

血液透析族群LTBI檢驗與治療經驗

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治療前注意事項

- 詳細向病人解釋
- 轉診前交班
- 仔細評估排除活動性結核，以及慢性共病
 - 1個月內的胸部X光
 - 慢性肝炎病人或肝炎高風險族群，治療前及治療中應追蹤肝功能檢驗
- 評估藥物交互作用
- 依據病人的需求選擇合適的藥物

LTBI 治療處方

- 1HP
- 3HP
- 4R
- 3HR
- 6H & 9H

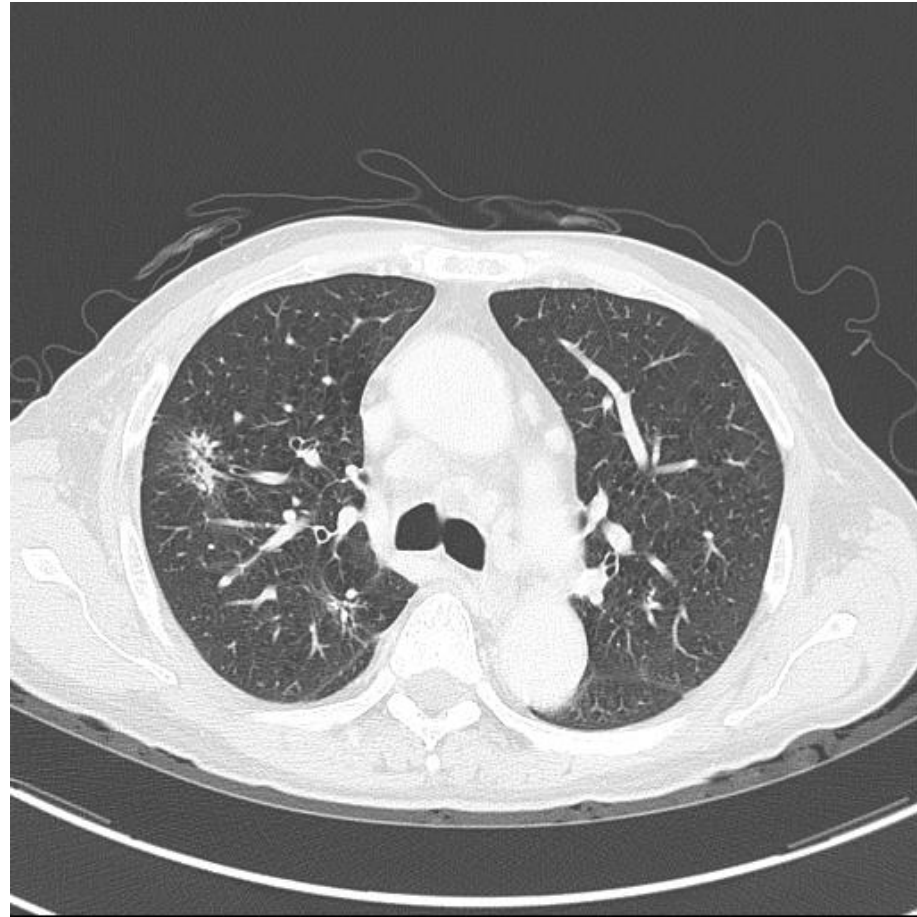
潛伏性結核感染活化高風險族群

- HIV/AIDS
- 密切接觸者
- 器官移植
- 慢性腎病透析病人
- 服用TNF-alpha blockers
- 矽肺病
- 慢性阻塞性肺病
- 糖尿病
- 藥癮者

Case

65 y/o male with fever of unknown origin, and
Right middle lung patch

- ADPKD, ESRD, Regular HD
- HTN
- Af
- Left posterior tongue cancer, pT3N0M0, stage III, s/p operation



2022.12.7

Surveys in the hospital

- BAL:
 - WBC: 45 (μ /L), Seg (22%), Lym (3%), GRAM (-), AFS (-), Culture: No growth of bacteria, fungus, and mycobacteria
 - GM (BAL & Serum): both negative
 - Rapid TB PCR: negative
- Gallium scan:
 - No definite inflammatory focus.
- Bone marrow study: hypocellular bone marrow

F/U at outpatient clinic

- Suspect neutrophilic dermatosis of the dorsal hands, sweet syndrome, r/o vasculitis, r/o pustular psoriasis
 - Lobular and partly septal panniculitis, consistent with erythema induratum
- Oral Prednisolone at OPD

Final diagnosis of pulmonary tuberculosis



2023.11.14

Sputum AFS/TB culture

2021.10.27 x 3:- ve

2022.02.07 x 3:- ve

2022.12.07 x3:- ve

2023.4.6 x 1:- ve

2023.11.21 x 3: *M. tuberculosis* (1/3)

慢性腎病及血液透析病人是結核病的高風險族群

WHO's recommendation for screening and treatment for LTBI⁴¹

Risk factor	TB risk ^a	Reference(s)	Country A ^b	Country B ^c
High-risk factors				
HIV/AIDS	10–100	Landry <i>et al.</i> , ⁴ Hourburgh <i>et al.</i> ⁹ and WHO ¹⁴	Required	Required
Close contacts	15	Landry <i>et al.</i> ⁴ and Sutherland <i>et al.</i> ¹⁵	Required	Required for close contacts (<five years old)
Organ-transplantation recipients	20–70	Aguado <i>et al.</i> ¹⁶ and Sakhuja <i>et al.</i> ¹⁷	Required	Not mentioned
Chronic renal failure requiring dialysis	6.9–52.5	Andrew <i>et al.</i> , ¹⁸ Lundin <i>et al.</i> , ¹⁹ Belcon <i>et al.</i> ²⁰ and Hussein <i>et al.</i> ²¹	Required	Not mentioned
TNF-alpha blockers	1.6–25.1	Solovic <i>et al.</i> ²²	Required	Not mentioned
Silicosis	2.8	Cowie <i>et al.</i> ²³	Required	Not mentioned
Moderate-risk factors				
Fibronodular disease on chest x-ray	6–19	Grzybowski <i>et al.</i> ²⁴	Not mentioned	Not mentioned
Immigrants from high-TB-prevalence countries	2.9–5.3	Baussano <i>et al.</i> ²⁵	Options to be considered	Not mentioned
Health-care workers	2.55	Chu <i>et al.</i> ²⁶	Options to be considered	Not mentioned
Prisoners, homeless persons, illicit drug users	–	–	Options to be considered	Not mentioned
Low-risk factors				
Diabetes mellitus	1.6–7.83	Harries <i>et al.</i> , ²⁷ Dobler <i>et al.</i> , ²⁸ Jeon <i>et al.</i> , ²⁹ Boucot <i>et al.</i> , ³⁰ Kim <i>et al.</i> ³¹ and Baker <i>et al.</i> ³²	Not recommended	Not mentioned
Smoking	2–3.4	Altet <i>et al.</i> , ³³ Slama <i>et al.</i> ³⁴ and Maurya <i>et al.</i> ³⁵	Not recommended	Not mentioned
Use of corticosteroids	2.8–7.7	Jick <i>et al.</i> ³⁶	Not recommended	Not mentioned
Underweight	2–3	Palmer <i>et al.</i> ³⁷ and Comstock <i>et al.</i> ³⁸	Not recommended	Not mentioned

我國各種結核病高風險族群成年人之潛伏結核感染率暨未進行治療之結核病發病率及相關指標

Risk Population	Sample Size	Age · Mean (year)	IGRA (+) 人數(%)	IGRA結果 Indeterminate 人數(%)	Active TB in IGRA positive 人數 (%)	Active TB in IGRA positive (每100人年)	Number needed to treat ***	Number needed to screen ****
Adult Contact ³	2203	45	414 (18.8%*)		10 (2.4%)		42	222.2
Leukemia and Hemaoncology ²	49	55.5	7 (14.3%)	12 (24.5%)	2 (28.6%)	25.6 (2/7.8人年)	3.5	24.4
Lung Cancer ²	244	68.6	63 (25.8%)	22 (9.0%)	1 (1.6%)	0.7 (1/150人年)	62.5	250.0
HIV ⁴ (Heterosexual)	97	39.8	10 (10.3%*)	(1.9%)	1 (10.0%)		10	97.1
HIV ⁶ (mainly IVDU)	772	36.8	90 (11.7%)	31 (4%)	6 (6.7%)		14.9	125
HIV ⁴ (IVDU)	362	36.4	42 (11.6%*)	(3.9%)	1 (2.4%)		41.7	357.1
IVDU ⁵ (HIV+)	4298				13**			333.3
HIV ⁴ (MSM)	450	35.5	29 (6.4%*)	(4.7%)	3 (10.3%)		9.7	149.3
HIV ⁷ (mainly MSM)	608		64 (10.5%)	10 (1.6%)	1 (1.6%)		62.5	500
IVDU ⁵ (HIV-)	32430				33**			1000
Type ² DM ²	1316	56.6	313 (23.8%)	7 (0.5%)	2 (0.6%)	0.2 (2/817人年)	166.7	666.7
CKD ²	63	61.8	7 (11.1%)	2 (3.2%)	0 (-)			
For Kidney Transplantation Evaluation ²	109	47.5	9 (8.3%)	10 (9.21%)	0 (-)			
Dialysis ²	940	59.3	193 (20.5%)	34 (3.6%)	3 (1.6%)	0.48	64.3	313
RA with TNF α Blocker ¹	242	54.7	45 (18.6%)	9 (3.7%)	3 (6.7%)		14.9	80.6
RA and other Autoimmune Diseases (RA: 55%,22% on TNF α Blocker) ²	229	50.1	26 (9.3%)	24 (8.6%)	0 (-)			
RA with TNF α Blocker ²	136		19 (14%)	10 (7.7%)	2 (1.5%)		9.5	68
RA without TNF α Blocker ²	173		24 (14%)	11 (6.4%)	0 (-)			

Case

- 78 y/o male
- ESRD, DM
- Agreed with 3HP for LTBI after discussion
- Suspended 3HP after 6 doses due to severe weakness

6M later

Chest tightness and low BP during HD, Af with SVR

CAD/3-v-d, sinus node dysfunction with AV nodal dysfunction

討論

- 3HP常見副作用
 - 全身性藥物反應(flu-like syndrome、急性過敏性休克反應，例如皮疹類，腸胃道和呼吸道症狀)
 - 常見於第3~4個劑量時發生
- 高齡病人接受3HP治療，並不會有較高比例發生副作用，但對於副作用耐受度較差，比較容易中斷治療。
- 副作用發生時，仔細評估，與病人討論，安全第一。
- 中斷治療後，衛教病人：一旦發現疑似結核病症狀，就醫時告知醫師自己是結核病接觸者，以免延誤治療。

Case

- 59 y/o male
- ESRD with HD for 15 years
- HBV carrier
- On KT waiting list
- Started on 9H x 4 weeks then shift to 3HP x 11 weeks due to concern of waiting kidney transplantation
- Completed LTBI treatment

討論

- 等待移植病人若確定LTBI，應在移植前完成治療
- LTBI治療若在移植前中斷，移植後應該盡快完成治療
- 建議處方：1HP, 3HP, 3HR, 4R, 6H and 9H
- 與Rifampine或rifapentine會產生交互作用的抗排斥藥物
 - Prednisolone, cyclosporine, tacrolimus

Case

- 64 y/o male
- ESRD, CAD, HTN, DM
- Started on INH 300mg qd for one week then shifted to 3HP due to personal choice
- Completed 3HP treatment

Discussion

- 各處方間若因副作用或其他因素，得相互轉換
- 轉換後處方按已服用比例，接續服用滿該處方的療程

Case

- 86 y/o female
- Exposure history: her husband and son had pulmonary tuberculosis
- ESRD, low grade fever for 2M, right UPJ tumor
- Started on 3HP after evaluation
- Shifted to 6H due to 3HP related AEs: fever, skin rash and low BP
- Suspended 6H due to weakness and low BP
- Hospice care at home



討論

- 仔細評估是否有活動性結核病感染
- 與病人及家屬討論LTBI治療的利弊得失

可能與rifampin 或 rifapentine 產生交互作用之藥物

- Antiarrhythmics
- Antibiotics
- Oral Anticoagulants
- Anticonvulsants
- Antipsychotics
- Benzodiazepines
- Beta-Blockers
- Calcium Channel Blockers
- Digoxin
- Corticosteroids
- Fibrates
- Oral Hypoglycemics
- Tricyclic antidepressants
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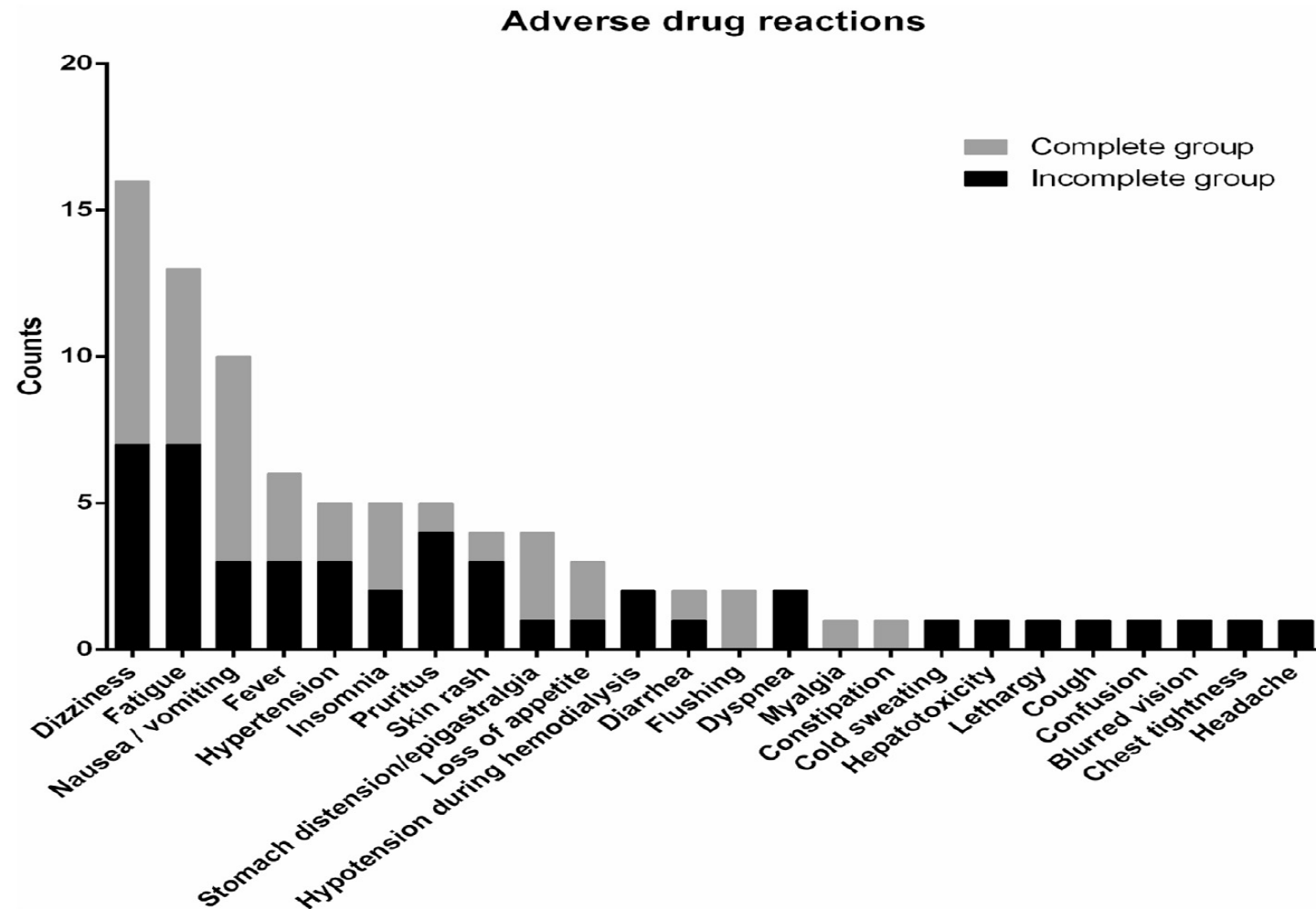
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Variable	Value for group ^a		P value ^b
	9H (n = 41)	3HP (n = 50)	
Treatment completed, no. (%)	25 (61.0)	41 (82.0)	0.046
Treatment not completed reasons, no. (%)			0.176
Participant refusal	10 (24.4)	2 (4.0)	
Termination due to ADE or other reasons ^c	6 (14.6)	7 (14.0)	
ADE, no. (%) ^d	9H (n = 37)	3HP (n = 48)	
Hypersensitivity	4 (10.8)	14 (29.2)	0.040
Flu-like syndrome	3 (8.1)	7 (14.6)	0.502
Gastrointestinal symptoms	6 (16.2)	14 (29.2)	0.163
Hepatotoxicity	0 (0)	0 (0)	1.000
Hospitalization, attributed to LTBI treatment	0 (0)	3 (6.3)	0.249
Reported maximal grade of ADE ^d	9H (n = 37)	3HP (n = 48)	0.001
Grade 1	12 (32.4)	17 (35.4)	
Grade 2	2 (5.4)	16 (33.3)	
Grade 3	3 (8.1)	5 (10.4)	
Grade 4	0	1 (2.1)	
Grade 2 or more	5 (13.5)	22 (45.8)	0.002
Grade 3 or more	3 (8.1)	6 (12.5)	0.725

治療中斷的風險因子

Variable	Crude OR	95% CI	<i>P</i> value	Adjusted OR	95% CI	<i>P</i> value
3HP vs 9H	0.39	0.15–0.99	0.049	0.17	0.04–0.69	0.013
Age over 60	0.58	0.23–1.49	0.259			
Male	1.30	0.47–3.56	0.616			
Active smoking	1.60	0.55–4.66	0.392			
Diabetes mellitus	2.08	0.78–5.54	0.141			
Peritoneal dialysis	1.79	0.46–6.94	0.401			
≥Grade 2 ADE	2.82	1.00–7.96	0.050	6.67	1.66–26.80	0.008
Eosinophil count ^b						
<349/ μ l	Reference					
350–699/ μ l	>100		0.999			
≥700/ μ l	>100		0.999			

3HP治療常見反應



LTBI 治療和安全性調查

	Overall	Age		p-Value
		≥60 years	<60 years	
Number of patients	406	167	239	
Occurrence of SARs	66 (16.3%)	<u>30 (18%)</u>	<u>36 (15.1%)</u>	0.436
SAR types				
Gastrointestinal reaction				
Abdominal pain	5 (1.2%)	1 (0.6%)	4 (1.7%)	0.653
Nausea/vomiting	17 (4.2%)	8 (4.8%)	9 (3.8%)	0.612
Anorexia	11 (2.7%)	5 (3%)	6 (2.5%)	0.768
Flu-like symptoms				
Fatigue	26 (6.4%)	12 (7.2%)	14 (5.9%)	0.591
Dizziness	21 (5.2%)	10 (6%)	11 (4.6%)	0.535
Headache	15 (3.7%)	6 (3.6%)	9 (3.8%)	0.928
Fever	14 (3.4%)	4 (2.4%)	10 (4.2%)	0.331
Myalgia/arthralgia	16 (3.9%)	5 (3%)	11 (4.6%)	0.412
Hypersensitivity reaction	8 (2.0%)	4 (2.4%)	4 (1.7%)	0.607
Other drug reactions	2 (0.5%)	0	2 (0.8%)	0.515
Elevated liver enzymes ^b				
Any	39 (9.6%)	11 (6.6%)	28 (11.7%)	0.084
1–3 × ULN	31 (7.6%)	11 (6.6%)	20 (8.4%)	
3–5 × ULN	6 (1.5%)	0	6 (2.5%)	
>5 × ULN	2 (0.5%)	0	2 (0.8%)	
Jaundice ^c				
Any	10 (2.5%)	5 (3%)	5 (2.1%)	0.564
1.5–3 mg/dl	8 (2%)	3 (1.8%)	5 (2.1%)	
>3 mg/dl	2 (0.5%)	2 (1.2%)	0	
Hepatotoxicity ^d	5 (1.2%)	1 (0.6%)	4 (1.7%)	0.334

嚴重副作用

	Overall	All patients		3HP		9H	
		≥60 years	<60 years	≥60 years	<60 years	≥60 years	<60 years
Number of patients	406	167	239	127	166	35	65
Treatment status							
Completed 完成率	332 (81.8%)	131 (78.4%)	201 (84.1%)	103 (81.1%)	147 (88.6%)	24 (68.6%)	47 (72.3%)
Discontinuation	74 (18.2%)	36 (21.6%)	38 (15.9%)	24 (18.9%)	19 (11.4%)	11 (31.4%)	28 (27.7%)
SARs	27 (36.5%)	15 (41.7%)	12 (31.6%)	14 (58.3%)	8 (42.1%)	1 (9.1%)	4 (22.2%)
Mild adverse reactions	10 (13.5%)	4 (11.1%)	6 (15.8%)	4 (16.7%)	5 (26.3%)	0	1 (5.6%)
Hepatotoxicity	5 (6.8%)	1 (2.8%)	4 (10.5%)	0	2 (10.5%)	1 (9.1%)	2 (11.1%)
Patient refusal	16 (21.6%)	8 (22.2%)	8 (21.1%)	3 (2.4%)	1 (5.3%)	5 (14.3%)	6 (33.3%)
Others	16 (21.6%)	8 (22.2%)	8 (21.1%)	3 (2.4%)	3 (15.8%)	4 (11.4%)	5 (27.8%)

	Overall patients, N = 406		≥60 years old, n = 167		<60 years old, n = 239	
	aOR (95% CI) ^a	p-Value	aOR (95% CI) ^a	p-Value	aOR (95% CI) ^a	p-Value
LTBI regimens						
3HP	1.00	–	1.00	–	1.00	–
9H	4.47 (1.29–15.52)	0.018	0.90 (0.06–13.50)	0.939	7.31 (1.74–30.81)	0.007
4R	1.67 (0.31–8.82)	0.549	1.19 (0.08–16.77)	0.898	1.87 (0.19–18.59)	0.595
Age years						
<35	1.00	–	–	–	1.00	–
35–59	1.63 (0.59–4.46)	0.344	–	–	1.68 (0.62–4.59)	0.310
60–79	1.72 (0.61–4.82)	0.304	1.00	–	–	–
≥80	4.96 (1.50–16.41)	0.009	3.62 (1.29–10.21)	0.015	–	–
ESRD	1.71 (0.78–3.73)	0.180	1.33 (0.40–4.45)	0.640	2.43 (0.82–7.16)	0.108
Autoimmune diseases	1.99 (0.92–4.29)	0.079	2.80 (0.79–9.90)	0.110	1.69 (0.61–4.65)	0.312
Having SARs	6.15 (3.18–11.89)	<0.001	11.27 (4.03–31.54)	<0.001	3.91 (1.58–9.67)	0.003
With DOPT	1.46 (0.41–5.11)	0.559	0.22 (0.02–3.37)	0.278	3.04 (0.69–13.56)	0.144

80歲以上病人有較高中斷治療風險

結論

- 治療前完整的溝通與評估
- 建議rifampin-based短期治療，副作用低於6H和9H 治療，但完成率高於6H和9H治療