IV congreso
de la Sociedad
Española
de Trasplante

Caso clínico 3

Natividad de Benito
UNIDAD DE ENFERMEDADES INFECCIOSAS
Hospital de la Santa Creu i Sant Pau

Mujer 68 años

Consulta por fiebre 10,5 meses post-trasplante renal

ANTECEDENTES

- Natural de China. Vive hace 8 años en Barcelona.
- **Nódulo tiroideo hiperfuncionante** en tratamiento farmacológico (tiamazol)
- **Hipercolesterolemia** en tratamiento
- **Insuficiencia renal crónica** no filiada
- **Trasplante de riñón** de donante cadáver en fosa ilíaca derecha el día 26.2.2012
- IQ: histerectomía, apendicectomía

- VHB, VHC: -
- CMV donante +/receptor +
- Cotrimoxaxol 3 meses
- Buena evolución post-trasplante (no infecciones, ni rechazo, buena función)

TRATAMIENTO ACTUAL

- Tacrolimus 15 mg-0-0
- Micofenolato 180-0-360 mg
- Prednisona 5 mg-0-0
- Tiamazol 5 mg-0-0
- Simvastatina 10 mg: 0-0-1

ENFERMEDAD ACTUAL

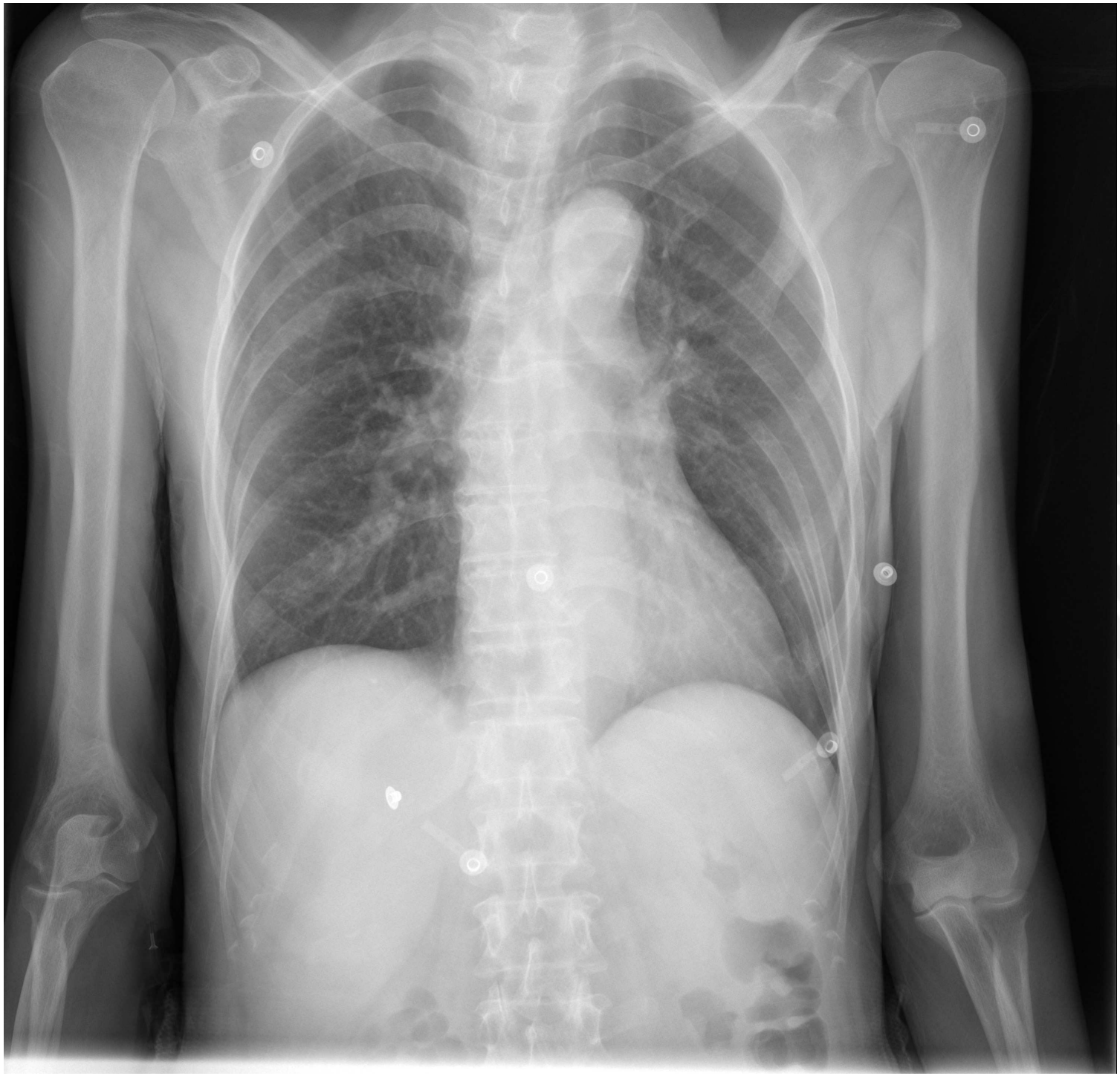
- Consulta el 8.1.2013 (10,5 meses post-trasplante)
- 10 días: malestar general, astenia, anorexia y sensación febril
- No síndrome miccional, tos, diarrea, ni otra sintomatología

EXPLORACIÓN

- Regular estado general
- TA 104/65 Tª 38,5ºC, nódulo tiroideo palpable.

ANALÍTICA

- Hemograma: 5350 L (fórmula normal), Hb 101 g/L, plaq 208.000
- Cr 91 umol/L – FG 53 mL/min/1.73 m
- Proteína C reactiva >320,0 mg/L (0,0 - 5,0)



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The most common cause of fever in renal transplant patients is infection. However, many other factors may be responsible, such as allograft rejection, drug hypersensitivity, and malignancy. Acute rejection occurs more frequently during the first six months after transplantation. Post-transplant lymphoproliferative disorders (PTLD) occur mainly within the first year.

Rev Clin Esp. 2012;212(4):193–197

ELSEVIER DOYMA

Revista Clínica Española

www.elsevier.es/rce

CONFERENCIA CLÍNICO-PATOLÓGICA

Fever in a kidney transplant recipient: No Facts and Many Interactions

Fiebre en un receptor de trasplante renal: ninguna evidencia y muchas interacciones

F. López-Medrano[a,*], J. Carratalà[b], J.M. Cruzado[c], M.J. Gutiérrez[d], J.M. Aguado[a]

¿Qué solicitaría a continuación?

1. Urocultivo y 2 hemocultivos
2. Ecografía abdominal
3. Detección ácidos nucleicos de CMV en sangre
4. Serología de fiebre Q y brucelosis
5. Urocultivo, hemocultivos y CMV (PCR)

SOLID-ORGAN TRANSPLANT RECIPIENTS

In addition to basic laboratory tests, the initial laboratory evaluation for transplant recipients presenting with an isolated fever should include urinalysis, urine culture, at least 2 sets of blood cultures, and a quantitative CMV polymerase chain reaction (PCR).

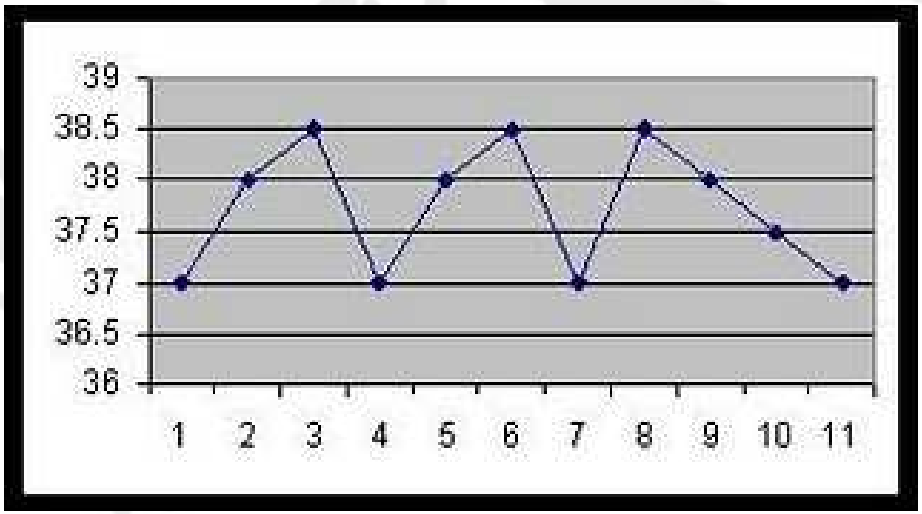
Fever in Immunocompromised Hosts

Emerg Med Clin N Am 31 (2013) 1059–1071

Devang M. Patel, MD*, David J. Riedel, MD

- **Urocultivo**: negativo
- **Hemocultivos**: x 3: negativos
- **Detección ácidos nucleicos CMV(VH5):** negativa
- **Ecografía abdominal:**
  - **Hígado, vesícula y vía biliar** normales
  - **Páncreas y bazo** de morfología conservada
  - **Riñón** trasplantado en fosa iliaca derecha de tamaño y grosor cortical conservado, con patrón ecográfico homogéneo
  - **Vía urinaria** sin litiasis, ni ectasias; vejiga normal
  - **Aorta abdominal** sin hallazgos valorables

- Se había iniciado al ingreso tratamiento antibiótico con ceftriaxona iv
- Los días siguientes la paciente continuó con fiebre



¿Qué haría a continuación?

1. Cambiar antibióticos a daptomicina + meropenem
2. Serología de fiebre Q y brucelosis
3. El 1 y el 2
4. TAC toraco-abdominal
5. PET-TAC

Timing of transplant-related infections	
First month	Donor-derived pathogens Bacteremia, candidemia from seeded allograft Health care–associated pathogens, including drug-resistant organisms Surgical site infections *Clostridium difficile* colitis
1–6 mo	Reactivation of herpes viruses (HSV, CMV, EBV, VZV) Hepatitis B and C TB *Nocardia, Listeria* Fungi Pneumocystis pneumonia Cryptococcosis *Aspergillus* Endemic fungi (eg, *Histoplasma*)
>6 mo	Community-Acquired Infections Respiratory viruses, community pneumonia, urinary infections With steroids or other enhanced immunosuppression for rejection CMV, *Aspergillus* Endemic fungi

Abbreviations: EBV, Epstein-Barr virus; HSV, herpes simplex virus; VZV, varicella zoster virus.

Cuadro 6.4 Factores de riesgo[a] de infección tardía (>6 meses) en el paciente con trasplante de órgano sólido

Profilaxis frente a CMV

Dos o más episodios de rechazo agudo

Infecciones bacterianas recurrentes

Insuficiencia renal que requiere diálisis

Disfunción crónica del injerto

[a]Presentes en los primeros 6 meses del trasplante.

American Journal of Transplantation 2007; 7: 964–971
Blackwell Munksgaard

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Journal compilation © 2006 The American Society of Transplantation and the American Society of Transplant Surgeons

doi: 10.1111/j.1600-6143.2006.01694.x

Incidence, Clinical Characteristics and Risk Factors of Late Infection in Solid Organ Transplant Recipients: Data from the RESITRA Study Group

Imaging can begin with conventional radiography of a focal area of complaint, but computed tomography and magnetic resonance imaging (MRI) are often necessary because of their higher sensitivity and frequent lack of overt physical examination findings.

Fever in Immunocompromised Hosts

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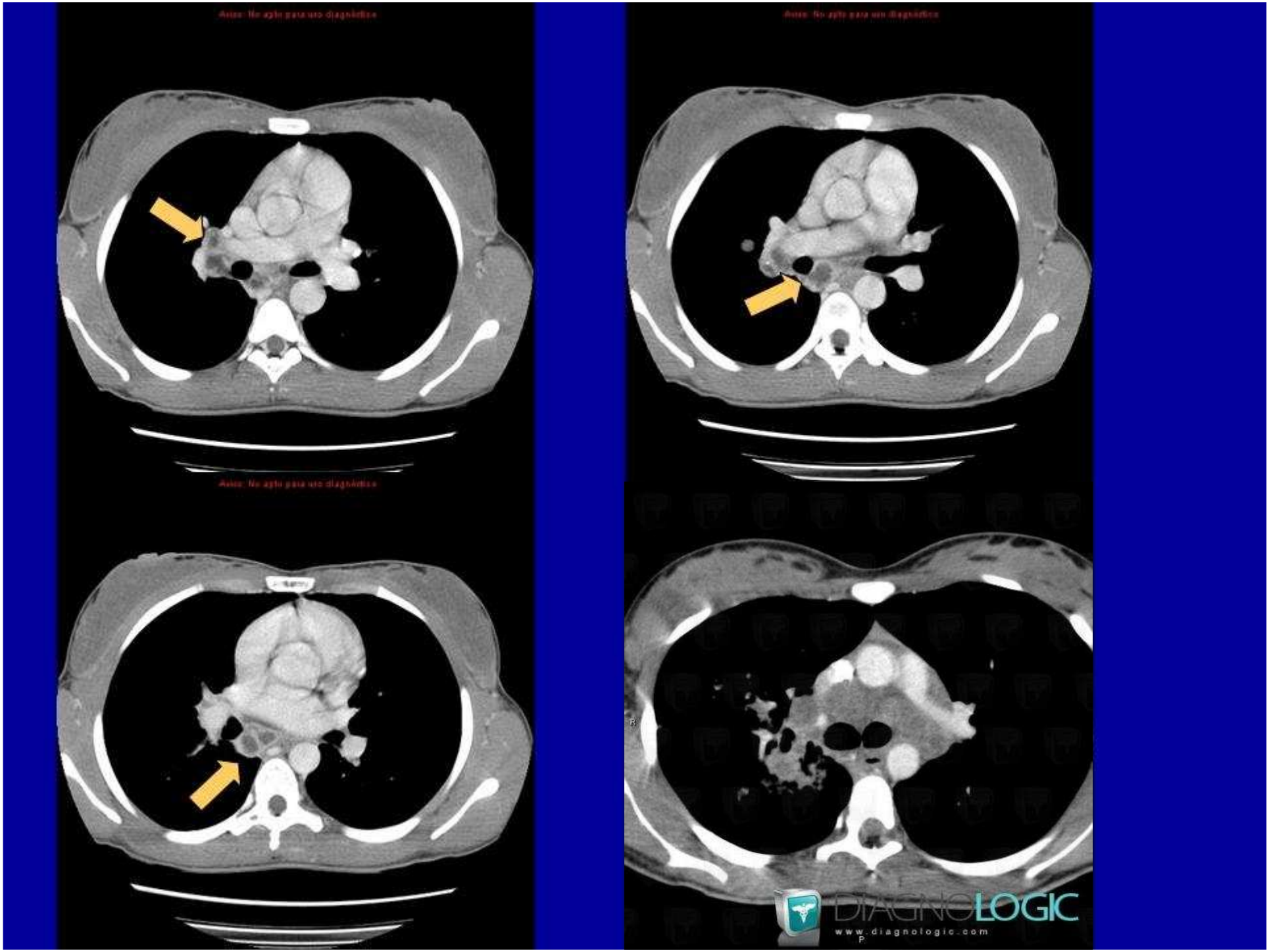
DIAGNOLOGIC
www.diagnologic.com

TORAX

- Múltiples **adenopatias mediatínicas**, subcarinales y paratraqueal derecha, hipodensas y de contornos irregulares (la mayor de 26 x 28 mm).
- **Lesión/adenopatía parahiliar izquierda** que podrían corresponder a neumonitis compresiva.
- Masa intratorácica en lóbulo tiroideo derecho (55 x 43 mm), heterogénea predominantemente hipodensa, con alguna calcificación.
- Discreto **derrame pericárdico y pleural** bilateral.

ABDOMEN

- Presencia de múltiples **adenopatías hipodensas** de gran tamaño (la mayor de 3 cm), de localización **mesentérica**, la mayoría adyacentes a la raiz mesentérica, en hilio hepático y precava.
- Colelitiasis. Vía biliar no dilatada.
- Hígado,vía biliar, bazo, suprarenales y páncreas: normales.
- Riñones propios esclerosos sin ectasia de vías. Injerto renal en FID de tamaño y morfología conservadas, sin dilatación de la vía excretora.
- Vejiga urinaria: notablemente repleccionada, globulosa.
- No líquido libre intrabdominal.

¿Qué diagnóstico le parece más probable?

1. Reacción de hipersensibilidad a tacrolimus
2. Histoplasmosis
3. Enfermedad linfoproliferativa post-trasplante (PTLD)
4. Brucelosis
5. Tuberculosis

¿Qué haría para llegar al diagnóstico?

1. Prueba de la tuberculina (PPD)
2. Quantiferon®
3. Cultivos de esputo seriados
4. Broncoscopia y biopsia transbronquial
5. Todos los anteriores

Variable	Transplant recipients (n = 22)	Patients from the general population (n = 88)	RR (95% CI)	p
Diagnosis of tuberculosis				
Median time (days) from onset of symptoms to diagnosis (IQR)	70 (48)	46 (70)	—	0.076
Median time (days) from clinical suspicion of tuberculosis to definitive diagnosis (IQR)	14 (51.5)	0 (1.25)	—	0.001
Sputum culture performed, no. (%)	12 (54.5)	77 (87.5)	0.17 (0.06–0.49)	<0.001
Positive sputum culture, no. (%)	10 (83.3)	70 (90.9)	0.5 (0.09–2.75)	0.769
Invasive procedures required, no. (%)	12 (54.5)[a]	15 (17)[b]	5.84 (2.14–15.98)	0.001
Post-mortem diagnosis, no. (%)	3 (13.6)[c]	0 (0)	—	<0.001
Positive tuberculin skin test result when tuberculosis was suspected, no. (%)[d]	0 (0)	16 (84.2)	—	0.022

Clinical features and outcomes of tuberculosis in transplant recipients as compared with the general population: a retrospective matched cohort study

Clin Microbiol Infect 2015; **21:** 651–658

N. Benito[1,2], E. García-Vázquez[3], J. P. Horcajada[4], J. González[5], F. Oppenheimer[6], F. Cofán[6], M. J. Ricart[6], A. Rimola[7], M. Navasa[7], M. Rovira[8], E. Roig[9], F. Pérez-Villa[10], C. Cervera[2,11] and A. Moreno[2,11]

Broncoscopia + biopsia

- Laringe normal.
- **Infiltración** irregular, de aspecto granulomatoso, con áreas más blanquecinas, que afecta a **carina traqueal e inicio del bronquio principal Izquierdo**. Se realizan biopsias a este nivel (x5) que se remiten a anatomía patológica y microbiología.
- Se realiza **punción de adenopatía subcarinal** que se remite a citología y microbiología.
- Resto de árbol bronquial sin alteraciones significativas.
- Moderada secreción seromucosa bilateral.

Quantiferon ®

- Resultado indeterminado

¿Cuál es la incidencia de tuberculosis en trasplantados?

1. En inmigrantes, se correlaciona más con la zona de origen
2. Similar a la de la población general
3. Se relaciona con la del área geográfica, pero es superior
4. Depende del tipo de órgano trasplantado
5. Son ciertas 1,3 y 4

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Table 3. Frequency and incidence of tuberculosis (TB) in the RESITRA (Spanish Network of Infection in Transplantation) cohort.

Transplant type	Recipients with TB, proportion (%)	Incidence[a] (95% CI)	RR (95% CI)
Heart	1/404 (0.25)	255 (6.5–1421)	13.7 (1.9–97.3)
Kidney	7/2052 (0.34)	358 (144–728)	19.0 (9.0–39.7)
Liver	8/1507 (0.53)	541 (269–1065)	29.5 (14.8–58.9)
Kidney-pancreas	1/122 (0.82)	1204 (30.5–6710)	45.5 (6.5–320.4)
Lung	4/303 (1.32)	2072 (565–5306)	73.3 (27.7–194.1)
All	21/4388 (0.48)	512 (317–783)	26.6 (17.4–40.8)

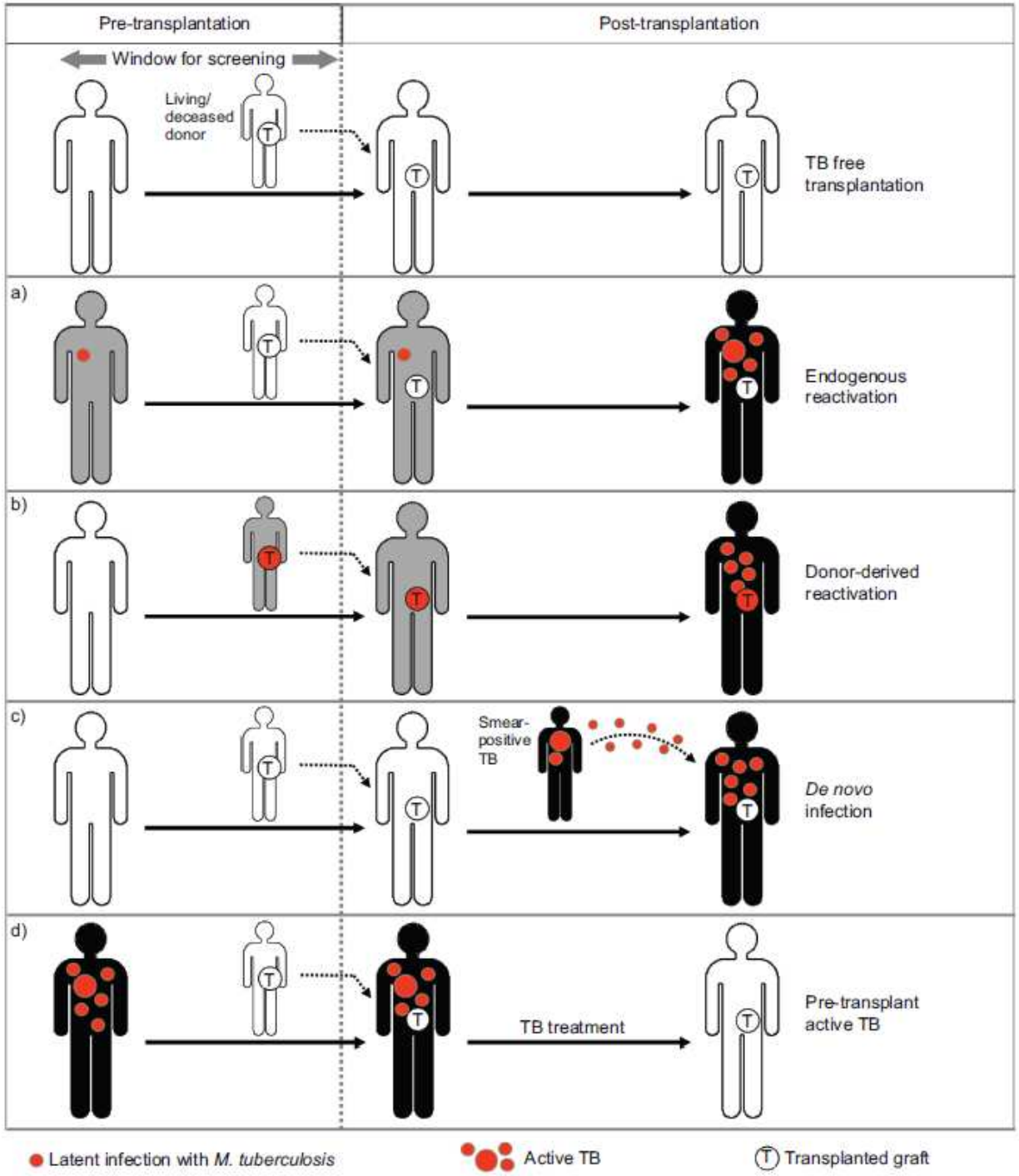
NOTE. CI, confidence interval; RR, relative risk.

[a] Cases per 10^5 transplant recipients per year.

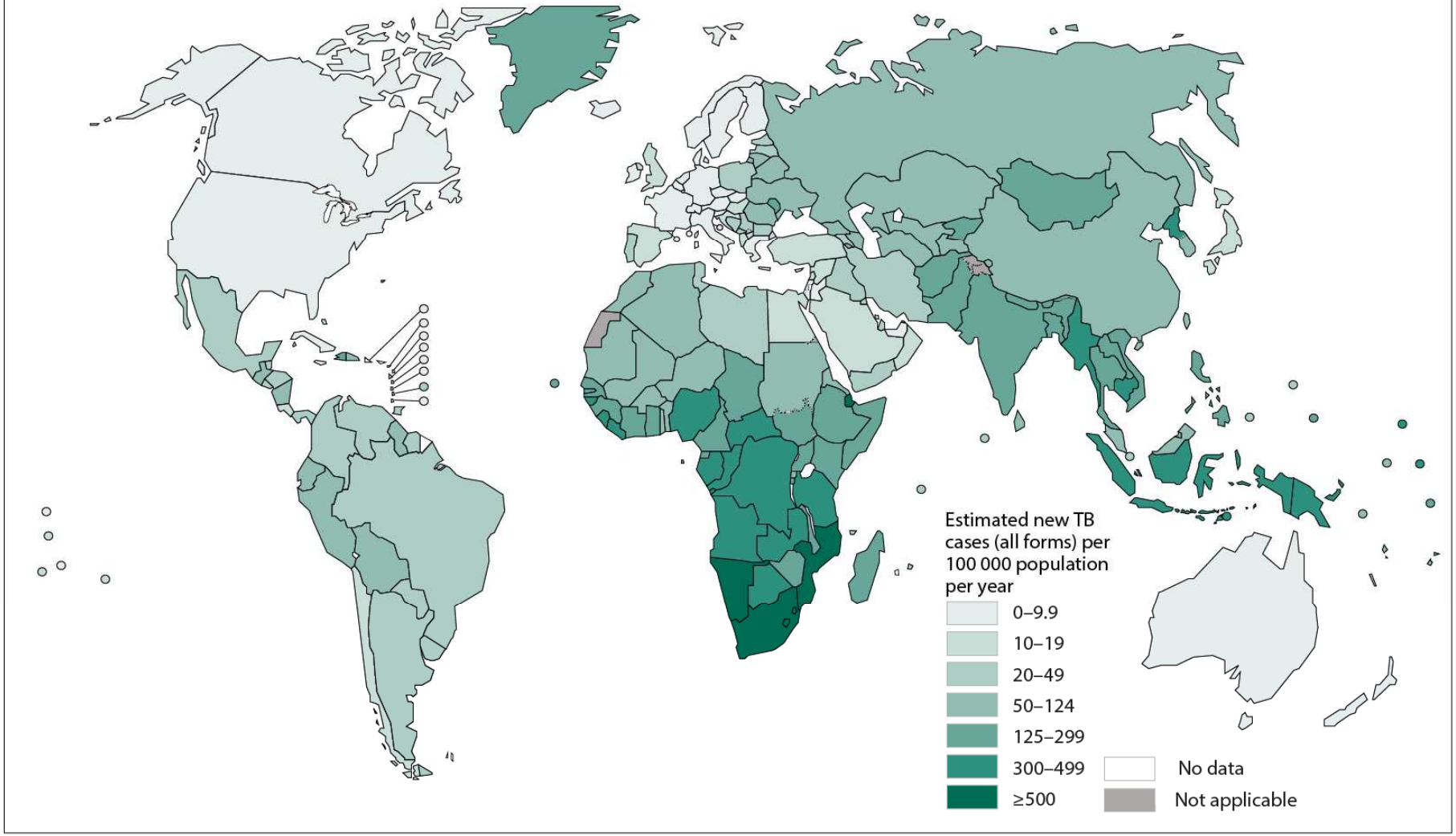
Tuberculosis after Solid-Organ Transplant: Incidence, Risk Factors, and Clinical Characteristics in the RESITRA (Spanish Network of Infection in Transplantation) Cohort

Clinical Infectious Diseases 2009; 48:1657–65

Julián Torre-Cisneros,[1] Antonio Doblas,[2] José María Aguado,[3] Rafael San Juan,[4] Marino Blanes,[5] Miguel Montejo,[6] Carlos Cervera,[10] Oscar Len,[11] Jordi Carratalá,[12] José Miguel Cisneros,[14] Germán Bou,[15] Patricia Muñoz,[5] Antonio Ramos,[5] Merce Gurgui,[13] Nuria Borrell,[16] Jesus Fortún,[7] Asunción Moreno,[10] and Joan Gavaldà,[11] for the Spanish Network for Research in Infectious Diseases


Pre-transplantation
Post-transplantation
Window for screening
Living/
deceased
donor
T
TB free
transplantation
a)
Endogenous
reactivation
b)
Donor-derived
reactivation
c)
Smear-
positive
TB
De novo
infection
d)
TB treatment
Pre-transplant
active TB
Latent infection with M. tuberculosis
Active TB
Transplanted graft

Estimated TB incidence rates, 2014



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: *Global Tuberculosis Report 2015*. WHO, 2015.

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World Health Organization

Descripció Macroscòpica:

Se reciben múltiples fragmentos de tejido. I.T.

Código Secciones

ID Muestra	Nº Bloque	Nº Fragmentos	Cod. Bloque	Nº Cortes
A	1	991	FX BR	4

Diagnòstic:

(BRONQUIO, CULMEN, LESIÓN, BIOPSIA):
- FRAGMENTOS DE MUCOSA RESPIRATORIA CON ABUNDANTE INFLAMACIÓN AGUDA Y CRÓNICA CON NECROSIS.

COMENTARIO:
En curso tinción específica para hongos y micobacterias, cuyo resultado se remitirá en un informe adicional.

Dr./a. ESPINOSA MARISCAL, IÑIGO
Resident: GARCÍA-CUERVA CALVAR, M. SOLEDAD

Data Informe: 24/01/2013

30/01/2013 12:42 | NOTA ADDICIONAL (Dr. IÑIGO ESPINOSA MARISCAL)

La tinción para micobacterias (Kinyoun) resultó positiva.
Tinciones para hongos (PAS y Plata) negativas.

Informe de Citopatologia

Mostres Rebudes:

Data Recepció: 21/01/2013

A) CITOLOGIA DE BRONCO-ASPIRADO
B) CITOLOGIA DE PUNCION TRANSBRONQUIAL

Descripció Macroscòpica:

a) Se reciben 6 cc. de líquido de coloración blanquecina.

Tinción de Papanicolaou.

b) Se recibe 2 extensión/es fijada/s.

Diagnòstic:

A)- NEGATIVO PARA CÉLULAS MALIGNAS

Intenso componente inflamatorio agudo inespecífico y marcados cambios reactivos en células bronquiales.

B)- Material necroinflamatorio inespecífico y grupos de células bronquiales degeneradas.

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Estudi de micobacteris No. Laboratori: 13K185A

Mostra Clinica: Biopsia bronquial

Auramina: S'observen alguns bacils alcohol-àcid resistents.

Detecció d'àcids nucleics M.tuberculosis complex: Positiu.
No es detecten mutacions responsables de resistència.

Cultiu micobacteris Positiu per:

1: *Mycobacterium tuberculosis complex*

Autoritzat per Pere Coll Figa el 11/03/2013 a les 14:26

HOSPITAL DE LA SANTA CREU I SANT PAU
UNIVERSITAT AUTÒNOMA DE BARCELONA

Estudi de micobacteris No. Laboratori: 13K184A

Mostra Clinica: Broncoaspirat

Auramina: S'observen alguns bacils alcohol-àcid resistents.

Detecció d'àcids nucleics M.tuberculosis complex: Estudi no realitzat.
Comentari La prova no esta indicada.
Per més informació contacteu amb el Laboratori.

Cultiu micobacteris Positiu per:

1: *Mycobacterium tuberculosis complex*

Autoritzat per Pere Coll Figa el 11/03/2013 a les 14:27

HOSPITAL DE LA SANTA CREU I SANT PAU
UNIVERSITAT AUTÒNOMA DE BARCELONA

Estudi de micobacteris No. Laboratori: 13K186A

Mostra Clinica: Adenopatia

Auramina: S'observen abundants bacils alcohol-àcid resistents.

Cultiu micobacteris Positiu per:

1: *Mycobacterium tuberculosis complex*

Diagnóstico

- **Tuberculosis endobronquial y ganglionar (afectación mediastínica, hiliar y mesentérica)**

Characteristics	Transplant recipients (*n* = 22), no. (%)	Patients from the general population (*n* = 88), no. (%)	RR (95% CI)	p
Tuberculosis form				
Pulmonary	12 (54.5)	77 (87.5)	0.12 (0.03–0.44)	0.001
Extrapulmonary	5[f] (22.7)	7[g] (8)	3.17 (0.94–10.70)	0.055
Disseminated	5[h] (22.7)	4[i] (4.5)	6.33 (1.29–31.11)	0.005
Number of involved organs				
Two or more organs involved with a definitive diagnosis	4 (18.2)	3 (3.4)	6.30 (1.30–30.60)	0.045
Two or more organs involved with a probable diagnosis	8 (36.4)	10 (11.4)	5.40 (1.64–17.77)	0.003

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Characteristics	Transplant recipients (n = 22), no. (%)	Patients from the general population (n = 88), no. (%)	RR (95% CI)	p
Clinical manifestations				
Fever	17 (81)	42 (49.4)	8.5 (1.81–39.81)	0.002
Constitutional symptoms[a]	9 (45)	54 (63.5)	0.57 (0.22–1.48)	0.207
Cough	9 (45)	53 (62.4)	0.6 (0.21–1.49)	0.245
Dyspnoea	1 (5)	13 (15.3)	0.27 (0.03–2.41)	0.396
Pleuritic chest pain	1 (5)	15 (17.6)	0.4 (0.05–3.04)	0.287
Haemoptysis	1 (5)	23 (27.1)	0.11 (0.01–1.11)	0.070
Symptoms suggestive of epididymo-orchitis	3 (15)[b]	0 (0)	—	0.004
Monoarticular or oligoarticular pain	2 (10)	1 (1.2)	8 (1.01–88.22)	0.043
Dysphonia	1 (5)	4 (4.7)	1 (0.08–12.56)	1.000
Other clinical manifestations	5 (25)[c]	4 (4.7)[d]	9 (1.57–51.74)	0.004
Physical findings	13 (65)	27 (31.4)	5.33 (1.55–18.39)	0.007
Ascites	7 (35)[e]	0 (0)	—	<0.001
Findings consistent with epididymo-orchitis	3 (15)[b]	0 (0)	—	0.004
Monoarthritis or oligoarthritis	2 (10)	1 (1.2)	8 (1.01–88.22)	0.043
Rales on chest examination	1 (5)	14 (16.3)	0.29 (0.04–2.04)	0.346
Findings consistent with pleural effusion	1 (5)	3 (3.5)	2 (0.18–22.06)	0.564
Peripheral lymphadenopathy	1 (5)	8 (9.3)	0.43 (0.04–4.29)	0.861

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Characteristics	Transplant recipients (n = 22), no. (%)	Patients from the general population (n = 88), no. (%)	RR (95% CI)	p
Chest radiograph findings				
None	6 (28.6)	5 (5.7)	5.75 (1.57–21.02)	0.003
Unilateral vs. bilateral pulmonary infiltrates	10 (66.7)	44 (56.4)	1.55 (0.48–4.95)	0.653
Cavitary infiltrates	0 (0)	50 (64.1)	—	<0.001
Diffuse infiltrates vs. focal infiltrates	5 (33.3)	0 (0)	—	<0.001
Pleural effusion	1 (5)	3 (3.5)	2 (0.181–22.156)	0.571

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Tratamiento

Table 1. Interactions between immunosuppressive and antituberculous drugs

Antituberculous medication	Immunosuppressive agent	Anticipated result
Rifamycins (eg, rifampin, rifabutin)	CNIs (eg, cyclosporine, tacrolimus)	Markedly decreased level of CNIs
	Sirolimus	Markedly decreased level of sirolimus
	Steroids	Decreased steroid effectiveness

Table 4. Tuberculosis (TB) treatment options, recommended doses, alternative dosing regimens, and drug interactions and contraindications.

Situation	Initial treatment	Maintenance treatment
Patients with localized, nonsevere forms of TB, without suspicion or evidence of resistance to isoniazid	Avoid the use of rifamycins; if rifamycins are used, the levels of immunosuppressors should be closely monitored, and the dose of cyclosporine or tacrolimus should be increased (A-II); if treatment is started early, it is not necessary to reduce the level of immunosuppression (C-III)	Isoniazid and ethambutol (or pyrazinamide) are recommended for 12–18 months (C-III); the incorporation of a third drug, such as pyrazinamide or levofloxacin,[a] could reduce this period to 12 months (C-III)
Severe forms or disseminated forms of TB or suspicion or evidence of resistance to isoniazid[b]	Consider adding rifampicin or rifabutin to the regimen (B-III)[c]	Complete treatment with isoniazid and rifampicin or rifabutin for at least 9 months
Multidrug-resistant TB or when there is some limitation for the use of the aforementioned drugs	If isoniazid and rifamycins cannot be used, induction treatment should include 4–6 drugs, including injectable antimicrobials (e.g., streptomycin,[d] amikacin, kanamycin, or capreomycin), linezolid, or other second-line drugs (C-III)[e]	The absence of isoniazid and rifamycin in the initial treatment makes it difficult to calculate the duration of treatment and the types of drugs to be used; therapy should be individualized

Tuberculosis in Solid-Organ Transplant Recipients: Consensus Statement of the Group for the Study of Infection in Transplant Recipients (GESITRA) of the Spanish Society of Infectious Diseases and Clinical Microbiology

Clinical Infectious Diseases 2009; 48:1276–84

José María Aguado,[1] Julián Torre-Cisneros,[4] Jesús Fortún,[2] Natividad Benito,[5] Yolanda Meije,[1] Antonio Doblas,[4] and Patricia Muñoz[3]

Summary

1. In general, the same short-course treatment regimen (2 HRZE/4 RH) is recommended for transplant recipients as for other patients with TB.

2. TB treatment in transplant recipients is often complicated by interactions between rifamycins and immunosuppressive drugs and the increased frequency of adverse anti-TB drug events.

3. A rifamycin-free anti-TB treatment regimen is an important option in non-severe cases in order to avoid drug interaction with immunosuppressive drugs and thus reduce the risk of graft rejection.

Eur Respir J 2012; 40: 990–1013
DOI: 10.1183/09031936.00000712
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REVIEW

The risk of tuberculosis in transplant candidates and recipients: a TBNET consensus statement

Dragos Bumbacea, Sandra M. Arend, Fusun Eyuboglu, Jay A. Fishman, Delia Goletti, Michael G. Ison, Christine E. Jones, Beate Kampmann, Camille N. Kotton, Christoph Lange, Per Ljungman, Heather Milburn, Michele I. Morris, Elmi Muller, Patricia Muñoz, Anoma Nellore, Hans L. Rieder, Urban Sester, Nicole Theodoropoulos, Dirk Wagner and Martina Sester

The major difficulty in administering antituberculous therapy to transplant patients is drug–drug interactions involving rifampin. Nevertheless, a rifamycin-containing regimen is strongly preferred due to the potent MTB sterilizing activity of this drug class. Rifampin is a strong

***Mycobacterium tuberculosis* Infections in Solid Organ Transplantatic**

American Journal of Transplantation 2013; 13: 68–76

A. K. Subramanian[a,]*, M. I. Morris[b] and the AST Infectious Diseases Community of Practice

Table 5 Comparison of patients who did and did not receive rifampin-based regimen

Factor	Odds of patients receiving rifampin-based regimen [95%CI]	Comparison (reference) group	P
Age	1.00 [0.97-1.03]	Continuous	.87
Male sex	0.54 [0.19-1.55]	Female	.25
Type of transplant			
Liver	1.02 [0.32-3.29]	Kidney transplant	.97
Heart	2.33 [0.44-12.22]		.32
Lung	3.50 [0.29-42.74]		.33
Kidney-pancreas	Unable to calculate[a]		.99
Time to onset of TB after transplant	1.00 [0.99-1.01]	Continuous	.58
Retransplant	Unable to calculate[b]	Initial transplant	.26
Prior rejection	Unable to calculate[c]	No prior rejection	.04
CMV infection	0.53 [0.14-1.97]	No CMV infection	.34
CMV disease			
Creatinine level[d] ≥2 mg/dL			
Dialysis			
Prior tuberculin test done			
Tuberculin positive			
Extrapulmonary TB			
Disseminated TB			
Signs and symptoms			
Fever			
Weight loss			
Malaise	0.43 [0.15-1.26]	No malaise	.13
Night sweats	0.30 [0.06-1.56]	No night sweats	.15
Outcomes at 12 months			
Rejection	1.46 [0.19-11.08]	No post-TB rejection	.72
Mortality	0.94 [0.24-3.72]	Alive at 1 year	.93

Tuberculosis in solid-organ transplant recipients: disease characteristics and outcomes in the current era

Progress in Transplantation, Vol 24, No. 1, March 2014

Hsin-Yun Sun, MD, Patricia Munoz, MD, Julian Torre-Cisneros, MD, Jose M. Aguado, MD, Roberta Gattes, MD, Miguel Montejo, MD, Ana Garcia-Reyne, MD, Emilio Bouza, MD, Maricela Valerio, MD, Rosario Lara, MD, Marilyn M. Wagener, MPH, George T. John, MD, Didier Bruno, Nina Singh, MD

Tratamiento

- Se inicia tratamiento con isoniacida, rifampicina, etambutol y pirazinamida

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Estudi de micobacteris No. Laboratori: 13K186A

Mostra Clinica: Adenopatia

Auramina: S'observen abundants bacils alcohol-àcid resistents.

Cultiu micobacteris Positiu per:

1: *Mycobacterium tuberculosis complex*

Antibiograma: CMI(mg/L)	1. MYCTBX	CMI
Isoniacida 0.1	R	>1
Pirazinamida 100	S	
Capreomicina 1.25	R	
Etionamida 2.50	S	
Amicacina 1	S	
Kanamicina 5	S	
Ofloxacino 2.0	S	
Rifabutina 0.5	S	
Rifampicina 1.0	S	
Etambutol 5.0	S	
Estreptomicina 1.0	S	

- Se suspende isoniazida
- Continúa 2 meses con:
  - rifampizina
  - etambutol
  - pirazinamida
  - moxifloxacino
- Dos meses → etambutol, rifampicina, moxifloxacino 18 meses
- Buena tolerancia y evolución; buena función renal (no rechazo)

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¿Se puede prevenir?

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TRANSPLANTATION
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DIAGNOSIS AND TREATMENT OF LATENT TUBERCULOSIS INFECTION IN LIVER TRANSPLANT RECIPIENTS IN AN ENDEMIC AREA

NATIVIDAD BENITO,[1,3] OMAR SUED,[1] ASUNCIÓN MORENO,[1] JUAN PABLO HORCAJADA,[1] JULIÀ GONZÁLEZ,[1] MIQUEL NAVASA,[2] AND ANTONI RIMOLA[2]

TABLE 3. Posttransplant tuberculosis (TB) in liver transplant patients who did not receive postoperative treatment of latent TB infection with isoniazid, classified according to their pre-operative tuberculin skin test (TST) and to whether they had clinical or radiologic features of previous TB

Features of past TB	No. of patients with posttransplant TB			
	TST positive	TST negative	TST unknown	Total
Yes (%)	0/9 (0)	2/19 (10.53)[b]	0/5 (0)	2/33 (6.06)[c]
No (%)	0/64 (0)	2/230 (0.87)	0/93 (0)	2/387 (0.52)
Unknown (%)	0/0	1/30 (3.33%)	1/56 (1.79)	2/86 (2.33)
Total (%)	0/73 (0)[a]	5/279 (1.79)	1/154 (0.65)	6/506 (1.19)

Proportion differences have been assessed using Fisher's exact test.

[a] TST positive versus TST negative patients, $P = 0.588$.

[b] Patients with features of past TB versus patients without such features, $P = 0.032$; RR, 11.8, 95% CI, 1.7–81.4.

[c] TST negative patients with features of past TB versus TST negative patients without features of past TB, $P = 0.03$; RR, 12.2, 95% CI, 1.8–81.9.

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Challenging Issues in Tuberculosis in Solid Organ Transplantation

David J. Horne,[1] Masahiro Narita,[1,4] Christopher L. Spitters,[2,4] Soumya Parimi,[1] Sherry Dodson,[3] and Ajit P. Limaye[2]

Clinical Infectious Diseases 2013;57(10):1473–82

Guideline	American Journal of Transplantation 2013 Subramainan at al	European respiratory Journal 2012 TBNET	Thorax 2010 British Thoracic Society	CID 2009 GESITRA (Spain)
Applicable population(s)	All SOT	All SOT	Kidney transplant only	All SOT
Who to routinely screen for LTBI: Candidates Timing of screening	 All candidates pre-transplant	 All candidates • Alternative: candidates with at least one additional risk factor pre-transplant	 All candidates pre-transplant	 All candidates pre-transplant
Recommended routine risk assessment Epidemiologic risk/history Chest X-ray	 Yes routine	 Yes routine	 Yes routine	 Yes Selective (if TST positive or symptomatic)
Routine diagnostic testing for LTBI in candidates pre-transplant TST & interpretive threshold	 Yes	 Yes	 Yes (IGRA preferred)	 Yes

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○ Threshold for positive	≥5 mm	≥ 10mm for BCG vaccinated ≥5 and <10mm w/o prior BCG	Not mentioned	≥ 5 mm
○ Booster testing	Yes	Yes	Not mentioned	Yes
IGRA	Yes	Yes	Yes (with or without TST)	not specifically mentioned
○ Sequential/booster testing	Yes, for high risk	Not mentioned	Not mentioned	Not mentioned
Treatment				
Selection of SOT candidates for LTBI treatment				
TST or IGRA positive	ALL	ALL	ALL	ALL
Other criteria	(i) have radiographic evidence of previous TB and no history of adequate treatment, (ii) have received an organ from a donor who is TST positive, had recent exposure to active TB or had radiographic evidence of untreated TB or (iii) have had close and prolonged contact	(i) fibrotic or calcified lesions on chest imaging, (ii) a strong history of exposure or documentation of a previous positive TST or IGRA, (iii) individuals originating from a country with a very high incidence (e.g. >100 per 100,000 population) -	(i) Consider in all black African and Asian patients born outside the UK (ii)CXR consistent with old TB, untreated. (iii) Recent contact	(i) Patients with chest radiograph findings consistent with untreated TB (ii)a history of contact with a patient with active TB

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Table 2. Analysis of latent *Mycobacterium tuberculosis* infection in the RESITRA (Spanish Network of Infection in Transplantation) cohort, as determined by the tuberculin purified protein derivative (PPD) skin test.

Transplant type	PPD performed/total patients[a] (%)	PPD positive/PPD performed[b] (%)	Prophylaxis/PPD positive[c] (%)
Heart	266/404 (65.8)	40/266 (15.0)	30/40 (75.0)
Kidney	625/2052 (30.5)	85/625 (13.6)	45/85 (52.9)
Liver	695/1507 (46.1)	162/695 (23.3)	48/162 (29.6)
Kidney-pancreas	17/122 (13.9)	4/17 (23.5)	2/4 (50.0)
Lung	172/303 (56.8)	47/172 (27.3)	22/47 (46.8)
All	1775/4388 (40.5)	338/1775 (19.0)	147/338 (43.5)

[a] Number of patients for whom a PPD test was performed per the total number of patients.
[b] Number of patients with a positive PPD test result per the number of patients for whom a PPD test was performed.
[c] Number of patients who received prophylaxis per the number of patients with a positive PPD test result.

Mensajes

- Alto índice de sospecha de TB en trasplantados
  - con fiebre sin foco
  - presentaciones atípicas
- Abordaje diagnóstico agresivo (rápido, pruebas invasivas si preciso)
- Preferibles regímenes terapéuticos con rifampicina – monitorización estrecha inmunosupresores
- PPD/IGRAs + evaluación factores de riesgo en el pretrasplante → tratamiento de tuberculosis latente


Gracias