

# Respiratory failure in a 46-year-old patient with recurrent acute myeloid leukemia and allogeneic stem cell transplantation

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# Late patient's history - Recurrent leukemia

## Admission to the hospital for induction therapy 01/2014

- First diagnosis of AML 1996, first relapse 2005 with allogeneic HSCT -> CR
- Exceeded dosages of anthracyclines in previous cycles
- Modified („7+3“-)chemotherapy regimen was planned

## Normal physical exam

- Sore throat, recurrent fever episodes
- Lung functioning/blood gas and echocardiography were normal
- Non-smoker
- Allergic to penicilline

## Refractory disease after induction therapy

## 2<sup>nd</sup> HLA-ident allogeneic stem cell transplantation with FLAMSA-re-induction 04/2014

- Outcome: Complete remission
- Complications: febrile neutropenia, radiologic suspicion for pulmonary fungal infection
- Discharge with oral voriconazole

# Re-admission: Respiratory failure 06/2014

## Physical exam:

- HR 100/min, BP 140/90 mmHg; Temperature = 38,5°C; RR >22/min, sO<sub>2</sub> ~ 80% while breathing ambient air
- Bilateral dry crackles

## Lung functioning 5 days before admission

- Decrease of total lung capacity (TLC) and diffusion capacity for Carbon monoxide (DLCO)

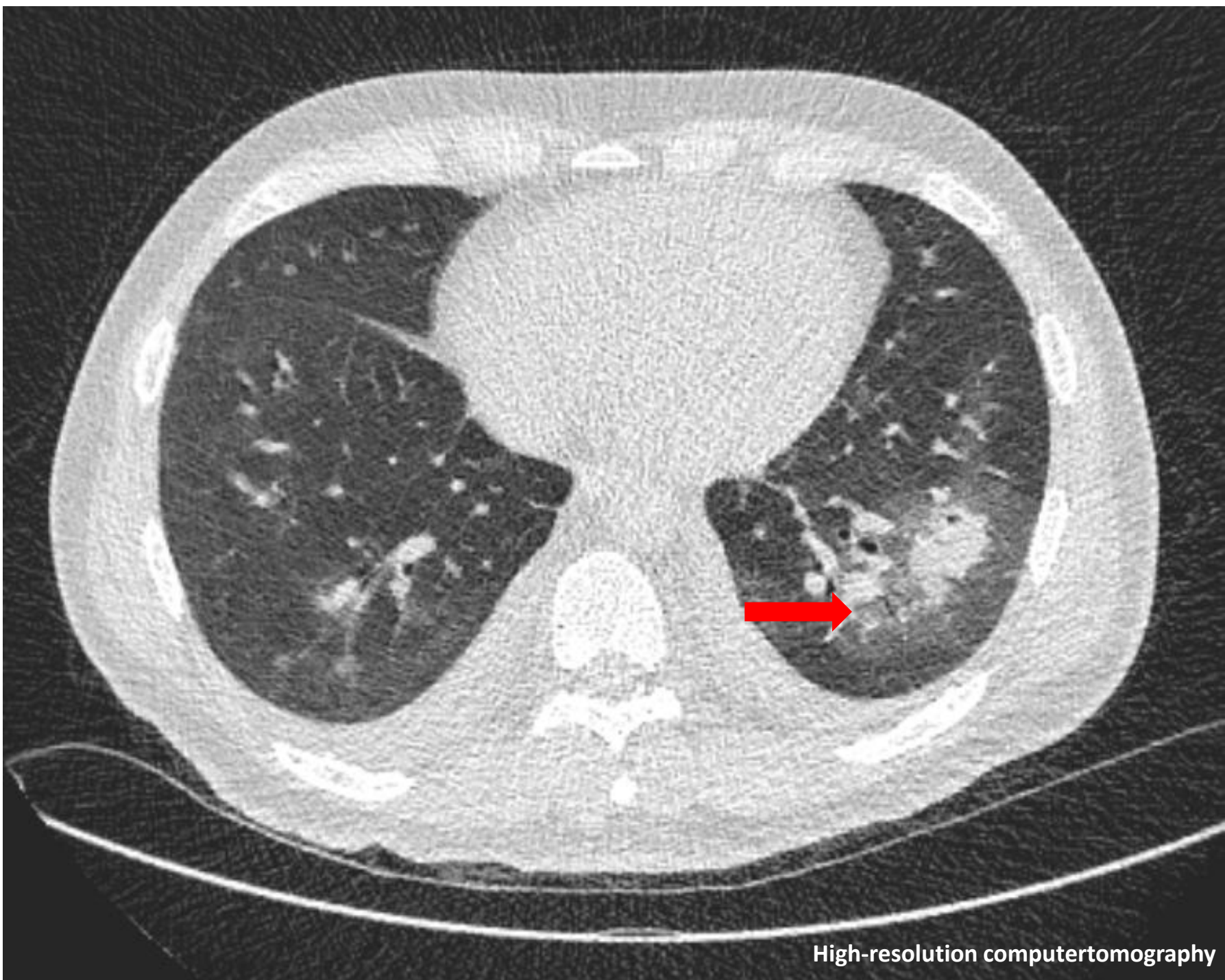
## Laboratory findings [->](#)

## Radiology: computertomography of the chest (HRCT) [->](#)

## Initial Therapy [->](#)

- Nasal oxygen supply
- Antibiotic treatment Imipenem/Cilastatin (Zienam)
- Antifungal treatment with high dose liposomal Amphotericin B (Ambisome)

<b>Bestimmung</b>	<b>Wert</b>	<b>Flag</b>	<b>Status</b>	<b>Vorwert vom</b>	<b>Einheit</b>	<b>Referenzbereich</b>
<b><u>Klinische Chemie (Li-Heparin-Plasma)</u></b>						
Natrium	141		validiert		mmol/l	136 - 145
Kalium	3.2	-	validiert		mmol/l	3.5 - 5.1
Creatinin	1.17		validiert		mg/dl	0.7 - 1.3
Harnstoff-N	16		validiert		mg/dl	9 - 21
Gesamt-Bilirubin	0.62		validiert		mg/dl	0.2 - 1.2
CRP	56	+	validiert		mg/l	- < 5
<b><u>Gerinnung (Citratplasma)</u></b>						
Quick	>133	+	validiert		%	70 - 120
INR	0.8		validiert			
APTT	28.3		validiert		sec	26 - 36
Antithrombin	79	-	validiert		%	80 - 120
<b><u>Hämatologie (EDTA-Blut)</u></b>						
Leukozyten	2.63	-	validiert		/nl	3.5 - 10
Erythrozyten	2.42	-	validiert		/pl	4.2 - 5.6
Hämoglobin	8.8	-	validiert		g/dl	13.5 - 17.5
Hämatokrit	26.8	-	validiert		%	39 - 49
MCV	110.7	+	validiert		fl	83 - 100
MCH	36.3	+	validiert		pg	27 - 33
MCHC	32.8		validiert		g/dl	32 - 35
EVB	23.0	+	validiert		%	11.0 - 15.0
Thrombozyten	38	--	validiert		/nl	150 - 360
MTV	8.6		validiert		fl	7.6 - 11.2



High-resolution computertomography

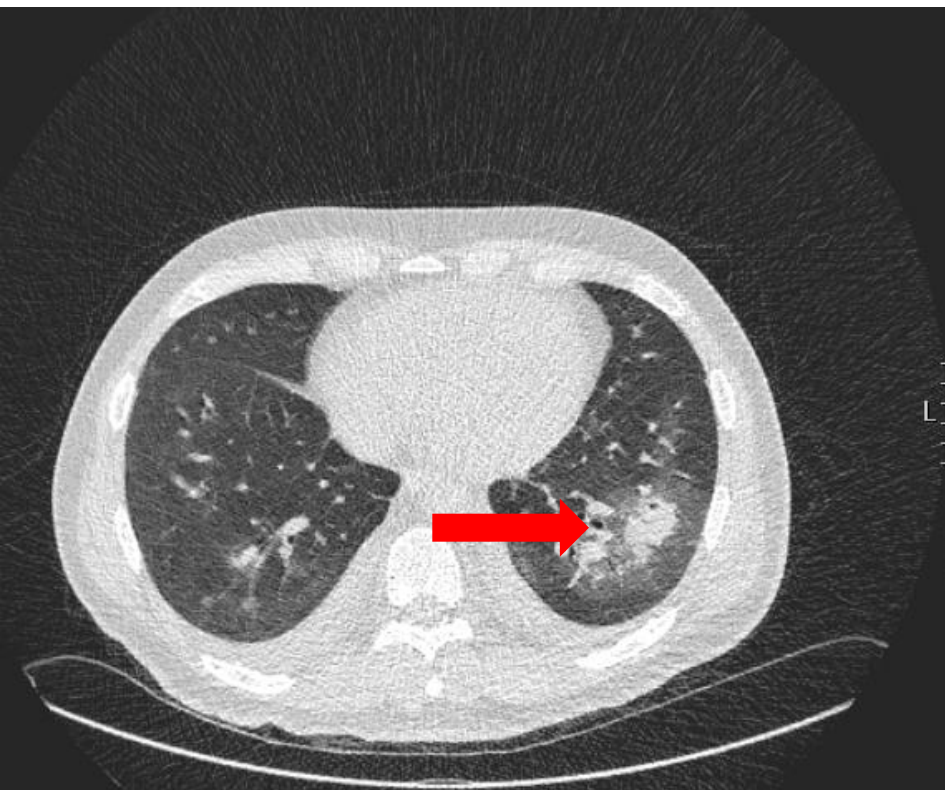
# Respiratory failure - further work-up 06-09/2014

## • Clinical course

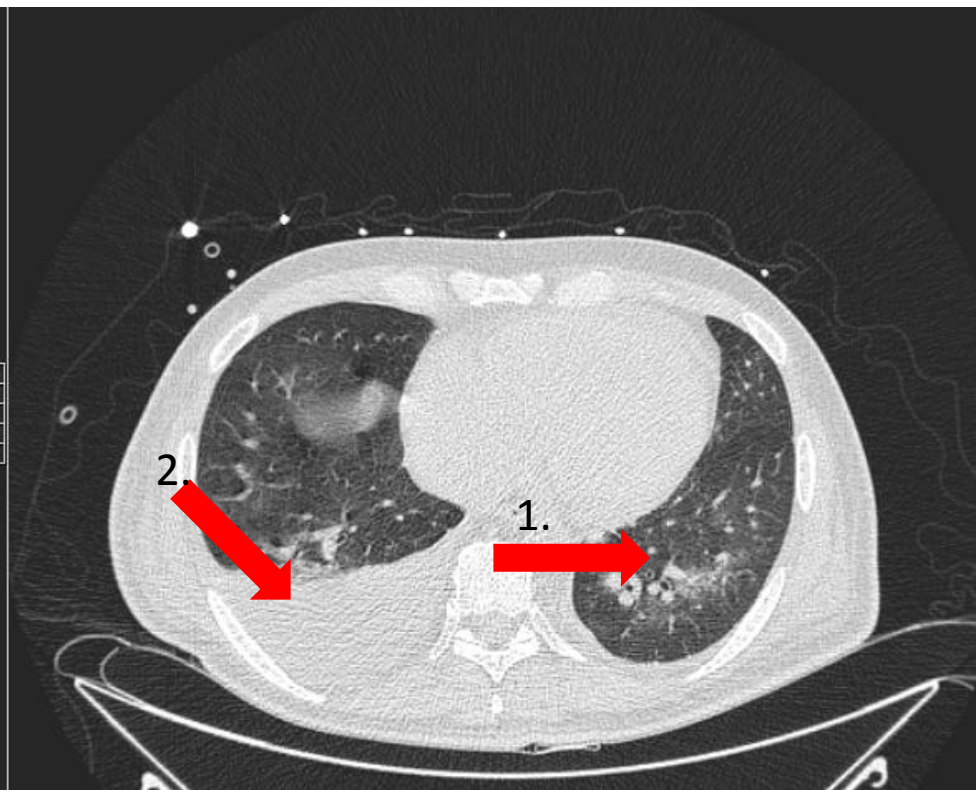
- **Initially decreasing inflammation parameters**
- **Increasing need for oxygen supply**
  - Up to 6L/min at rest
- **Moist Crackles**
- **Severe edema of arms and legs**
  - Reduced urine output
  - Continuous application of diuretics
- **Intubation because of respiratory failure and septic shock**
- **Resuscitation twice due to PEA**
  - Time to ROSC 5-10 min
  - CPC=1

## Further Diagnostics

- **Microbiology/Virology**
  - Cytomegalovirus reactivation
  - Klebsiella pneumoniae (3-MRGN)
- **Laboratory findings**
  - Increasing Inflammation
  - Renal failure
- **Radiology [->](#)**
  - Regressive fungal disease
  - Pleural and pericardial effusion
- **Echocardiography**
  - Pulmonary hypertension with right heart failure (sPAP > 60 mmHg)
- **Ventilation-Perfusion Szintigraphy**
  - No pulmonary embolism
- **Right heart catheterization [->](#)**



HR-CT on admission



HR-CT 6 weeks after admission:  
1. Regressive fungal disease  
2. Pleural effusion

Pressure		[mmHg]	Reference [mmHg]
Mean <a href="#">pulmonary</a> capillary wedge pressure	PCWP mean	16	9-23
Systolic pulmonary artery pressure	sPAP	79	15-25
Mean systolic artery pressure	PAP mean	55	10-22
Right ventricular end diastolic pressure	RVEDP	20	3-12
Mean right atrial pressure	RAP(ZVD) mean	20	1-8
<b>Diagnosis: Severe pulmonary hypertension resp. Class III pulmonary hypertension owing to lung diseases/or hypoxia</b>			



# Class III pulmonary hypertension due to lung disease/hypoxia – Differential diagnoses

## Infection of the lung

- Cytomegalovirus (serum)
- Klebsiella pneumoniae (blood cultures), Pseudomonas spp.

## Toxicity due to cytotoxic agents

- Cyclophosphamide, Busulfan, Fludarabine

## Acute/Chronic graft-versus-host disease of the lung

- Bronchiolitis obliterans

## Veno-occlusive disease (VOD) of the lung, etc

Biopsy  
wanted...needed...

# Bronchiolitis obliterans (syndrome)

**Definition:** Small airway inflammation and narrowing due to fibrous scar

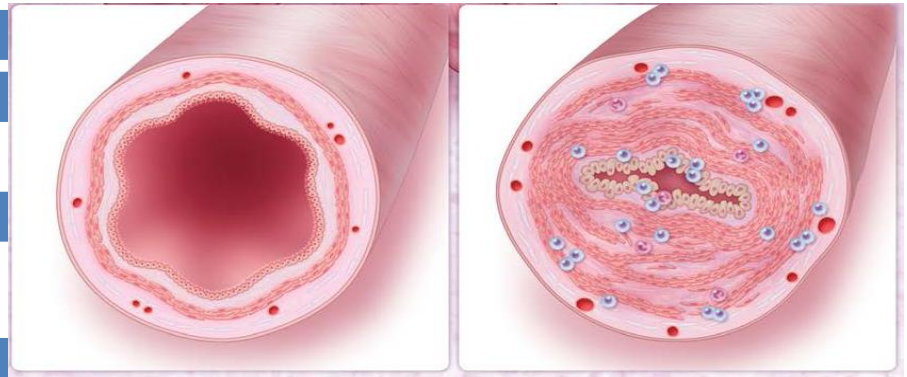
**Clinical findings:** Airflow limitation  $\geq$

- Respiratory Obstruction/Restriction
- Reduced DLCO

**Primary noninfectious pulmonary complication in patients after HSCT**

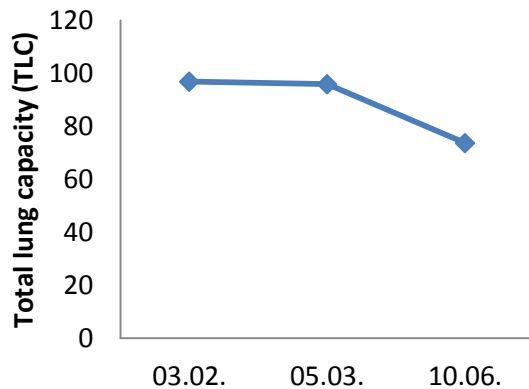
- Manifestation of chronic GvHD of the lung
- Risk factors: older donor age/recipient, degree of HLA mismatch, busulfan-based conditioning regimen, eg.

**Therapy:** Increase of immunosuppression; ECP, steroids,...

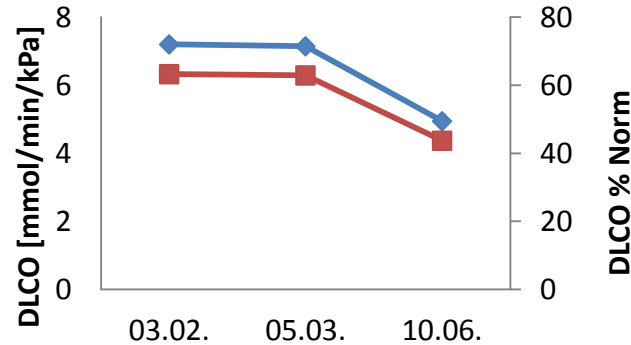


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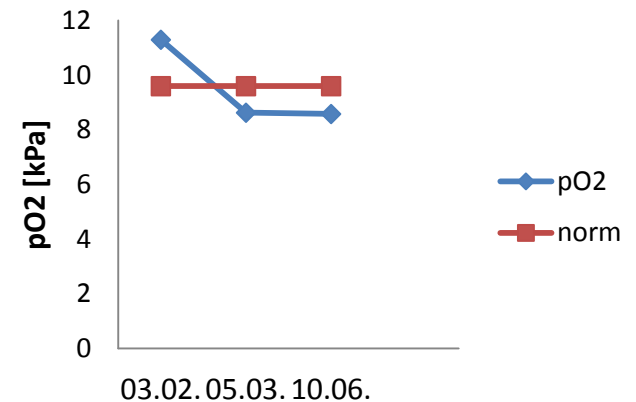
**Restrictive changes**



**Diffusing capacity for carbon monoxide**



**Blood gas analysis**



# Therapeutic management of the pulmonary hypertension/bronchiolitis obliterans syndrome

## Symptomatic

### Prostacyclin pathway agonists/PD5E inhibitors

- Intravenous Iloprost /oral sildenafil
- Initial decrease of sPAP down to 40 mmHg
- Multiple resuscitations because of PEA
  - CPC Score 1
  - Long term dependency on catecholamines

### Continuous hemodialysis

### Low dose catecholamines

### Tracheostomy

- Continuous oxygen supply

### Physical therapy

### Psychological therapy

## Causal

### Infection

- Klebsiella pneumoniae (4- MRGN), Pseudomonas, CMV
- Antibiotic treatment: Inhaled Colistin/Meropenem
- Antiviral treatment: Ganciclovir

### Extracorporeal photopheresis (ECP)

# Outcome 09/2014 – 03/2015

## Pulmonary hypertension and circulation

- Continuous increase of sPAP
- Multiple arrhythmias -> high frequency catheter ablation

## Infection of the lung

- Controlled by high dose meropenem/inhaled colistin
- Successful CMV treatment
- Continuous need for oxygen supply via tracheostomy

## Renal impairment

- Regular hemodialysis treatment three times a week

## Physical therapy

- Mobilization into a chair
- Oral food intake
- Neurological rehabilitation scheduled

## Psyche

- Depression
- Patient's will for continued intensive care treatment

# Unfortunately...

- 5th PEA
  - Unsuccessful resuscitation
  - Death because of right heart failure in 03/2015
- Curing the underlying disease (AML) is not necessarily curative for the patient...

Thank you for  
listening!



SCHUKZ