Supplemental Digital Content, containing 3 tables. The Supplemental Digital Content was not copyedited by *Archives of Pathology & Laboratory Medicine*.

Supplemental Table 1. Histopathological patterns of disease in confirmed infectious diseases identified in non-neoplastic space-occupying mass lesions (*n*=43).

Histological phenotype of confirmed infectious process	Resection cases with phenotype, *n* (%)	Infectious agents identified (*n*)
Necrotizing granuloma	19 (44)	*Blastomyces dermatitidis/gilchristii* (2)
		Histoplasma spp. (11)
		Mycobacteroides chelonae (1)
		Mycobacterium kansasii (1)
		Mycobacterium tuberculosis (1)
		Polymicrobial infection, ≥3 pathogens identified (1)
		Pseudallescheria boydii (1)
		Unidentified yeast (1)
Angioinvasive mycosis	5 (12)	*Aspergillus fumigatus* (1)
		Aspergillus versicolor (1)
		Hyaline septated mold (3)
Lung abscess	5 (12)	*Histoplasma* spp. (2)
		Polymicrobial infection, ≥3 pathogens identified (2)
		Streptococcus pyogenes (1)
Hyalinized Granuloma	3 (7)	*Histoplasma* spp. *(3)*
Acute and organizing pneumonia	2 (5)	Adenovirus / Viridans *Streptococcus* sp. (1)
		Staphylococcus aureus / Unidentified yeast (1)
Fungal ball	2 (5)	*Aspergillus flavus / Pseudomonas aeruginosa* (1)
		Hyaline septated mold (1)
Fungal necrotizing mycosis	2 (5)	*Aspergillus fumigatus* (1)
		Aspergillus sp. (1)
Pneumatocele	2 (5)	Methicillin Resistant Staphylococcus aureus (MRSA; 1)
		Polymicrobial infection, ≥3 pathogens identified (1)
Organizing pneumonia	2 (5)	*Cryptococcus gattii/neoformans* (1)
		Staphylococcus aureus (bacteremic patient; 1)
Hydatid cyst	1 (2)	*Echinococcus granulosus* (1)

Supplemental Table 2. Microbiologically and histopathologically confirmed infectious diseases pathogens in thoracic resection specimens (*n*=43).

Pathogens identified	**N (%)**
Monomicrobial infections	36 (84)
Histoplasma spp.	16 (37)
Hyaline septated mold	4 (9)
Blastomyces dermatitidis/gilchristii	2 (5)
Staphylococcus aureus	2 (5)
Aspergillus fumigatus	2 (5)
Aspergillus sp.	1 (2)
Aspergillus versicolor	1 (2)
Cryptococcus gattii/neoformans	1 (2)
Echinococcus granulosus	1 (2)
Mycobacteroides chelonae	1 (2)
Mycobacterium kansasii	1 (2)
Mycobacterium tuberculosis	1 (2)
Pseudallescheria boydii	1 (2)
Streptococcus pyogenes	1 (2)
Unidentified yeast	1 (2)
Polymicrobial infections	7 (16)
Adenovirus / Viridans *Streptococcus* sp.	1 (2)
Aspergillus flavus / Pseudomonas aeruginosa	1 (2)
Staphylococcus aureus / Unidentified yeast	1 (2)
≥3 bacterial pathogens identified [a]	4 (9)

[a] In four cases ≥3 bacterial pathogens were identified. In two of those, species identification was not further pursued. The other two cases included the following pathogens:
- Polymicrobial anaerobic abscess containing: *Peptostreptococcus anaerobius*, *Prevotella timonensis*, *Fusobacterium gonidiaformans*, *Actinomyces turicensis*, *Porphyromonas asaccharolytica*, *Gemella morbillorum*, small anaerobic gram-positive coccus, anaerobic gram-positive bacillus (probably not *Clostridium* sp.).
- Polymicrobial abscess containing: *Citrobacter freundii* complex, *Clostridium* sp., unidentified yeast, gram-negative bacilli, gram-positive bacilli, and gram-positive cocci.

Supplemental Table 3: Summary of molecular findings observed from CGP testing in primary pediatric thoracic neoplasms occurring in patients aged ≤21 years

Case	Pathologic Diagnosis	Age (years)	Sex	SNVs/ delins (pathogenicity[a])	Copy Number Alterations	Fusion and Splice Variants	MSI Status	TMB Status	Gene-level Amplification
1	Typical carcinoid	20	F	*ARID1A* c.6747dupA p.E2250fs*28 (likely pathogenic)	None observed	None observed	3.92 (MSS)	0.8 (TMB-L)	None observed
2	Typical carcinoid	19	F	No pathogenic or likely pathogenic alterations observed	Loss of chr 13, 21 and 22	None observed	3.95 (MSS)	1.6 (TMB-L)	None observed
3	Typical carcinoid	21	M	No pathogenic or likely pathogenic alterations observed	Loss of chr 22 and the majority of 15q26.1	None observed	3.92 (MSS)	0.8 (TMB-L)	None observed
4	Typical carcinoid	20	F	No pathogenic or likely pathogenic alterations observed	None observed	None observed	0 (MSS)	2.4 (TMB-L)	None observed
5	Atypical carcinoid	20	F	No pathogenic or likely pathogenic alterations observed	Loss of chr 13; gain of chr 7 and 8	None observed	3.06 (MSS)	0 (TMB-L)	None observed
6	Atypical carcinoid	20	M	*DNMT1* c.445+1G>A (likely pathogenic)	None observed	NA. Testing failure	0.96 (MSS)	0 (TMB-L)	None observed
7	Pleuropulmonary blastoma	<1	M	*DICER1* c.5126A>G p.D1709G (likely pathogenic)	None observed	None observed	0 (MSS)	2.4 (TMB-L)	None observed
8	Inflammatory myofibroblastic tumor	14	M	No pathogenic or likely pathogenic alterations observed	None observed	NA. Testing failure	2.44 (MSS)	0 (TMB-L)	None observed
9	Paraganglioma	19	F	*SDHD* c.167delA p.H56fs*30 (pathogenic) *VHL* c.598C>T p.R200W (pathogenic)	None observed	None observed	0 (MSS)	1.6 (TMB-L)	None observed
10	Schwannoma	21	F	*ATM* c.7865C>G p.A2622G (variant of unknown significance)	Loss of chr 22	None observed	0.95 (MSS)	1.6 (TMB-L)	None observed
11	Synovial sarcoma	21	M	No pathogenic or likely pathogenic alterations observed	Loss of the majority of chr22 and 11q12.2-q24.33	*SS18-SSX1*†	1.69 (MSS)	0 (TMB-L)	None observed

[a] Pathogenicity as determined by Qiagen Clinical Insights Interpret-One (QCI-II; Hilden, Germany). The UCSC Genome Browser on Human GRCh37/hg19 was used to visual chr bands when listed.

Abbreviations: CGP= comprehensive genomic profiling; SNV=single nucleotide variant, delins= deletion/insertions, Chr=chromosome; MSI=microsatellite instability; MSS=microsatellite stable; TMB=tumor mutational burden; TMB-L= tumor mutational burden-low; NA=not applicable. MSI status of MSS is assigned to samples with <20% unstable sites and MSI-H with ≥20% unstable sites. TMB values <10 mut/Mb are categorized as TMB-Low and ≥10 mut/MB as TMB-High.

†The SS18-SSX1 fusion was detected clinically by a separate reverse transcriptase-polymerase chain reaction (RT-PCR) assay.