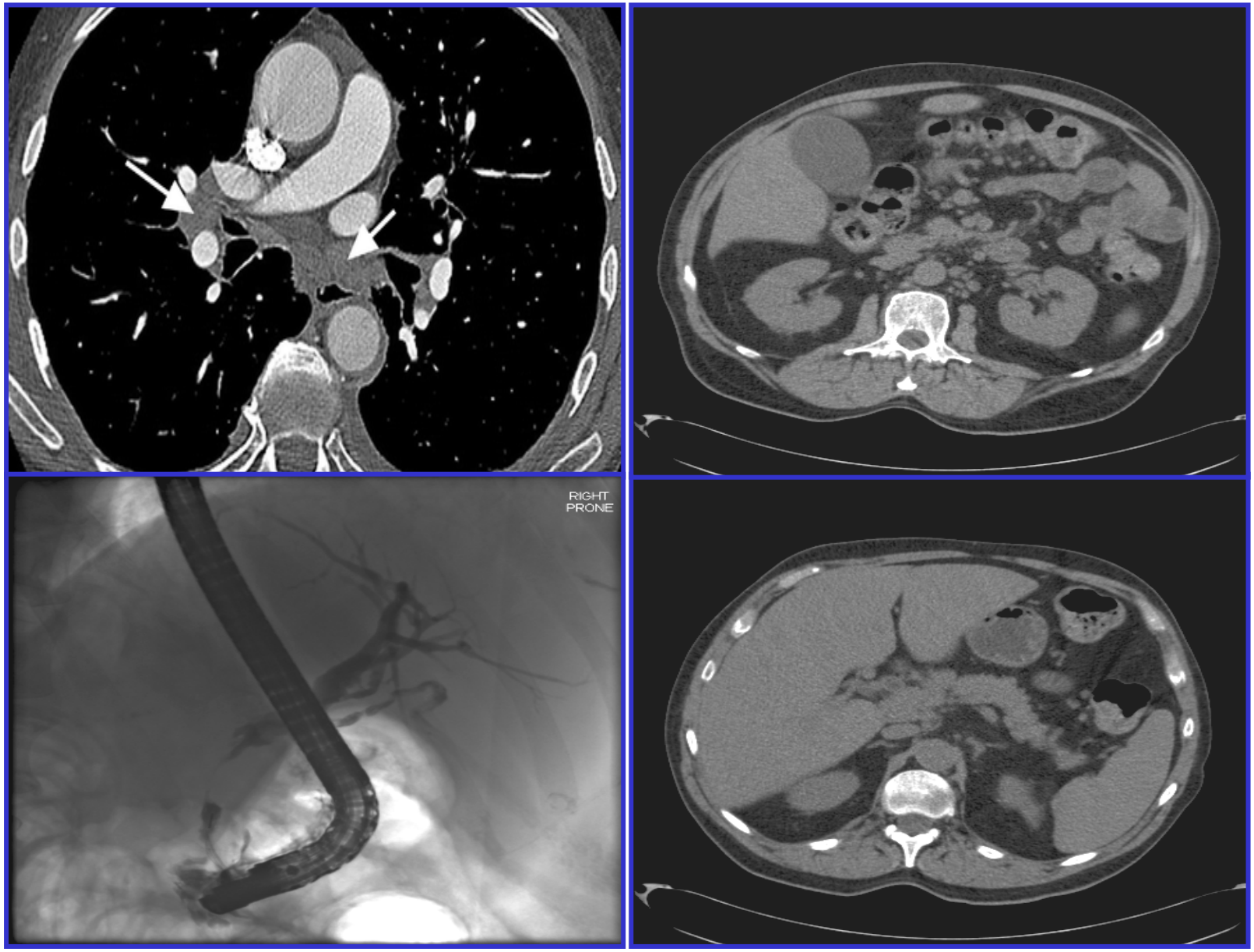
Directorate of Gastroenterology
Pancreatobiliary Medicine
& General Gastroenterology

22/03/2007

Clinical Problems:

1. Obstructive jaundice, January 2007, due to low bile duct stricture (probably inflammatory, with possible diagnosis of autoimmune pancreatitis with associated mediastinal and intraabdominal lymphadenopathy).
2. Ulcerative colitis.

The cause of his biliary obstruction remains a little uncertain, with options including a focal pancreatitis, perhaps related to the passage of small gallstones/sludge, or an autoimmune pancreatitis. This would fit well with his background of colitis and the associated lymphadenopathy, but the serum IgG4, which is often elevated in this condition is low. His liver biopsy also did not show a high level of IgG4 plasma cells.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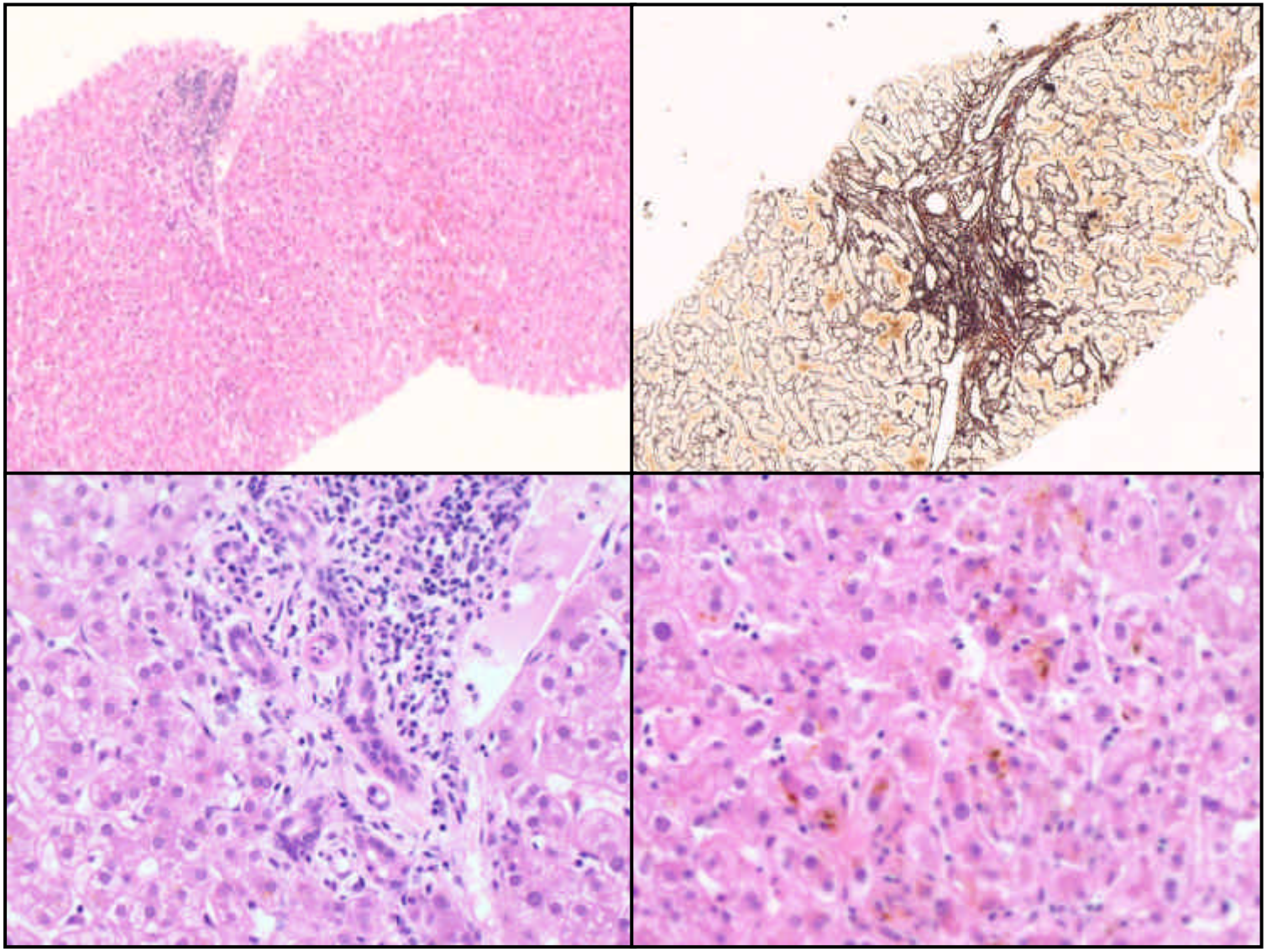
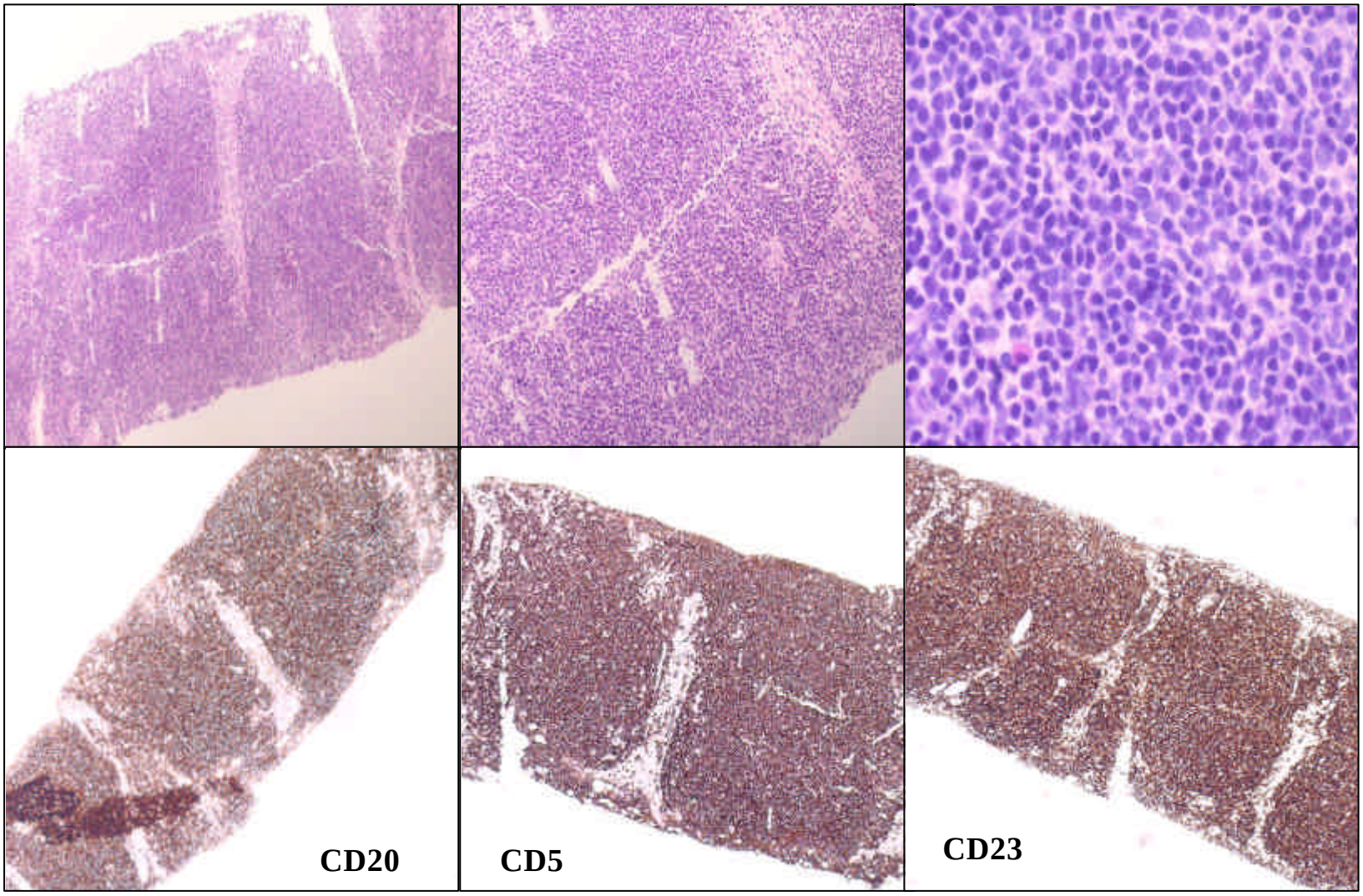
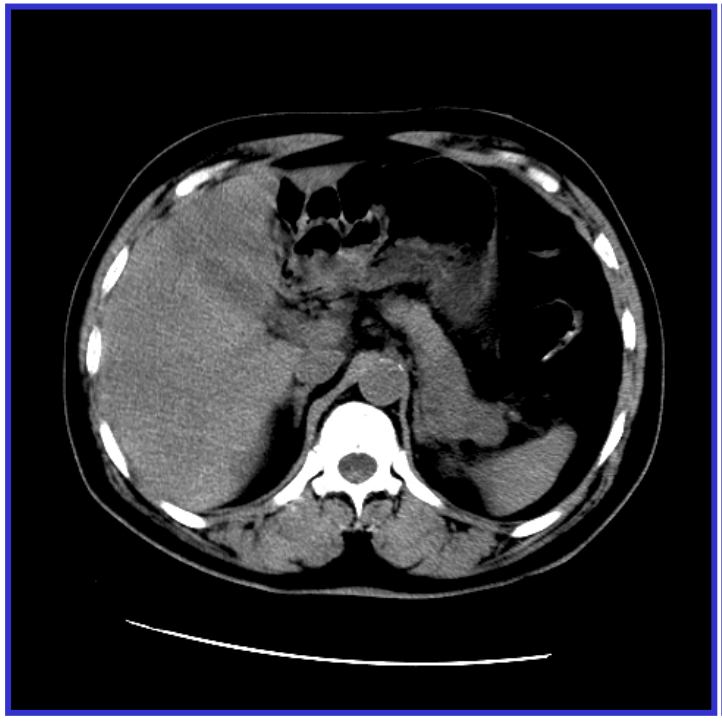
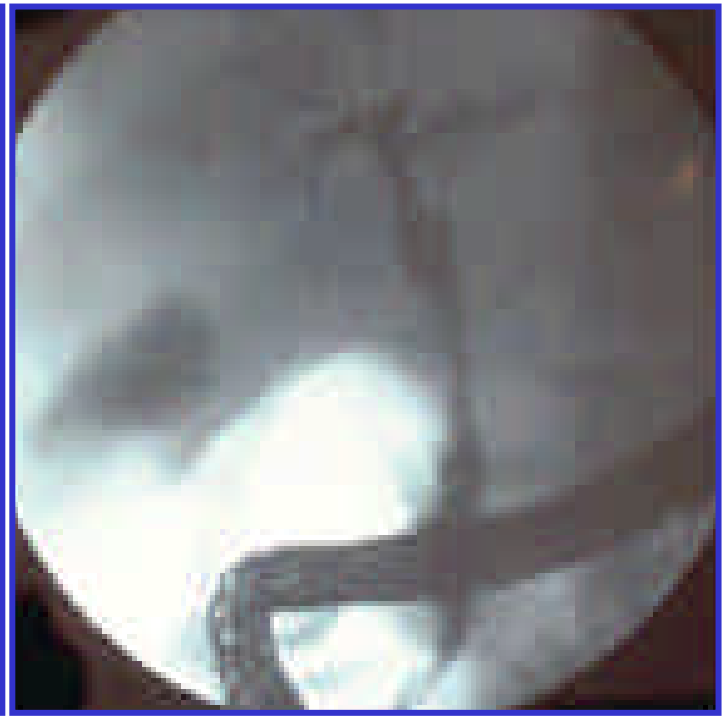
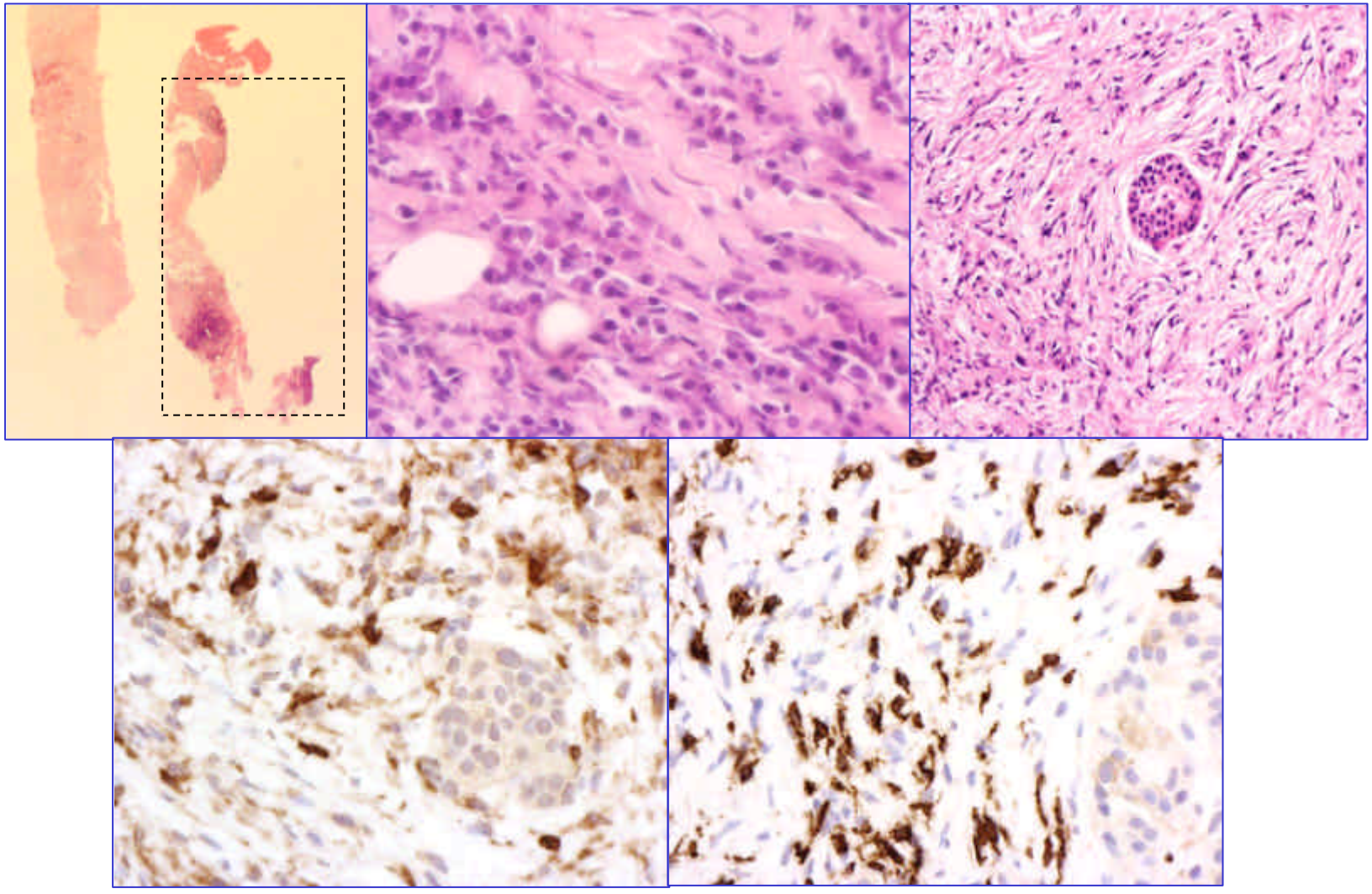


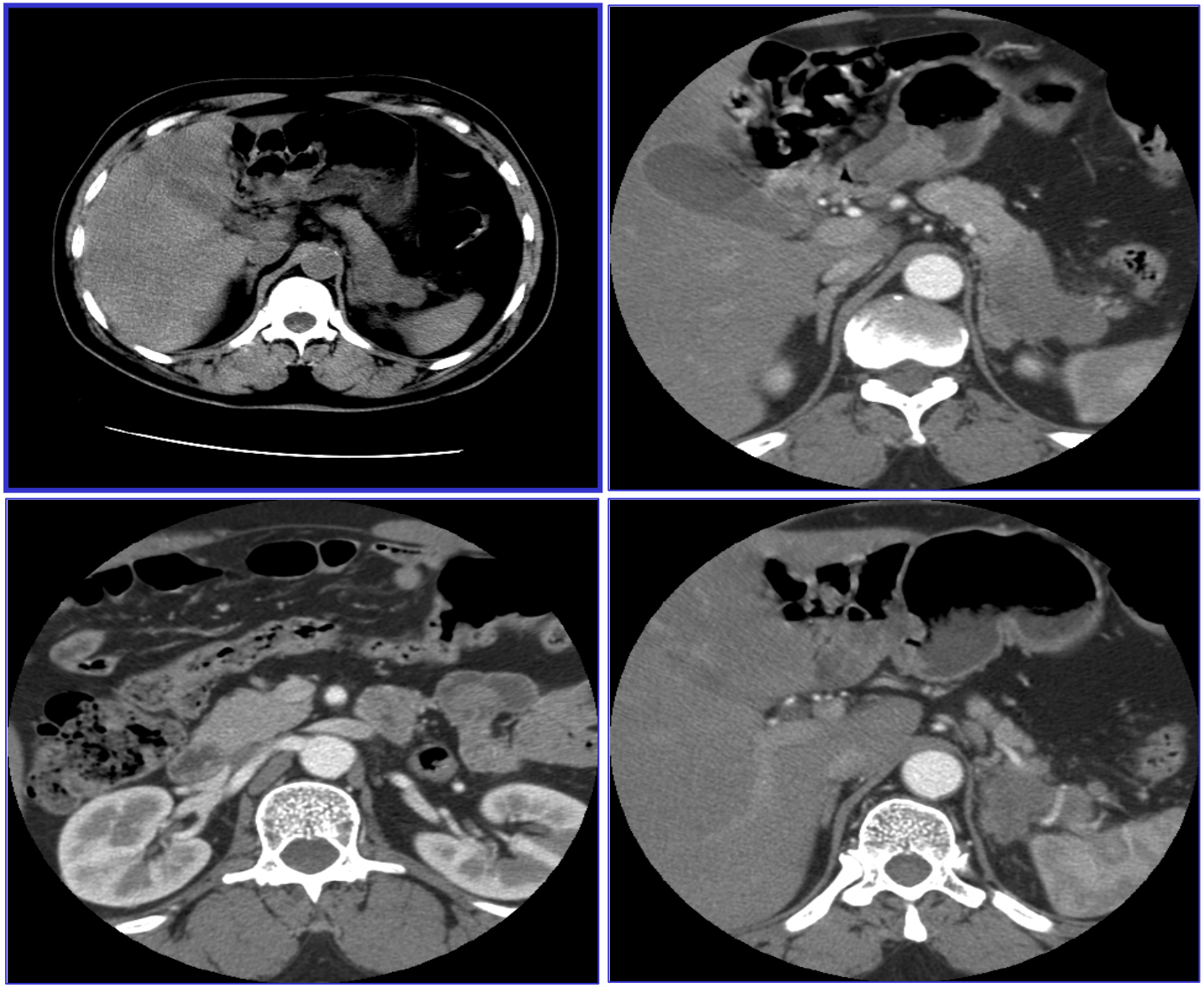

CD20
CD5
CD23

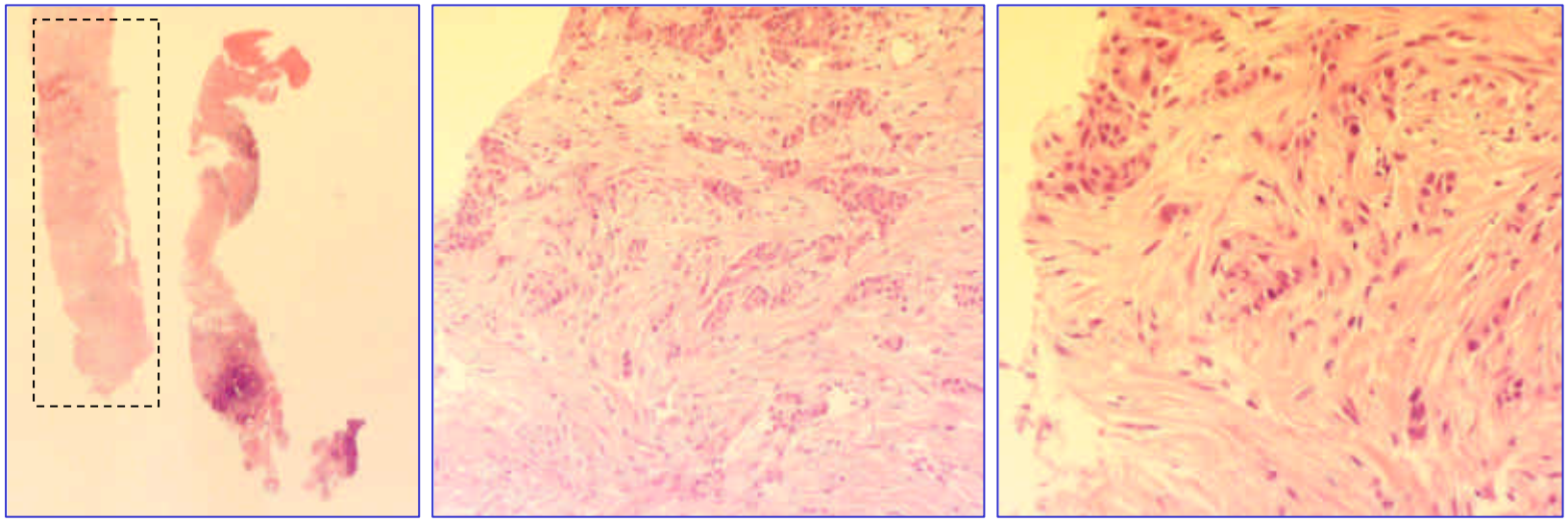
Último caso clínico:











PO Box 2345, Beijing 100023, China
www.wjgnet.com
wjg@wjgnet.com

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World Journal of Gastroenterology ISSN 1007-9327

CASE REPORT

Pancreatic cancer with a high serum IgG4 concentration

Terumi Kamisawa, Pong Yui Chen, Yuyang Tu, Hitoshi Nakajima, Naoto Egawa, Kouji Tsuruta, Atsutake Okamoto, Tsunekazu Hishima

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Value of Serum IgG4 in the Diagnosis of Autoimmune Pancreatitis and in Distinguishing It From Pancreatic Cancer

Amaar Ghazale, M.D.,[1] Suresh T. Chari, M.D.,[1] Thomas C. Smyrk, M.D.,[2] Michael J. Levy, M.D.,[1] Mark D. Topazian, M.D.,[1] Naoki Takahashi, M.D.,[3] Jonathan E. Clain, M.D.,[1] Randall K. Pearson, M.D.,[1] Mario Pelaez-Luna, M.D.,[1] Bret T. Petersen, M.D.,[1] Santhi Swaroop Vege, M.D.,[1] and Michael B. Farnell, M.D.[4]
[1]*Division of Gastroenterology and Hepatology,* [2]*Department of Pathology,* [3]*Department of Radiology, and* [4]*Division of Gastroenterologic and General Surgery, Mayo Clinic College of Medicine, Rochester, Minnesota*

Elevated serum IgG4 levels are characteristic of AIP. However, mild (<2-fold) elevations in serum IgG4 are seen in up to 10% of subjects without AIP including pancreatic cancer and cannot be used alone to distinguish AIP from pancreatic cancer.

J Gastroenterol 2007; 42[Suppl XVIII]:39–41
DOI 10.1007/s00535-007-2046-8

Journal of Gastroenterology

Diagnosis of autoimmune pancreatitis using its five cardinal features: introducing the Mayo Clinic's HISORt criteria

Suresh T. Chari

Division of Gastroenterology and Hepatology, Mayo Clinic College of Medicine, 200 First Street SW, Rochester, MN 55905, USA

Histology

Pancreatic Imaging

Serology

Other organ involvement

Response to steroid treatment

Cellular Pathology

Dr MG Deheragoda

Prof M Novelli

Ms P Munson

Gastroenterology

Dr NI Church

Dr N Sandanayake

Dr EW Seward

Dr SP Pereira

Dr ARW Hatfield

Dr GJM Webster

Radiology

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Dr A Gillams

Nephrology

Prof GH Neild

Dr JO Conolly

Dr C Wall

H.U.Getage

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