

Table S1. Details of 83 paediatric histoplasmosis cases included in this review.

Ref	Country	Age (yrs)	Sex	Disseminated/Single Organ Disease	Organs Effected	Underlying condition	Signs and Symptoms	Diagnostic Technique	Specimens Used for Diagnosis	Treatment	Outcome
17	US	3m	M	Disseminated	Bone marrow	-	Fever HSM	Histopathology	Bone marrow	AmB + Itra	Improved
								Ag Detection	Serum Urine		
18	India	11	M	Disseminated	Lymph-nodes	HIV	Fever Abdominal pain Vomiting	Histopathology	Lymph Node Bone marrow	AmB	Death
					Bone marrow			Culture	Lymph Node Bone marrow		
19	US	16	M	Disseminated	Lungs	HIV Tx-Kidney	Fever Cough Malaise Vomiting Weight Loss Respiratory distress	Microscopy	BAL	AmB + Itra	Improved
					Bone marrow			Ag Detection	Urine Serum		
	US	11	F	Disseminated	Lungs	Tx-Kidney	Fever Cough Headache Splenomegaly	Ag Detection	Urine	Itra + Vori	Recurrence (compliance issues)
	US	16	F	Disseminated	Pericard Lungs Bone marrow	Tx-Kidney	Fever Diarrhoea Vomiting Weight loss Respiratory Distress	Ag Detection	Pericardial fluid BAL Urine Serum	AmB + Itra	Lost to Follow Up
	US	11	F	Disseminated	Lungs Bone marrow	Tx-Kidney	Fever Fatigue Cough Abdominal pain Weight loss	Microscopy	BAL	AmB + Itra	Not specified
								Ag Detection	Urine		
								Ab Detection (CF)	Serum		
20	India	15	M	Disseminated	Lung Lymph nodes Bone marrow	Tx-Kidney	Fever Cough Malaise Abdominal Pain Chest pain Splenomegaly	Histopathology	Lymph Node Bone marrow	AmB+ Itra + Vori	Cure
21	Brazil	13	M	Disseminated	Lung Lymph-nodes	Not specified	Cough Lymphadenopathy	Ag Detection	Serum	Itra	Improved
22	India	13	M	Disseminated	Bone CNS Lymph-nodes	Not Specified	Fever Anorexia Lymphadenopathy HSM Weight loss	Histopathology	Bone (skull + tibia)	AmB + Itra	Cure
								Culture	Bone (skull + tibia)		Treatment ongoing

23	US	6m	F	Disseminated	Lung Bone Marrow	HLH	Fever Lethargy HSM Respiratory distress	Histopathology	Bone marrow	AmB	Cure Treatment ongoing
								Ag Detection	Serum Urine CSF		
								Ab Detection (ID)	Serum		
24	Nepal	14	M	Disseminated	Lung Skin	Rheumatic Heart Disease	Fever Cough HSM Skin lesions Weight loss	Histopathology	Lung Skin	AmB + Itra	Improved Treatment ongoing
25	US	10	M	Disseminated	Lung Skin Bone marrow	HIES (STAT-3 def)	Fever Abdominal pain Skin lesions	Microscopy	BAL	AmB + Posa	Improved
								Ag Detection	Serum Urine		Treatment ongoing
	US	13	F	Disseminated	GI	HIES (STAT-3 def)	Abdominal pain Weight loss	Histopathology	GI Tissue	AmB + Itra	Improved
								Culture	GI Tissue		Treatment ongoing
								Ag Detection	Urine		
26	India	7	F	Disseminated	Bone marrow Lymph nodes Skin Lungs	-	Fever Ostalgia Weight loss HSM Respiratory distress	Histopathology	Lymph Node Bone marrow	AmB	Death
								Culture	Bone marrow Skin Blood		
								Gene Sequencing	Skin		
27	US	13	M	Disseminated	Lymph	Crohn's Disease	Lymphadenopathy	Serology (Ab/Ag not specified)	Not Specified	Itra	Cure
28	Colombia	7	M	Laryngeal	Larynx	Tx-Kidney	Diarrhoea Odynophagia Tonsillitis Anorexia Headache Fever Stridor Lymphadenopathy	Ab Detection (ID)	Serum	AmB + Itra	Cure
								Histopathology	Epiglottis biopsy		
29	India	17	M	Disseminated	Bone Soft Tissue	Previous MTB Common Variable Immunodeficiency	Arthralgia Joint swelling Abdominal pain Ascites Fever Weight loss HSM	Microscopy	Joint Aspirate	AmB + Itra	Cure
30	US	6	M	Disseminated	CNS	EBV	Fever Nausea Abdominal pain Headache Phonophobia	Ag Detection	Urine CSF	AmB + Itra	Not Specified
								Ab Detection (CF)	Serum		

							Photophobia				
31	US	8	M	Pulmonary	Lungs	Not Specified	Fever Cough Abdominal pain	Ag Detection	Serum	Itra	Cure
								Ab Detection (CF)	Serum		
	US	5	F	Pulmonary	Lungs	Not Specified	Fever Cough Abdominal pain	Ag Detection	Serum	Itra	Cure
								Ab Detection (CF)	Serum		
32	Nigeria	13	F	Disseminated	CNS Lungs Lymph nodes	Not Specified	Lymphadenopathy Oliguria Seizures Respiratory distress Ascites	Histopathology	Lymph Node	No treatment	Death
33	US	17	M	Disseminated	Lymph-nodes	EBV	Fatigue Night-sweats Headaches Weight loss Lymphadenopathy	Histopathology	Lymph node	Itra	Not Specified
34	US	6	M	CNS	CNS	-	Headache Reduced mobility Facial droop Slurred speech	Culture	CSF	AmB + Itra	Cure
								Ab Detection (CF)	CSF Serum		
								Ag Detection	CSF Serum		
35	India	5	F	Disseminated	Bone marrow	Not Specified	Abdominal distention Petechiae	Histopathology	Bone marrow	AmB	Improved
								Serology (not specified)	Not Specified		
36	US	12	F	Disseminated	Lung Lymph-nodes	Not Specified	Neck and shoulder pain Chest pain SOB	Histopathology	Lymph node Lung Tissue	AmB + Itra	Recurrence
								Ab Detection (CF+ID)	Serum		
37	US	4m	F	Disseminated	Bone marrow	-	Fever HSM	Ag Detection	Urine	AmB + Itra	Not Specified
38	US	17	M	Disseminated	Liver Bone marrow Lymph-nodes	STAT1 mutation	Lymphadenopathy Fever Weight loss	Not specified	Not specified	Not specified	Recurrence
	US	7	F	Disseminated	Lymph-nodes Lung	STAT1 mutation	Fever HSM Lymphadenopathy SOB	Not specified	Not specified	Itra	Recurrence
39	Brazil	13	F	Pulmonary	Lung	Lymphoma	Not specified	Histopathology	Lung	Itra	Improved
		13	M	Pulmonary	Lung	-	Not specified	Histopathology	Lung	Itra	Improved
40	China	11	M	Osseous	Bone	-	Bone/joint swelling Skin nodule	Histopathology	Bone	Debridement Vori	Cure
41	US	17m	M	Disseminated	Lung Bone marrow	T-cell deficiency	Fever	Histopathology	Bone marrow	AmB	Improved Persistently elevated urine

								Microscopy	BAL		Ag
								Ag Detection	Urine		
42	Brazil	14	F	Disseminated	Lung Lymph-nodes	Juvenile SLE	Cough Abdominal Pain Fever Diarrhoea Vomiting Impetigo HSM	Histopathology	Lymph node	AmB	Death
								Culture	GI Tissue Lymph node		
								Ab Detection (ID)	Serum		
43	Guinea-Bissau	12	M	Disseminated	Lung Lymph-nodes	-	Lymphadenopathy with cutaneous fistulas	Culture	Lymph node	AmB + Itra + Posa	Cure
44	India	4	F	Disseminated	GI Lymph-nodes	HIES	Fever Abdominal pain Diarrhoea Weight loss Lymphadenopathy HSM	Histopathology	GI Tissue	Antibiotics	Improved
45	US	6m	M	Disseminated	Bone marrow	-	Fever HSM	Histopathology	Bone Marrow	AmB + Itra	Cure
								Ag Detection	Urine Serum		
								Ab Detection (CF)	Serum		
46	US	13	F	CNS	CNS	-	Confusion Headaches Neck Pain Back Pain Abdominal pain Hearing loss Facial Numbness Slurred Speech Fever Altered mental status	Ag Detection	Blood CSF	AmB + Itra	Improved
								Ab Detection (ID)	Serum		Treatment ongoing
47	US	8	M	Pulmonary	Lung	Not Specified	Wheeze	Histopathology	Lung tissue	Itra	Not Specified
	US	4	M	Pulmonary	Lung	Wilms tumour Chemotherapy	None (incidental finding)	Histopathology	Lung tissue	Antifungal (not specified + resection	Not Specified
48	US	16	M	Disseminated	Lung Lymph nodes	Idiopathic chronic anterior uveitis	Fever Night sweats Cough Headache Dysphagia Lymphadenopathy Chest Pain	Ab Detection (CF)	Serum	AmB + Itra	Cure
								Ag Detection	Urine		
49	Us	12	M	Pulmonary	Lung	-	Cough Fever Chest pain	Histopathology	Lung Tissue	AmB + Itra	Cure
								Ab Detection (ID)	Serum		
								Ag Detection	Pleural Fluid		

50	Brazil	13	M	Pulmonary	Lung	Not Specified	Fever Headache Myalgia Malaise	Serology (not specified)	Not specified	Not specified	Improved Persistent pulmonary nodule on CT
51	India	3	-	Disseminated	Skin	-	Skin lesions HSM Mouth ulceration	Histopathology	Skin	AmB + Itra	Recurrence
52	US	16	F	Disseminated	Lung Lymph-nodes	Crohn's Disease	Abdominal Pain Fatigue Anorexia Nausea Headache Myalgia Dysuria SOB	Ag Detection	Serum Urine	Itra	Cure
	US	14	F	Pulmonary	Lung	Crohn's Disease	Fever Headache Myalgia Arthralgia Cough Anorexia Weight loss Dizziness	Serology (not specified)	Not specified	AmB + Itra	Cure
	US	13	M	Pulmonary	Lung	Crohn's Disease	Fever Malaise	Serology (not specified)	Serum Urine	AmB + Itra	Lost to Follow Up
	US	15	F	Disseminated	Lung Lymph-nodes	Crohn's Disease	Fever Abdominal pain Cough Fatigue	Ab Detection (not specified)	Serum	AmB + Itra	Improved Persistent urine Ag positive
								Ag Detection	Serum Urine		
53	India	16	F	Disseminated	Skin Bone	AIDS	Fever Diarrhoea Skin lesions Lymphadenopathy HSM Weight loss	Histopathology	Bone marrow	AmB	Death
54	US	8	M	Disseminated	Lung Lymph-nodes	Crohn's Disease	Fever Night sweats Cough Anorexia Abdominal pain Diarrhoea HSM	Culture	Lymph Node	Itra	Cure
								Ag Detection	Urine		
								Ab Detection (CF)	Serum		
55	US (mother from Guatemala)	4wk	F	Disseminated	Skin	HIV	Fever Skin rash Respiratory distress Seizures	Culture	CSF	AmB + Itra	Cure
					Lung			Ag Detection	Urine		
					CNS			Microscopy	CSF		

	– vertical transmissi on)						Hepatomegaly				
56	US	15	F	Disseminated	Lung Lymph-nodes	GIST Chemotherapy	Fever Cough	Ab Detection (CF+ID)	Serum	No treatment	Cure
57	US	8	F	Unclear	Unclear	Juvenile RA	Not specified	Ab Detection (not specified)	Serum	AmB + Itra	Cure
								Ag Detection	Not specified		
		10	F	Unclear	Unclear	Juvenile RA	Fever	Ab Detection (not specified)	Serum	AmB + Itra	Cure
								Ag Detection	Not specified		
		17	F	Unclear	Unclear	Juvenile RA	Fever	Ab Detection (not specified)	Serum	AmB + Itra	Cure
								Ag Detection	Not specified		
		13	F	Unclear	Unclear	Juvenile RA Psoriasis	Fever	Ab Detection (not specified)	Serum	AmB + Itra	Cure
								Ag Detection	Not specified		
		16	M	Unclear	Unclear	Uveitis	Not specified	Ab Detection (not specified)	Serum	AmB + Itra	Cure
								Ag Detection	Not Specified		
58	India	6	F	Disseminated	Lung Bone marrow	Not Specified	Fever Cough Abdominal pain Oedema HSM	Histopathology	Bone marrow	Not specified	Not specified
		1	M	Disseminated	Bone marrow	HIV	Fever Night sweats Abdominal distention Oedema Weight loss Anorexia Malaise Myalgia	Histopathology	Bone marrow	Not specified	Not specified
59	US	14	F	Disseminated	Lung GI Lymph-nodes	HIES	Abdominal pain Fever Weight loss Fatigue Cough	Histopathology	GI Tissue	Itra	Cure
								Ag Detection	Urine		
								Ab Detection (CF +ID)	Serum		
60	US	15	F	Disseminated	Not specified	Sarcoidosis Tx-Kidney	Fever Multi-organ failure	Autopsy	Not specified	No treatment	Death
61	US	5m	M	Pulmonary	Lung	-	SOB	Ab Detection (CF + ID)	Serum	Itra	Cure
								Ag Detection	Urine		
62	Brazil	13	M	Disseminated	Skin	AML	Skin nodules	Histopathology	Skin	AmB + Itra + Fluc	Cure
63	US	15	F	Disseminated	Lung	Tx-Kidney	Not specified	Ag Detection	Serum	Itra + Vori	Improved

									Urine		
64	Africa	10	F	Disseminated	Skin Lymph-nodes	-	Skin lesions Lymphadenopathy	Histopathology	Lymph node	AmB	Improved Residual Skin Lesions
								Ab Detection (ID)	Serum		
65	Pakistan	5	M	Disseminated	Lymph-nodes	Not Specified	Fever Weight loss	Histopathology	Lymph node	Not specified	Not specified
66	US	8m	F	Disseminated	Lungs Bone marrow	-	Fever Cough HSM	Histopathology	Bone marrow	AmB + Itra	Cure
								Ag Detection	Urine		
								Ab Detection (ID)	Serum		
								Culture	Blood		
67	France (Recent Travel to Africa)	2	F	Disseminated	Skin Bone	HIV	Frontal Bone Swelling Fever Weakness	Histopathology	Skin Bone	AmB + Itra + Fluc	Improved
								Culture	Skin		
68	US	7	F	Disseminated	Lung Lymph-nodes	Juvenile RA	Fever Sore throat Weight loss Splenomegaly	Histopathology	Lymph Node	Itra	Improved Persistent symptoms
								Ag Detection	Urine		
69	US	11	F	Disseminated	Lung Skin Lymph-nodes	HIV	Weight Loss Cough Skin Lesions Lymphadenopathy HSM	Histopathology	Skin	AmB	Death
70	Venezuela	3m	M	Disseminated	Lung Lymph-nodes	Not Specified	Fever SOB Jaundice	Histopathology	Lymph node	No treatment	Death
								Culture	Lymph Node		
71	US	3	M	Disseminated	Lung Bone marrow Lymph-nodes	Interferon-gamma receptor-1 Deficiency	Fever HSM Lymphadenopathy	Ab Detection (ID + CF)	Serum	AmB + Keto	Recurrence
								Culture	BAL Bone marrow		
72	Africa	17	M	Disseminated	Skin Bone Soft Tissue	Not Specified	Skin ulceration Pharyngeal fistula	Histopathology	Bone Soft tissue	AmB	Cure
73	US	8	M	Disseminated	Lymph-nodes	-	Flu-like illness Vomiting Weight loss	Ab Detection (CF + ID)	Serum	No treatment	Improved Oesophageal diverticulum due to extensive lymphadenopathy
	US	10	M	Disseminated	Lymph-nodes	Not Specified	Cough Fatigue Weight loss Chest Pain Dysphagia Lymphadenopathy	Ab Detection (CF)	Serum	Itra	Cure
	US	14	M	Disseminated	Lymph-nodes Lung	-	Dysphagia Night Sweats Cough	Ab Detection (CF+ID)	Serum	Itra	Cure
74	US	17	F	Disseminated	Lung Bone	Juvenile RA	Cough Fever	Ag Detection	Urine	AmB + Itra	Cure

					marrow		Nausea Vomiting SOB	Ab Detection (ID + CF)	Serum		
75	US	5m	F	Disseminated	Bone marrow	-	Fever Diarrhoea Rhinorrhoea Abdominal distention HSM Irritability	Histopathology	Bone Marrow	Not specified	Not specified
76	US	11	F	Disseminated	Lymph- nodes	-	Neck pain Lymphadenopathy	Histopathology Ab Detection (CF+ID)	Lymph Node Serum	Itra	Cure
77	Paraguay	11m	F	Disseminated	Bone Lungs	-	Fever Cough Respiratory Distress Anorexia Weight loss Arthralgia Joint swelling Periorbital swelling	Histopathology	Joint tissue		
78	Africa	3	M	Disseminated	Skin Lymph- nodes Bone marrow	HIV	Skin rash Lymphadenopathy HSM	Histopathology	Not specified	AmB + Itra	Lost to Follow Up
79	Panama	14	F	Disseminated	Bone marrow CNS Liver Spleen Pancreas	ALL HIV	“Sepsis-like-picture”	Culture	Blood Bone marrow	AmB + Itra	Improved
80	US	6	F	Disseminated	Bone Ocular	ALL Chemothera py	Fever Malaise HSM Choroidal lesions on fundus	Histopathology	Bone Marrow	AmB	Cure
								Ag Detection	Urine		
								Culture	Bone Marrow Blood		
81	US	3	F	Pulmonary	Lungs	-	Fever SOB Malaise Weight loss Abdominal pain	Ab Detection (ID +CF)	Serum	No treatment	Cure

F=female, M=male, SOB = shortness of breath, Itra = itraconazole, Keto = ketoconazole, AmB = Amphotericin B, Vori = voriconazole, ID = immunodiffusion, CF = complement fixation, BAL = Broncho-alveolar lavage, d = day, m = month(s), HIV = Human Immunodeficiency Virus, Ab = Histoplasma antibody, Ag = Histoplasma antigen, ALL = Acute Lymphoblastic Leukaemia, RA = Rheumatoid Arthritis, AML = Acute Myeloid Leukaemia, GIST = Gastrointestinal stromal tumour, Tx = transplant, HIES = hyper-immunoglobulin E syndrome, SLE = systemic lupus erythematosus, EBV = Epstein Barr Virus infection, MTB = Mycobacterium tuberculosis infection, HLH = hemophagocytic lymphohistiocytosis, HSM = hepatosplenomegaly.