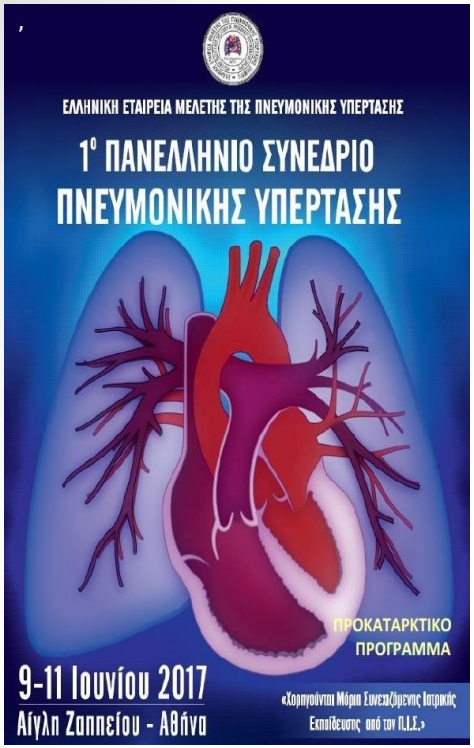

Σύγχρονες προκλήσεις στην αντιμετώπιση περιστατικών με ΡΗ κατηγορίας 5

Κορνέλια Μητράκου
Πνευμονολόγος – Εξειδικευόμενη ΜΕΘ

Β' Πανεπιστημιακή Κλινική Εντατικής Θεραπείας
& Ιατρείο Πνευμονικής Υπέρτασης
Π.Γ.Ν. «Αττικόν»

Clinical classification of Pulmonary Hypertension (ESC/ERS guidelines 2015)

1. Pulmonary arterial hypertension

- 1.1 Idiopathic
- 1.2 Heritable
  - 1.2.1 BMPR2 mutation
  - 1.2.2 Other mutations
- 1.3 Drugs and toxins induced
- 1.4 Associated with:
  - 1.4.1 Connective tissue disease
  - 1.4.2 Human immunodeficiency virus (HIV) infection
  - 1.4.3 Portal hypertension
  - 1.4.4 Congenital heart disease (Table 6)
  - 1.4.5 Schistosomiasis

1'. Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis

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1''. Persistent pulmonary hypertension of the newborn

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- 2.1 Left ventricular systolic dysfunction
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- 3.1 Chronic obstructive pulmonary disease
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- 3.4 Sleep-disordered breathing
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- 3.7 Developmental lung diseases (Web Table III)

4. Chronic thromboembolic pulmonary hypertension and other pulmonary artery obstructions

- 4.1 Chronic thromboembolic pulmonary hypertension
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  - 4.2.3 Arteritis
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  - 4.2.5 Parasites (hydatidosis)

5. Pulmonary hypertension with unclear and/or multifactorial mechanisms

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- 5.2 Systemic disorders, sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
- 5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
- 5.4 Others: pulmonary tumoral thrombothic microangiopathy, fibrosing mediastinitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension

Pulmonary hypertension with unclear and/or multifactorial mechanisms (group 5)

- includes several disorders with multiple patho-aetiologies

- the mechanisms of PH are poorly understood, may include:
  - pulmonary vasoconstriction
  - proliferative vasculopathy
  - extrinsic compression
  - intrinsic occlusion
  - high-output cardiac failure
  - vascular obliteration
  - left heart failure

- These patients need **careful diagnosis**

- Treatment is tailored for that diagnosis

!! **treatment of PH is secondary**

- There are no RCTs regarding the use of PAH-approved drugs in the treatment of group 5 disorders

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

Γυναίκα 34 ετών

- **Διάγνωση Ιστιοκύττωσης Langerhans** (Ιστιοκύττωσης – Χ) **σε ηλικία 7 ετών** (με **βιοψία** ανώδυνων λεμφαδένων τραχηλικής χώρας)
  - ✓ Υπό παρακολούθηση έως 18 ετών στο Νοσοκομείο «Παίδων»
    - !!! Έκτοτε χωρίς παρακολούθηση για το νόσημα…….
  - ✓ Έλαβε κορτιζονοθεραπεία για ≈ 2 χρόνια (χωρίς ΧΜΘ)

- **Άποιος διαβήτης σε ηλικία 9 ετών**
  - ✓ Έκτοτε υπό θεραπεία με Desmopressin

- **Πολυκυστικές ωοθήκες** υπό ορμονοθεραπεία
- **Σακχαρώδης διαβήτης** υπό δισκία
- **Αλλεργική ρινίτιδα**

- **Πρώην καπνίστρια**
  - ✓ Διακοπή ≈ προ έτους, 15 PY

Γυναίκα 34 ετών - διάγνωση Ιστιοκύττωσης-Χ

- προ έτους νοσηλεύτηκε σε επαρχιακό νοσοκομείο λόγω δύσπνοιας

↓

Παραπέμφθηκε στο Ιατρείο Πνευμονικής Υπέρτασης λόγω παθολογικού U/S καρδιάς (υπολογιζόμενη PASP =85-90mmHg)

- ≈ από διετίας αναφέρει

↓

✓δύσπνοια κοπώσεως

✓προσυγκοπτικά επεισόδια

Αρχική διερεύνηση – αξιολόγηση

PFTs: FEV1 85%, FVC 93%
FEV1/FVC 79, RV124%
TLC 127%, **DLCO 64%**

MRI καρδιάς:αναστροφή ΜΚΔ κατά τη διαστολή, διάταση ΔΕ κοιλίας με υποκινησία-ακινησία τοιχ. και έκπτωση συστολικής λειτουργιας, **ΚΕΔΚ 42%**

HRCT: κυστικές αλλοιώσεις άνω+μέσα πνευμονικά πεδία
Διάταση ΡΑ , διόγκωση ΔΕ καρδιακών κοιλοτήτων

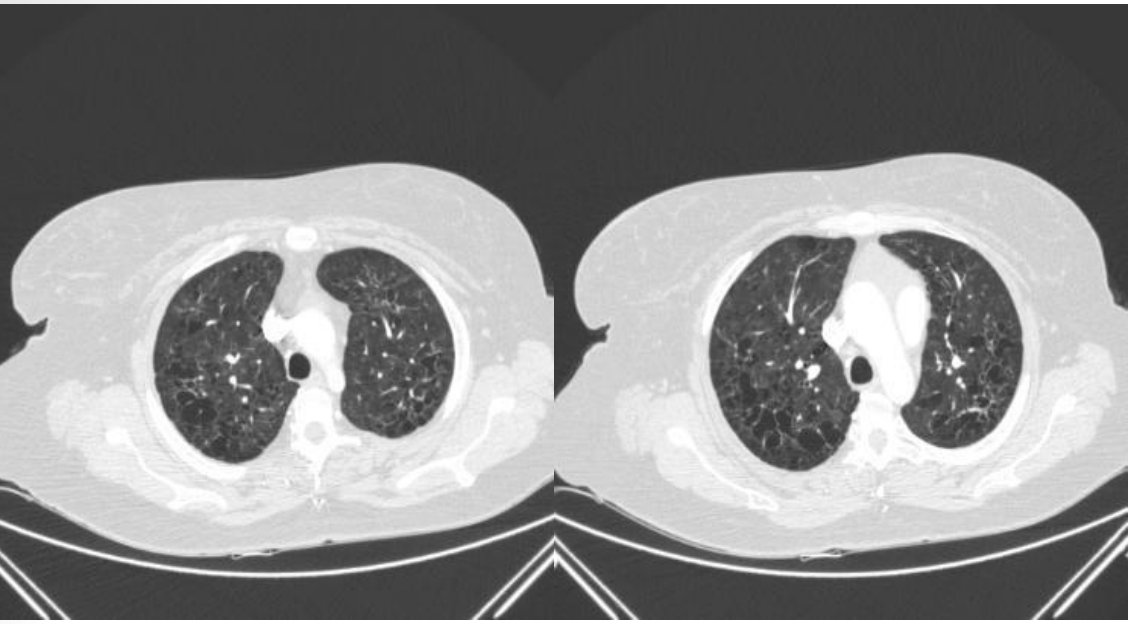
Δύσπνοια, **προ-συγκοπτικά**
+
U/S καρδιάς παθολογικό

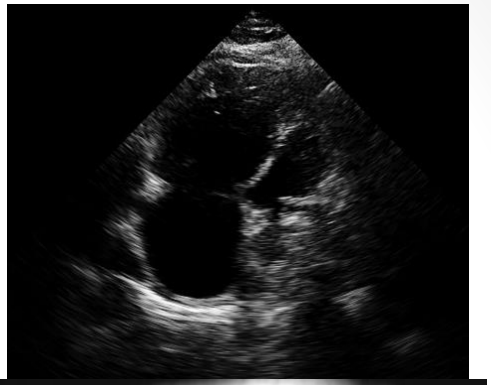
U/S καρδιάς:
TRVmax 4.2 m/s, **D-shape**, μεγάλη διάταση ΔΕ κοιλ.

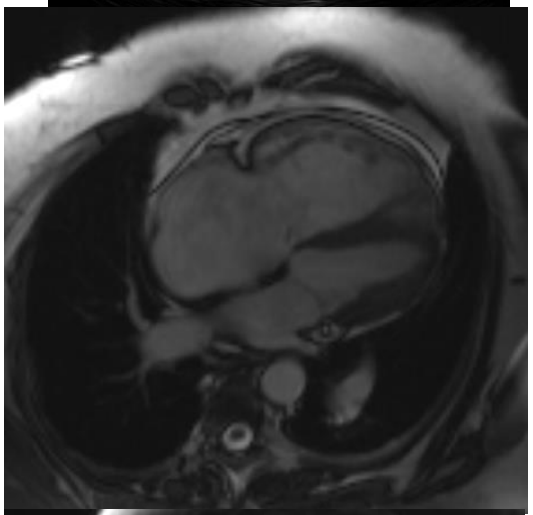
Σπινθηρογράφημα αιμάτωσης:
-μελέτη αρνητική για ΠΕ,
-ήπια ανομοιογενής πρόσληψη στα ανώτερα πνευμονικά πεδία

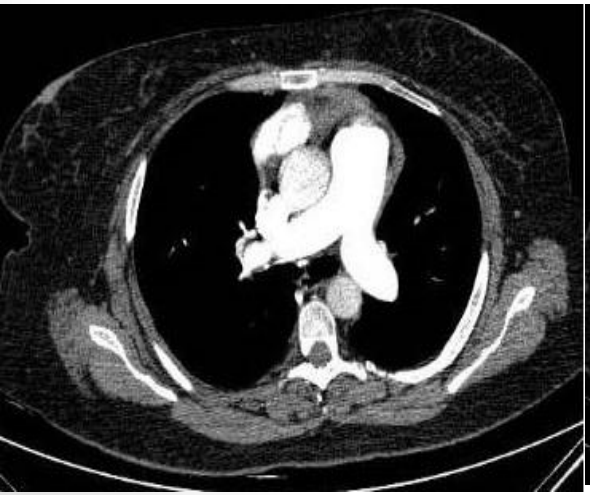
WHO class II late
6MWD 411m
(SaO2 95% → 83%)

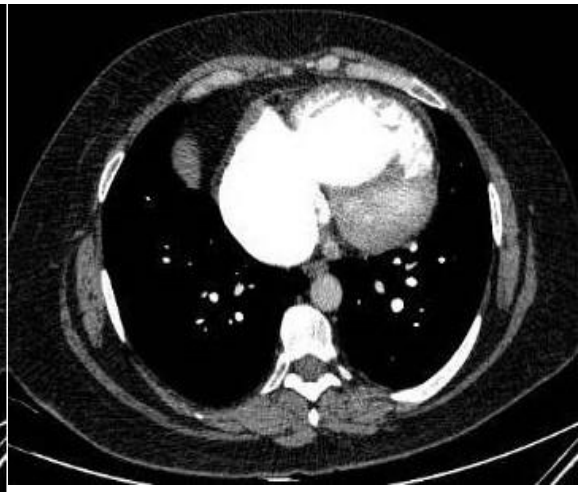
Αρχική διερεύνηση – αξιολόγηση

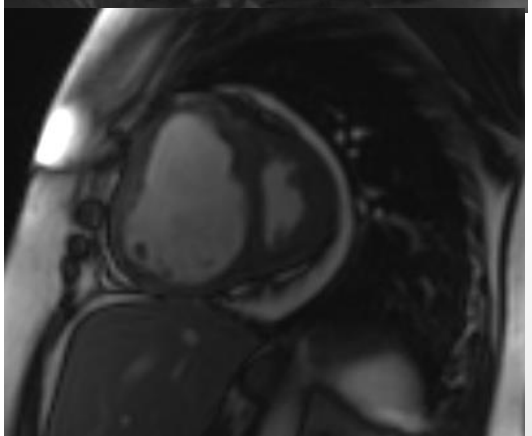












Αρχική διερεύνηση – αξιολόγηση

	RHC 1st
RAP	20 mmHg
PAP	**114/33/60** mmHg (S/D/M)
PAWP	**11** mmHg
CO	**4** l/min
CI	2,2 l/min/m^2
PVR	**12,2** Wood Units
SvO2	**53 %**

NT-proBNP: **3240** pg/ml

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Πως θα αντιμετωπισθεί η ασθενής ;

LANGERHANS CELL HISTIOCYTOSIS

HISTIOCYTE SOCIETY

Histiocyte Society

Evaluation and Treatment Guidelines

April 2009

Contributors:

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Girschikofsky *et al. Orphanet Journal of Rare Diseases* 2013, **8**:72
http://www.ojrd.com/content/8/1/72

ORPHANET JOURNAL OF RARE DISEASES

REVIEW **Open Access**

Management of adult patients with Langerhans cell histiocytosis: recommendations from an expert panel on behalf of Euro-Histio-Net

Michael Girschikofsky[1*], Maurizio Arico[2], Diego Castillo[3], Anthony Chu[4], Claus Doberauer[5], Joachim Fichter[6], Julien Haroche[7], Gregory A Kaltsas[8], Polyzois Makras[9], Angelo V Marzano[10], Mathilde de Menthon[11], Oliver Micke[12], Emanuela Passoni[10], Heinrich M Seegenschmiedt[13], Abdellatif Tazi[14] and Kenneth L McClain[15]

Abstract

Langerhans Cell Histiocytosis (LCH) is an orphan disease of clonal dendritic cells which may affect any organ of the body. Most of the knowledge about the diagnosis and therapy is based on pedriatic studies. Adult LCH patients are often evaluated by physicians who focus on only the most obviously affected organ without sufficient evaluation of other systems, resulting in patients being underdiagnosed and/or incompletely staged. Furthermore they may be treated with pediatric-based therapies which are less effective and sometimes more toxic for adults. The published literature on adult LCH cases lacks a comprehensive discussion on the differences between pediatric and adult patients and there are no recommendations for evaluation and comparative therapies. In order to fill this void, a number of experts in this field cooperated to develop the first recommendations for management of adult patients with LCH. Key questions were selected according to the clinical relevance focusing on diagnostic work up, therapy, and follow up. Based on the available literature up to December 2012, recommendations were established, drafts were commented by the entire group, and redrafted by the executive editor. The quality of evidence of the recommendations is predominantly attributed to the level of expert opinion. Final agreement was by consensus.

Keywords: Langerhans, Adult, Histiocytosis

Risk organs (RO)

Hematopoietic involvement: (with or without bone marrow involvement*)	**At least 2 of the following:** • **anemia:** hemoglobin <10 g/dl, infants <9 g/dl (not due to other causes; e.g. iron deficiency) • **leukocytopenia:** leukocytes <4,0 x 10^9/l, • **thrombocytopenia:** platelets < 100 x 10^9/l
Spleen involvement:	• **enlargement** > 2 cm below costal margin in the midclavicular line
Liver involvement:	• **enlargement** > 3 cm below costal margin in the midclavicular line and/or • liver **dysfunction** (i.e. hypoproteinemia <55g/l, hypoalbuminemia <25g/l not due to other causes) and/or • **histopathological** diagnosis
Lung involvement:	• typical changes on **HR-CT** (low dose multi-detector CT if available) and/or • **histopathological** / **cytological** diagnosis

The disease may affect any organ or system, more frequently bones, skin, and pituitary gland. Lymph nodes, liver, spleen, gut, the central nervous system, pituitary, and the hematopoietic system are less frequently affected. Lungs may be affected simultaneously or consecutively with other organs, but isolated pulmonary LCH (PLCH) occurs frequently in adults and may proceed to multisystem involvement. PLCH requires a different management in contrast to multi-organ involvement and is therefore discussed in a separate section.

Suri et al. Orphanet Journal of Rare Diseases 2012, 7:16
http://www.ojrd.com/content/7/1/16

ORPHANET JOURNAL OF RARE DISEASES

REVIEW Open Access

Pulmonary langerhans cell histiocytosis

Harpreet S Suri[1], Eunhee S Yi[2], Gregorz S Nowakowski[3] and Robert Vassallo[1,4*]

Table 1 Contrasting pediatric and adult PLCH

	Pediatric PLCH	Adult PLCH
Demographic features		
Peak age at presentation	1-3 yrs [16]	20-40 yrs [5]
Smoking history	Infrequently described [16,17]	Reported in > 95% [5,12]
Imaging findings; chest CT		
Distribution of abnormalities	Frequently involves lower lobes [18]	Sparing of bases and costo- phrenic angles is typical [19-21]
Biological character		
Clonality	Invariably reported [22-24]	Suspect reactive rather than clonal [25]
Clinical Presentation		
Single system vs multi-system presentation	Typically part of multi-system LCH [16]	Single system disease in > 80% of patients [5]
Management		
Pharmacotherapy with prednisone/ vinblastine	Complete or partial response frequently observed [26,27]	Insufficient data available; likely limited response
Smoking cessation	Limited role as tobacco exposure not involved in most cases	Main and first line therapy in all adult smokers [28,29]

cigarette smoking is less clear [17], although it has been reported that the commencement of smoking in teenage years can precipitate PLCH in young adults with a history of non-pulmonary childhood LCH [30]. Smoking

Girschikofsky et al. Orphanet Journal of Rare Diseases 2013, 8:72
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Systemic therapy should be considered in case of the following disease category:

- MS-LCH with/without involvement of “risk organs”
- SS-LCH with multifocal lesions
- SS-LCH with “special site” lesions [Vertebral lesions with intraspinal or cranofacial bone lesions with soft tissue extensions (orbit, mastoid, sphenoid or temporal bones)]

Pulmonary hypertension and PLCH

- The **natural history** of PLCH is **widely variable and unpredictable** (resolve spontaneously or after smoking cessation / remain stable / progress to respiratory failure in a minority of patients)

- **Pulmonary hypertension**
  - ✓ is a common and underrecognized complication that occurs several years after PLCH diagnosis in the majority of cases
  - ✓ severe precapillary PH is frequent in patients with advanced PLCH

- PH confirmed by RHC was present in 92% of the 36 patients with PLCH referred for lung transplantation (mPAP >35 mm Hg in 72.5% of cases)

  (Dauriat G, Mal H, Thabut G, et al. Lung transplantation for pulmonary Langerhans' cell histiocytosis:a multicenter analysis. Transplantation 2006; 81: 746–750)

Severe Pulmonary Hypertension in Histiocytosis X

MURIEL FARTOUKH, MARC HUMBERT, FRÉDÉRIQUE CAPRON, SOPHIE MAÎTRE, FLORENCE PARENT, CATHERINE LE GALL, OLIVIER SITBON, PHILIPPE HERVÉ, PIERRE DUROUX, and GÉRALD SIMONNEAU

UPRES EA 2705 (Maladies Vasculaires Pulmonaires), Service de Pneumologie et Réanimation Respiratoire, Service d'Anatomie Pathologique, et Service de Radiologie, Hôpital Antoine Béclère, Assistance Publique des Hôpitaux de Paris, Clamart, France

- Evidence from histopathological assessment of lung tissue samples examined prior to and following establishment of PH found that **progression of pulmonary vascular involvement occurs** independently of **progression of parenchymal involvement**
- Pulmonary hypertension in PLCH is associated with a **primary pulmonary vasculopathy**, which may be observed histopathologically as intimal fibrosis and remodeling of both venous and arterial systems

AM J RESPIR CRIT CARE MED 2000;161:216–223.

PLCH – related PH Therapy

- There are no RCTs regarding the use of PAH-approved drugs in the treatment of group 5 disorders (2015 ESC/ERS Guidelines)
- The efficacy of advanced PH therapies is uncertain in group 5 PH disease
- There is **no currently approved therapy** for PH that develops in the context of PLCH

- Whether therapy for PH may affect long-term outcomes of disease and impact timing of transplantation is currently unknown

- **Lung transplantation** remains the treatment of choice for end-stage PLCH, especially among patients with severe PH

CHEST

Original Research

PULMONARY VASCULAR DISEASE

Pulmonary Langerhans Cell Histiocytosis-Associated Pulmonary Hypertension

Clinical Characteristics and Impact of Pulmonary Arterial Hypertension Therapies

Jérôme Le Pavec, MD, PhD; Gwenaël Lorillon, MD; Xavier Jaïs, MD; Colas Tcherakian, MD; Séverine Feuillet, MD; Peter Dorfmüller, MD, PhD; Gérald Simonneau, MD; Marc Humbert, MD, PhD; and Abdellatif Tazi, MD, PhD

- 29 patients with PLCH – related PH
- Average mPAP of 45 (± 14) mmHg (19 had mPAP ≥ 40 mmHg, indicative of severe PH)
- 14 patients underwent PAH therapies (ERA / PDE-5i / ERA + PDE-5i / Iloprost)
- A follow-up assessment at 5.5 ± 2.5 mo and 16 ± 4 mo after baseline in 12 and 10 patients, respectively

Table 3—*Response to PAH Therapy at Follow-up Evaluations*

Measure	Baseline	Short-term Evaluation[a]	Long-term Evaluation[a]	*P* Value[b]	*P* Value[c]
WHO functional class I-II/III-IV, No.	1/11	6/6	4/6	.12	.37
6MWT, m	376 ± 96	403 ± 74	415 ± 90	.25	.20
Hemodynamics					
HR, bpm	89 ± 10	82 ± 12	80 ± 8	.17	.08
Mean BP, mm Hg	102 ± 24	98 ± 15	90 ± 13	.57	.20
RAP, mm Hg	8 ± 4	6 ± 4	8 ± 5	.18	.59
PCWP, mm Hg	11 ± 4	10 ± 3	11 ± 3	.40	.71
mPAP, mm Hg	56 ± 14	45 ± 12	43 ± 11	.03	.04
CO, L/min	5.5 ± 1.7	6.4 ± 1.7	6.9 ± 1.1	.08	< .01
Cardiac index, L/min/m^2	2.9 ± 0.8	3.4 ± 0.8	3.6 ± 0.5	.09	< .01
PVR, dyne/s/cm^5	701 ± 239	469 ± 210	348 ± 104	.01	< .01
Oxygen requirement in patients on oxygen at baseline, mean ± SD (No.), L/min	3.7 ± 2.1 (3)	2.0 ± 3.5 (3)	2.0 ± 3.4 (3)	.20	.20
Arterial oxygen saturation, %					
Entire population	91 ± 4	91 ± 5	89 ± 8	.96	.68
Patients without oxygen at baseline, mean ± SD (No.)	90 ± 4 (9)	91 ± 4 (9)	92 ± 2 (7)	.50	.16
Patients on oxygen at baseline, mean ± SD (No.)	93 ± 4 (3)	90 ± 9 (3)	83 ± 13 (3)	.66	.41

PAH-specific therapy may improve the WHO function class and hemodynamics

Respiratory Medicine Case Reports 14 (2015) 13–15

Contents lists available at ScienceDirect

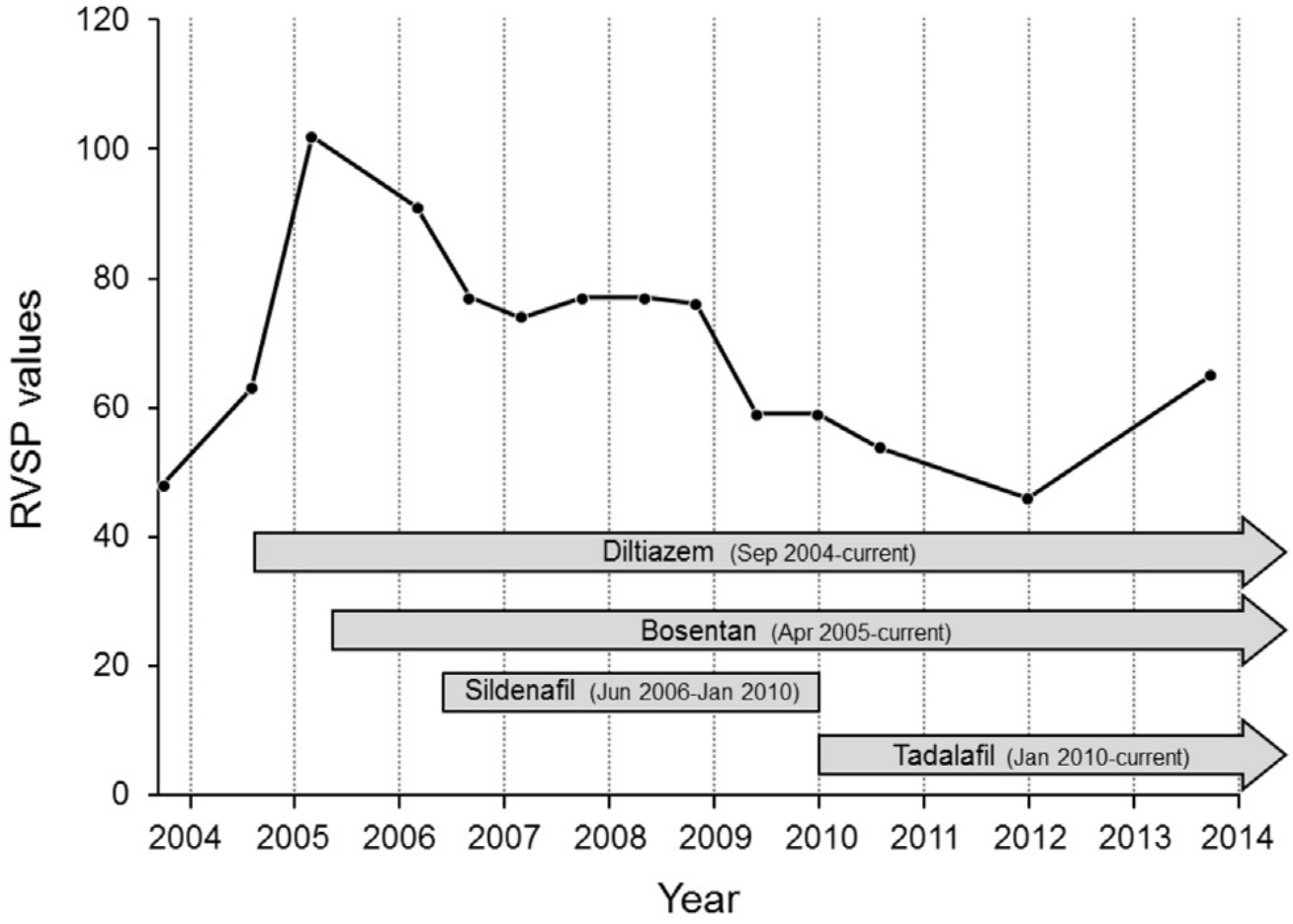
Respiratory Medicine Case Reports

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

Case report

Dramatic and sustained responsiveness of pulmonary Langerhans cell histiocytosis-associated pulmonary hypertension to vasodilator therapy

Adam May [a], Garvan Kane [b], Eunhee Yi [c], Robert Frantz [b], Robert Vassallo [d, *]



Respiratory Medicine Case Reports 18 (2016) 54–57

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

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

Case report

Long-term improvement during tadalafil therapy in a patient with pulmonary hypertension secondary to pulmonary Langerhans cell histiocytosis

Kenji Nemoto [a, *], Shuji Oh-ishi [a], Toshihide Inui [a], Mariko Nakazawa [a], Kentaro Hyodo [a], Masayuki Nakajima [a], Jun Kanazawa [a], Yukiko Miura [a], Takio Takaku [a], Yuko Minami [b], Kenji Hayashihara [a], Takefumi Saito [a], Yoshinori Kawabata [c]

Overview of clinical, function and haemodynamic features before and after tadalafil therapy.

Variables	2007	2009	2010 (Baseline)	1 month	15 months	30 months	40 months	50 months
NYHA class	I	II	IV	III	II	II	II	II
NT pro BNP (pg/ml)	ND	61.6	63.3	43.3	25.7	21.5	39.1	26.3
6MWT distance (m)	ND	265[a]	255[a]	200[a]	ND	230[a]	305[a]	310[a]
6MWT SpO_2, percentage of decrease (%)	ND	2[a]	5[a]	9[a]	ND	2[a]	5[a]	7[a]
PaO_2 at rest (mmHg)	83.1	74.2[b]	56.6[b]	52.9[b]	ND	70.3[b]	74.2[b]	83.8[b]
$PaCO_2$ at rest (mmHg)	41.8	44.7[b]	42.8[b]	46.5[b]	ND	39.7[b]	41.5[b]	46.9[b]
VC, % pred (%)	106.9	97.4	64.5	61.9	75.1	72.8	66.2	73.5
FEV_1, % pred (%)	103.3	72.9	49.8	49.8	50.4	52.6	48.4	52.4
DLco, % pred (%)	70.2	49.1	34.6	37.3	44.2	38.4	34.9	50.0
PAP systolic/diastolic (mmHg)	ND	ND	51/24	51/27	ND	34/18	34/16	32/13
Mean PAP (mmHg)	ND	ND	34	34	ND	25	24	21
Mean PCW (mmHg)	ND	ND	6	13	ND	8	9	5
PVR (dynes/s/cm^5)	ND	ND	638.3	342.5	ND	376.1	321.1	387.7
CI (L/min/m^2)	ND	ND	2.02	2.97	ND	2.23	2.33	2.00
Therapy	Smoking cessation	Nasal oxygen	Nasal oxygen Tadalafil commenced	Nasal oxygen plus Tadalafil	Nasal oxygen plus Tadalafil	Nasal oxygen plus Tadalafil	Nasal oxygen plus Tadalafil	Nasal oxygen plus Tadalafil

Πως θα αντιμετωπισθεί η ασθενής ;

Risk assessment in pulmonary arterial hypertension

Determinants of prognosis[a] (estimated 1-year mortality)	Low risk <5%	Intermediate risk 5–10%	High risk >10%
Clinical signs of right heart failure	Absent	Absent √	Present
Progression of symptoms	No	Slow √	Rapid
Syncope	No	Occasional syncope[b] √	Repeated syncope[c]
WHO functional class	I, II √	III	IV
6MWD	>440 m	165–440 m √	<165 m
Cardiopulmonary exercise testing	Peak VO_2 >15 ml/min/kg (>65% pred.) VE/VCO_2 slope <36	Peak VO_2 11–15 ml/min/kg (35–65% pred.) VE/VCO_2 slope 36–44.9	Peak VO_2 <11 ml/min/kg (<35% pred.) VE/VCO_2 ≥45
NT-proBNP plasma levels	BNP <50 ng/l NT-proBNP <300 ng/ml	BNP 50–300 ng/l NT-proBNP 300–1400 ng/l	√ BNP >300 ng/l NT-proBNP >1400 ng/l
Imaging (echocardiography, CMR imaging)	RA area <18 cm^2 No pericardial effusion	RA area 18–26 cm^2 No or minimal, pericardial effusion √	RA area >26 cm^2 Pericardial effusion
Haemodynamics	RAP <8 mmHg CI ≥2.5 l/min/m^2 SvO_2 >65%	RAP 8–14 mmHg CI 2.0–2.4 l/min/m^2 SvO_2 60–65% √	RAP >14 mmHg CI <2.0 l/min/m^2 SvO_2 <60%

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Macitentan → **Tadalafil**

WHO class	**II late**		**II**
6MWD	411 m		497 m

	RHC 1st		RHC 2nd
RAP	**20** mmHg		**18** mmHg
PAP	**114/33/60** mmHg (S/D/M)		**106/34/58** mmHg (S/D/M)
PAWP	**11** mmHg	**3 months**	**13** mmHg
CO	**4** l/min		**4.4** l/min
CI	**2,2** l/min/m^2		**2,4** l/min/m^2
PVR	**12,2** Wood Units		**9.7** Wood Units
SvO2	**53 %**		**61** %

NT-proBNP:	**3240** pg/ml	**2379** pg/ml

➢ PET-CT:

- υπερμεταβολισμός στις πνευμονικές πύλες αμφω,
- υπερμεταβολισμός σε αριστερό μασχαλιαίο λεμφαδένα
- εστιακή υπερμεταβολική αλλοίωση στη δερματική επιφάνεια αριστερής κατώτερης κοιλιακής χώρας

➢ Αιματολογική εκτίμηση

Girschikofsky et al. Orphanet Journal of Rare Diseases 2013, 8:72
http://www.ojrd.com/content/8/1/72

ORPHANET JOURNAL OF RARE DISEASES

REVIEW Open Access

Management of adult patients with Langerhans cell histiocytosis: recommendations from an expert panel on behalf of Euro-Histio-Net

Michael Girschikofsky[1*], Maurizio Arico[2], Diego Castillo[3], Anthony Chu[4], Claus Doberauer[5], Joachim Fichter[6], Julien Haroche[7], Gregory A Kaltsas[8], Polyzois Makras[9], Angelo V Marzano[10], Mathilde de Menthon[11], Oliver Micke[12], Emanuela Passoni[10], Heinrich M Seegenschmiedt[13], Abdellatif Tazi[14] and Kenneth L McClain[15]

First line systemic therapy

Recommendation	Grade
Mild Symptoms, No Risk Organ Involved:	
• Methotrexate 20 mg per week p.o/i.v.	C1
• Azathioprine 2 mg/kg/d p.o	D1
• Thalidomide 100mg/d p.o in skin or soft tissue multifocal single system LCH	C2
Additionally In Multifocal Bone LCH	
• zoledronic acid 4 mg i.v.	C2
q 1 (- 6) month (depending on extent and response)	C1
Symptomatic, MS-LCH, No Risk Organs involved	
• Cytarabine 100 mg/m^2 d1-5 q4w i.v.	C1
• Etoposide 100 mg/m^2 d1-5 q4w i.v.	D1
• Vinblastin/Prednisolone (like in pediatric studies)	C1
MS-LCH, Risc Organs Involved	
• 2-CDA 6 mg/m^2 d1-5 q4w s.c./i.v.	C2

LANGERHANS CELL HISTIOCYTOSIS

HISTIOCYTE SOCIETY

Histiocyte Society
Evaluation and Treatment Guidelines

April 2009

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First line systemic therapy

- An initial 6-week course of therapy with **vinblastine** and **prednisone is** suggested for all patients with MS-LCH <u>regardless of risk organ involvement</u>
- Maintenance therapy with vinblastine and prednisone for a total treatment duration of 12 months

Ασθενής 34 ετών με συστηματική ιστιοκύττωση Langerhans και πνευμονική υπέρταση

- ολοκλήρωσε δωδεκάμηνη θεραπεία με Vinblastine + Prednisolone
- PET-CT…….
- βρίσκεται υπό θεραπεία με Macitentan + Tadalafil
- Πρόσφατη επανεκτίμηση με RHC και MRI καρδίας (χωρίς ιδιαίτερες διαφοροποιήσεις)

Risk assessment in pulmonary arterial hypertension

Determinants of prognosis[a] (estimated 1-year mortality)	Low risk <5%	Intermediate risk 5–10%	High risk >10%
Clinical signs of right heart failure	Absent √	Absent	Present
Progression of symptoms	No	Slow √	Rapid
Syncope	No √	Occasional syncope[b]	Repeated syncope[c]
WHO functional class	I, II √	III	IV
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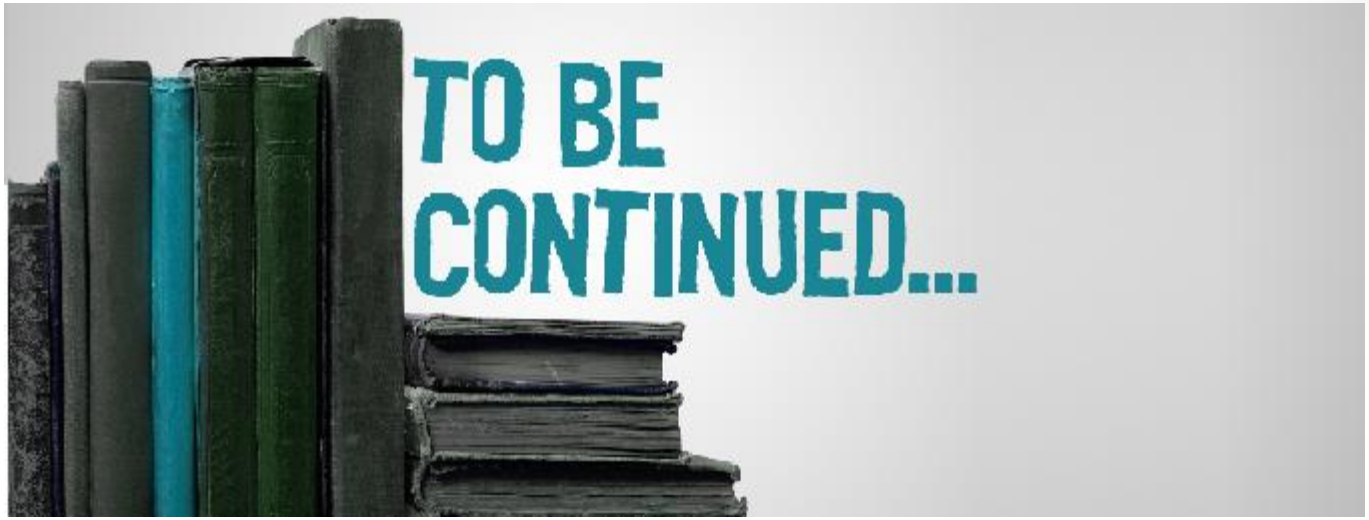

Σας ευχαριστώ.....