Clinical Grand Round
An Unexpected Opportunist

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History of Presenting Illness

A 23 year old male is admitted to the hospital with 3 days of fevers, nausea, lightheadedness, and falls

Has chronic myelogenous leukemia (CML) and is Day #27 from a hematopoietic stem cell transplant (HSCT)

Review of systems

- Positive: longstanding skin rash
- Negative: headache, shortness of breath, cough, abdominal pain, vomiting, diarrhea, urinary symptoms, weakness, or numbness

Past Medical History

1 Year Ago

- CML
- Failed therapy

Additional History

INFECTIOUS COMPLICATIONS

- *Candida krusei* blood stream infection
- Cytomegalovirus viremia
- *Klebsiella pneumoniae* urinary tract infection

SOCIAL HISTORY

- No current tobacco, alcohol, or illicit drug use
- Born in United States
- No recent travel outside of Ohio
- Pet snake

Additional History

MEDICATIONS

- Tacrolimus 2mg twice daily
- Mycophenolate mofetil 750mg three times daily
- Prednisone 60mg twice daily
- Valacyclovir
- Voriconazole
- Inhaled pentamidine
- Azithromycin

ALLERGIES/INTOLERANCES

- Trimethoprim/sulfamethoxazole: rash
- Piperacillin/tazobactam: thrombocytopenia

Physical Examination

Vitals

- Temperature - 38.6 degrees Celsius
- Heart Rate – 137 beats/minute
- Respirations – 36 breaths/minute
- Blood Pressure – 172/106 mmHg
- Oxygen Saturation – 92% on 60% high flow oxygen supplementation

General – ill appearing, somnolent

Heart – tachycardic, no murmurs/rubs

Lungs – clear to auscultation bilaterally

Abdomen – soft, non-tender, non-distended, bowel sounds present

Neurologic – no weakness or sensory deficits

Skin – patchy, erythematous rash in bilateral upper extremities

Laboratory Studies: Pre-Transplant

- Cytomegalovirus IgG antibody positive
- Herpes simplex virus 1 and 2 IgG antibodies negative
- Varicella zoster virus IgG antibody negative
- Epstein Barr virus serologies showed immunity through previous infection
- HIV antigen/antibody screen negative
- Syphilis IgG antibody non-reactive
- Toxoplasma IgG antibody positive

Laboratory Studies: Current Presentation

Complete Blood Count	
White Blood Cell Count	35 400 cells/uL
Neutrophils	95%
Immature neutrophils	2%
Lymphocytes	1%
Monocytes	1%
Eosinophils	<1%
Basophils	<1%
Hemoglobin / Hematocrit	10.8 g/dL / 32%
Platelets	72 000 cells/uL

Renal function and electrolytes were normal

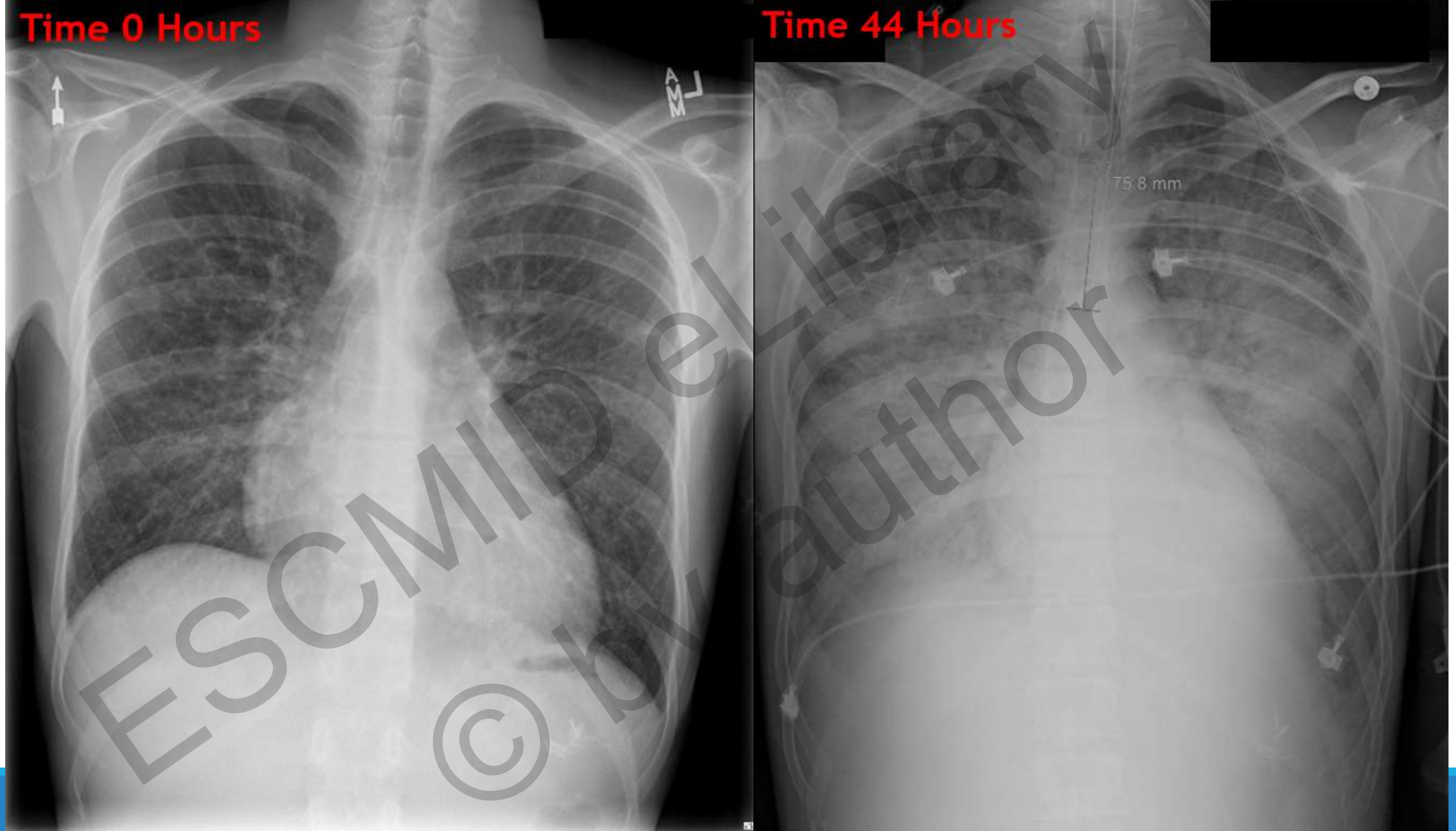
ALT (SGPT): 318 U/L

AST (SGOT): 264 U/L

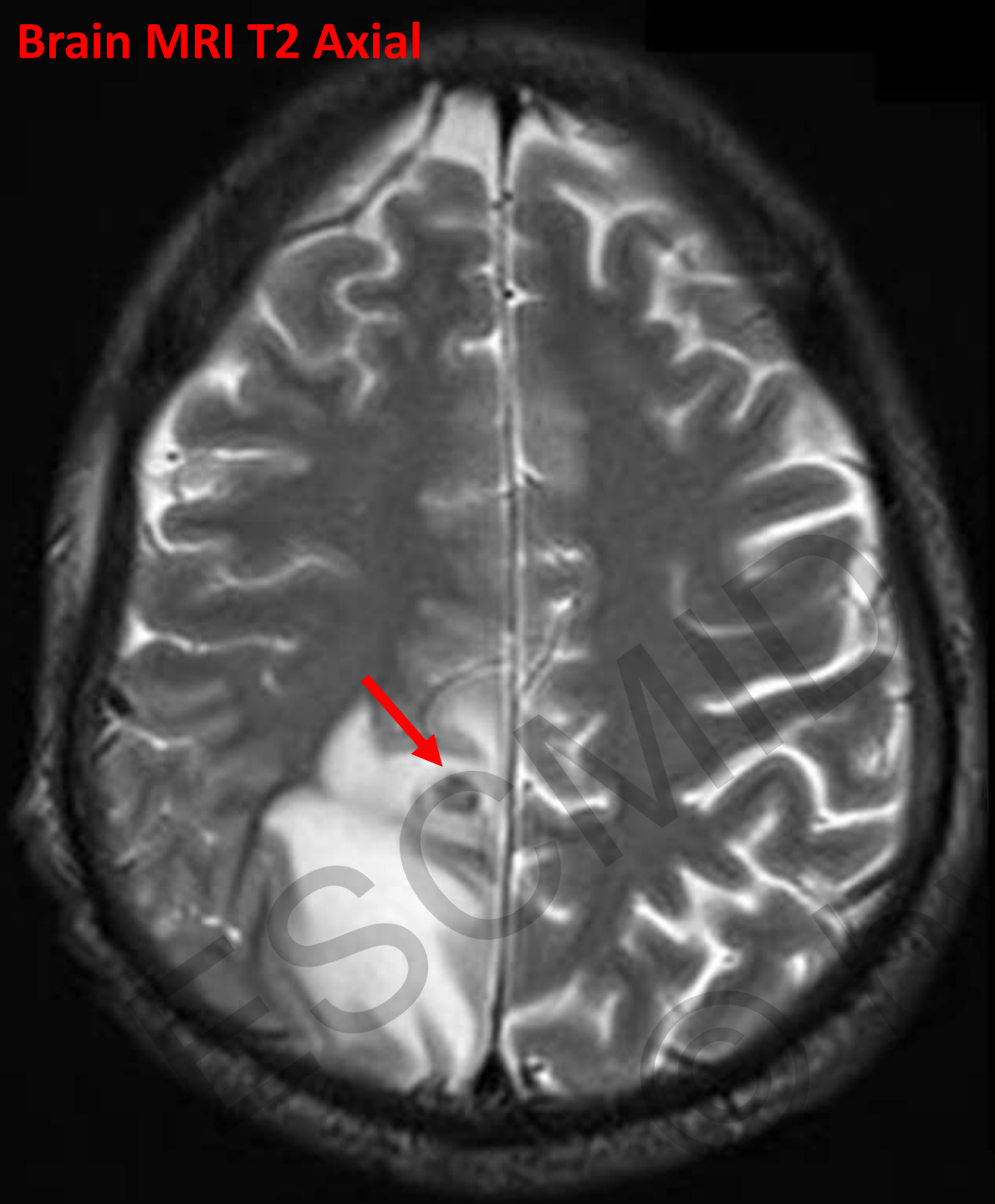
Total bilirubin 1.5 mg/dL

Direct bilirubin 1.2 mg/dL

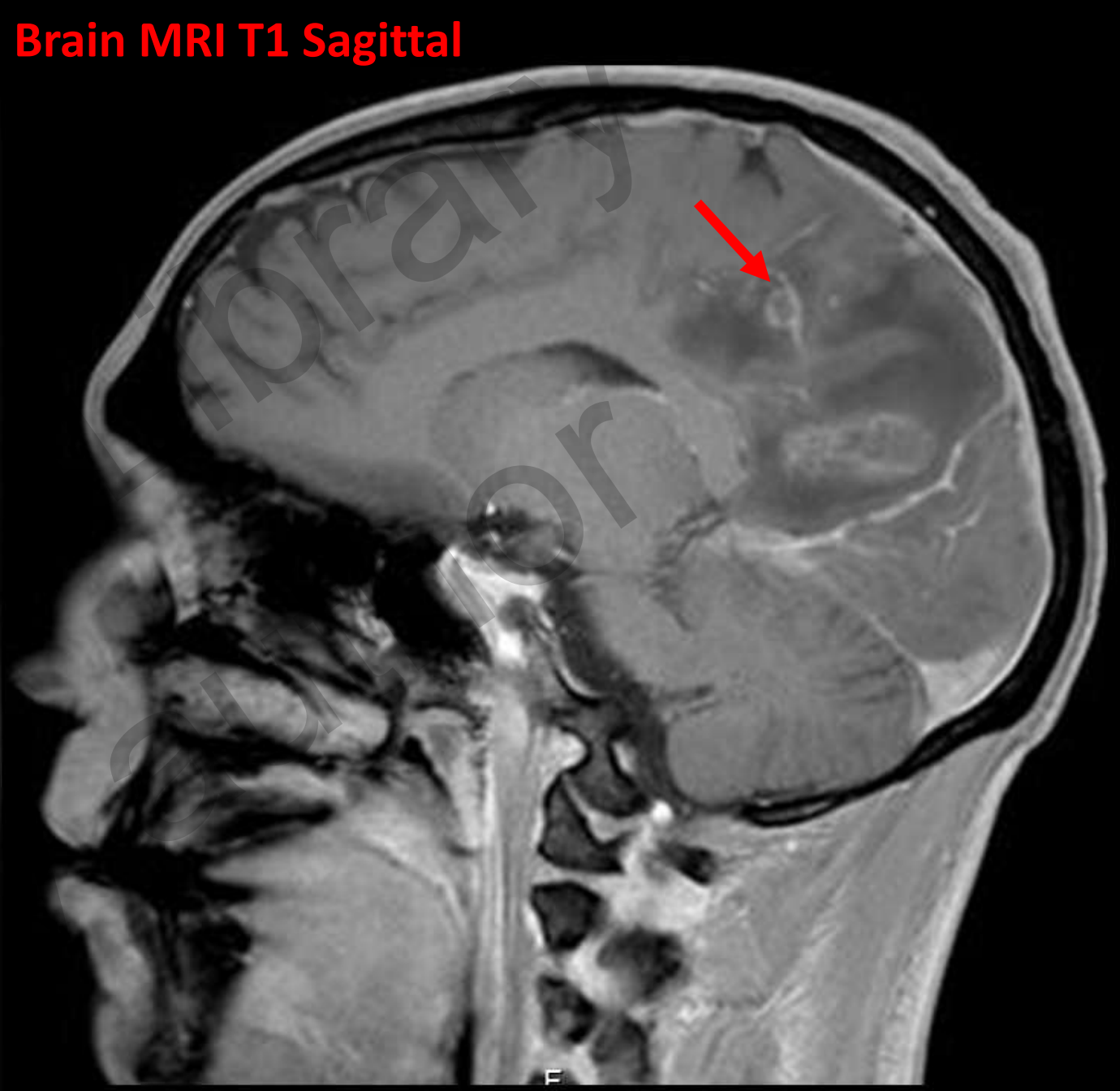
Alkaline phosphatase 348 mg/dL



Brain MRI T2 Axial



Brain MRI T1 Sagittal



Discussion

Differential diagnosis?

Additional testing?

Management?

Hospital Course

Antimicrobials:

- IV vancomycin 1g every 12 hours
- IV meropenem 2g every 8 hours
- IV metronidazole 500mg every 6 hours
- IV ganciclovir 300mg every 24 hours (5mg/kg)
- IV liposomal amphotericin B 290mg every 24 hours (5mg/kg)
- Oral pyrimethamine 150mg once and then 75mg every 24 hours
- Oral atovaquone 750mg every 6 hours

Hospital Course Continued

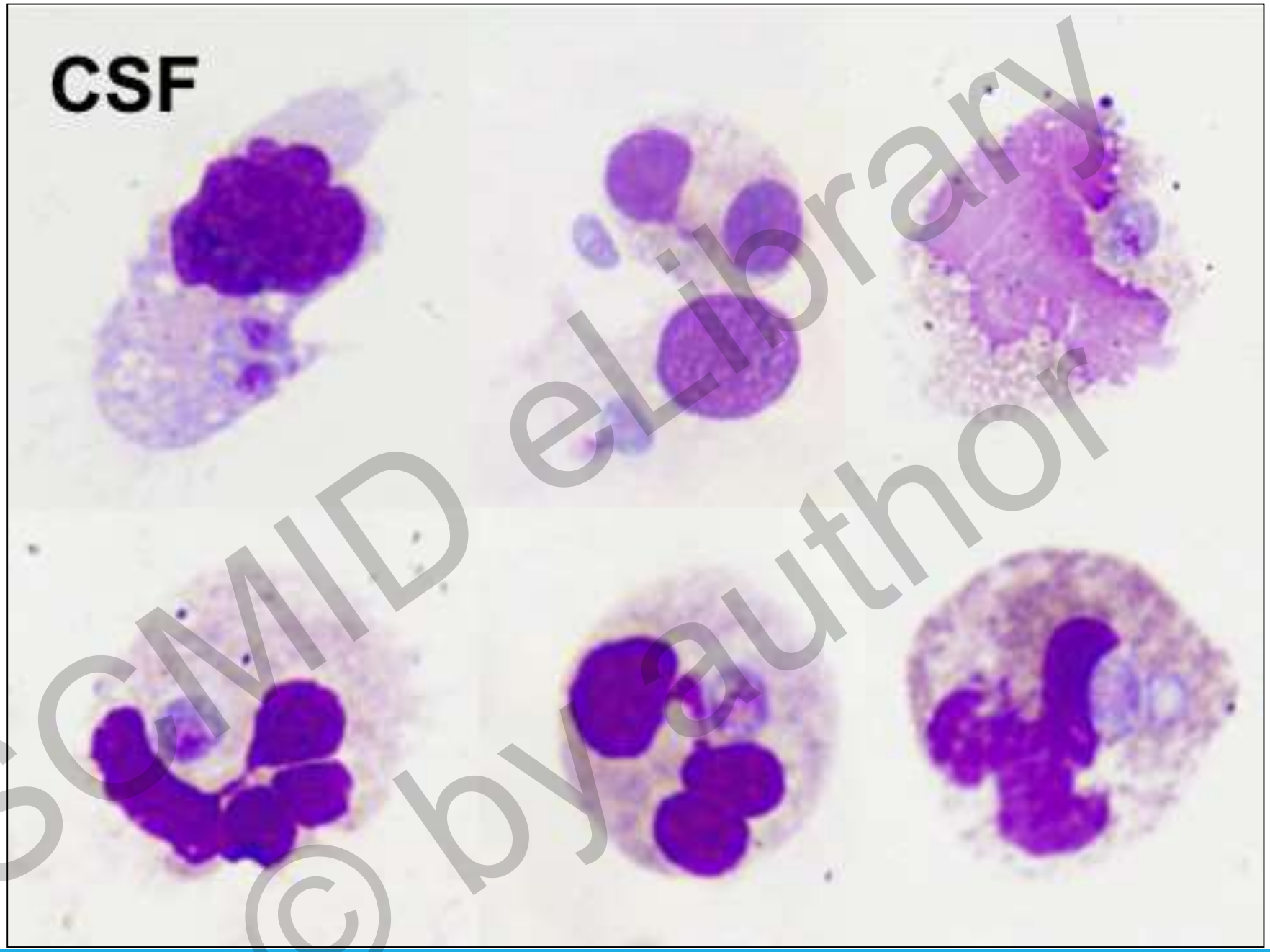
Developed worsening hypoxic respiratory failure needing intubation

Bronchoscopy performed

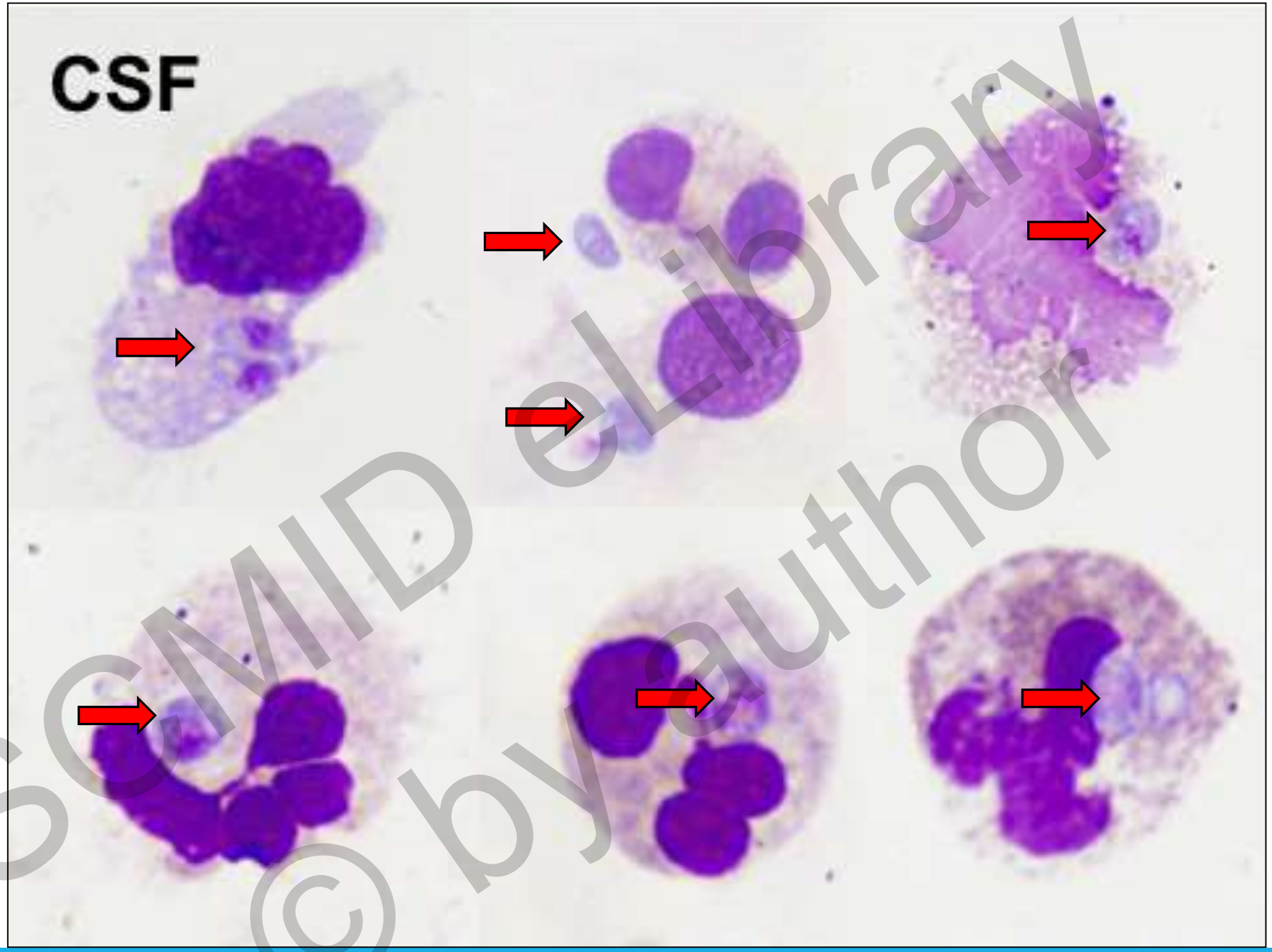
- Bronchial washing and bronchoalveolar lavage (BAL) had negative bacterial stain/culture, fungal stain/culture, acid fast smear, gomori methenamine silver stain

Lumbar Puncture: CSF Analysis

	Tube #1	Tube #4
Appearance	Red, cloudy	Clear
White Blood Cells	139 cells/uL	28 cells/uL
Red Blood Cells	8 000 cells/uL	51 cells/uL
% Neutrophils	95%	89%
% Lymphocytes	1%	1%
% Monocytes	4%	10%
Glucose	67 mg/dL	
Protein	90 mg/dL	



Trophozoites of *Toxoplasma gondii*



Patient Follow-Up

Developed hypotension needing pressor support and hypoxia worsened despite maximum ventilator support

Extracorporeal membranous oxygenation was considered but decision made by family not to escalate care

Patient died despite aforementioned interventions

Toxoplasma gondii PCR on both BAL and CSF later came back positive

Autopsy revealed disseminated toxoplasmosis involving lungs, brain, spinal cord, liver, kidneys, heart, gastrointestinal tract, bone marrow

Learning Points

Disseminated toxoplasmosis is an opportunistic infection in patients with cell mediated immunosuppression

- 1/3 seropositive patients with AIDS will develop toxoplasmosis if they do not receive prophylaxis

Toxoplasmosis is rare in patients with HSCT, occurring in only 1% of patients within 6 months of transplant

- Risk factors include seropositivity pre-transplant and GHVD with increased immunosuppression

This patient was seropositive for *Toxoplasma gondii* but only on inhaled pentamidine for prophylaxis targeting *Pneumocystis jiroveci* due to trimethoprim/sulfamethoxazole allergy

Patients undergoing HSCT should have prophylaxis with trimethoprim/sulfamethoxazole when possible to cover for *Toxoplasma gondii*

- Atovaquone or pyrimethamine/leucovorin are alternatives
- Surveillance PCR testing is an alternative strategy in seronegative patients

Thank You!