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Acute lung pathology in the immunocompromised child

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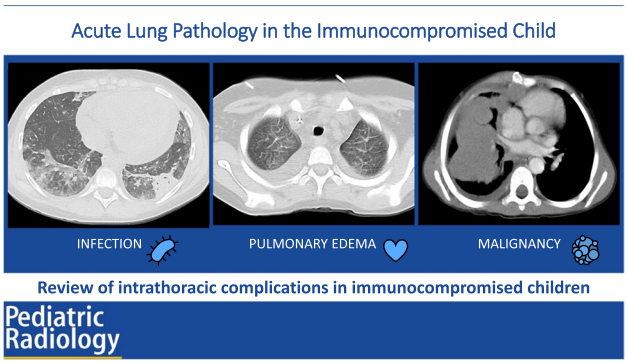
Abstract

Children with compromised immune systems, whether due to primary or secondary immunodeficiencies, are susceptible to a broad spectrum of acute intrathoracic pathologies. These include infections, pulmonary edema, and malignancies. Pulmonary issues are common and perilous in this population, necessitating prompt and precise diagnosis for effective management. This review aims to provide an overview of such conditions, focusing on the imaging appearances of the most prevalent acute lung conditions affecting immunocompromised children. It emphasizes the critical importance of an integrated clinical and radiological approach when diagnosing these acute pulmonary disease states.

Graphical Abstract



Keywords Child · Immunosuppression · Infection · Lung · Neoplasm · Computerized tomography

Introduction

Acute pathology involving intrathoracic structures represents a common and potentially life-threatening class of disorders in children lacking an intact immune system. The chest is the site of many of the most severe complications that occur in immunodeficient children. It is intuitive that the respiratory tract should serve as an organ of acute susceptibility for complications. The respiratory system, including the sinuses, airways, and lungs, acts as the primary line of defense against the invasion of pathogens. Infection, therefore, is the leading cause of pulmonary disease in immunocompromised children. For children with weakened immune systems, pulmonary infections are not only the most common complication but also a leading cause of morbidity and even mortality. These children are particularly susceptible to otherwise unusual infections, including those caused by fungal, protozoan, viral, and mycobacterial pathogens. Radiographic manifestations of these infections can vary and may be atypical, depending on the specific pathogen involved and the variable integrity of the child's immune status. Rapid

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and accurate diagnosis of pulmonary infections is of great importance to initiate prompt treatment. The importance of early radiologic diagnosis in these patients cannot be overstated. In addition to acute infection, immunodeficiency constitutes a relatively common cause of recurrent/chronic pneumonia. Studies on the underlying causes of recurrent pneumonia in the otherwise normal child have shown that primary immunodeficiencies constitute the underlying etiology in 14–20% of cases [1].

The complications of immune deficiency are not limited to infections. Children with immunocompromised systems are also more susceptible to malignancies, iatrogenic toxic interventions, and idiopathic alterations in pathophysiology. Although these entities can result in variable symptomatology, each of these alone can result in significant morbidity and even mortality when severe. The severity of morbidity depends on several complex and sometimes intertwined issues. For example, the lung and mediastinum can become sites of malignancy, a not uncommon complication in immunocompromised children. Pulmonary edema from heart failure can occur as a complication of chemotherapy and radiation treatments. Furthermore, bone marrow transplantation (BMT) carries with it a range of thoracic complications. It is estimated that 40–60% of children who undergo BMT will manifest some form of clinically significant pulmonary complication, responsible for 10–40% of post-transplant mortality [2]. In children who have undergone BMT, complications are even categorized into different phases of the transplant process that may have varying rates of immune reconstitution. Consequently, complications vary based on the type of immune compromise and the type of pulmonary complication.

This review provides an overview of the most prevalent acute lung conditions affecting immunocompromised children—namely infections, pulmonary edema, and neoplastic processes—and their corresponding imaging appearances.

Infection

Primary immunodeficiencies

Children with primary, congenital immune deficiencies may manifest similar infectious susceptibilities as those whose immune deficiency is iatrogenically induced. However, their clinical presentations are frequently quite different. Since primary immunodeficiencies can be selective in their involvement of the complex immune system, they sometimes manifest in a more easily identifiable setting.

Innate locoregional factors form the first barrier to infection. The mucociliary apparatus acts as an initial, broad-spectrum barrier to pulmonary infection. As such, children with cystic fibrosis or ciliary deficiencies could be considered as having a form of selective immunodeficiency. The lack of an efficient mucociliary clearance is the basis for the development of pneumonia, and recurrent pneumonias can result in subsequent bronchiectasis. These infections are usually suppurative in nature, caused by specific bacteria that are normally removed by mucociliary clearance. *Staphylococcus* and *Pseudomonas* are common pathogens that tend to persist in these children and can remain both commensal and pathogenic. In these children, computerized tomography (CT) can be useful to demonstrate and qualify the presence and extent of bronchiectasis. As well, the presence of a tree-in-bud pattern can indicate superimposed atypical mycobacterial infection [3] (Fig. 1). Children with ciliopathies such as primary ciliary dyskinesia may demonstrate similar, if not more focal, findings (Fig. 2).

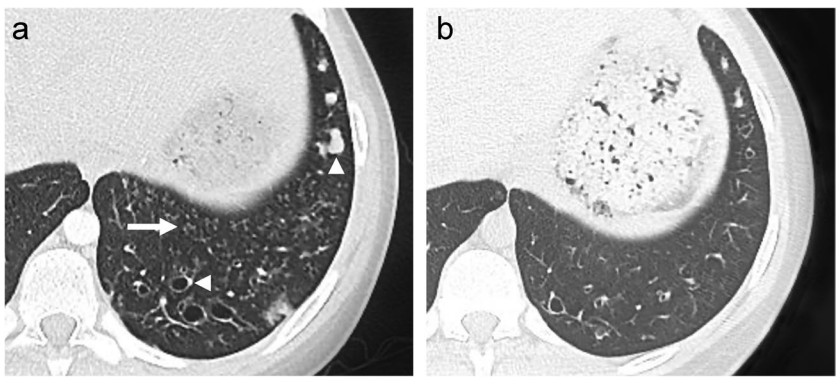

Fig. 1 Axial computed tomography (CT) unenhanced chest images (window width 2000, window level 500) in a 15-year-old boy with cystic fibrosis and *Mycobacterium abscessus* infection. **a** Pre-treatment image demonstrates tree-in bud changes in the left lower lobe (*arrow*), along with tubular bronchiectasis in the posterior segment of the left lower lobe and mucus-filled bronchiectasis in the lower lingula (*arrowheads*). **b** The tree-in-bud opacities resolved after treatment on follow-up CT

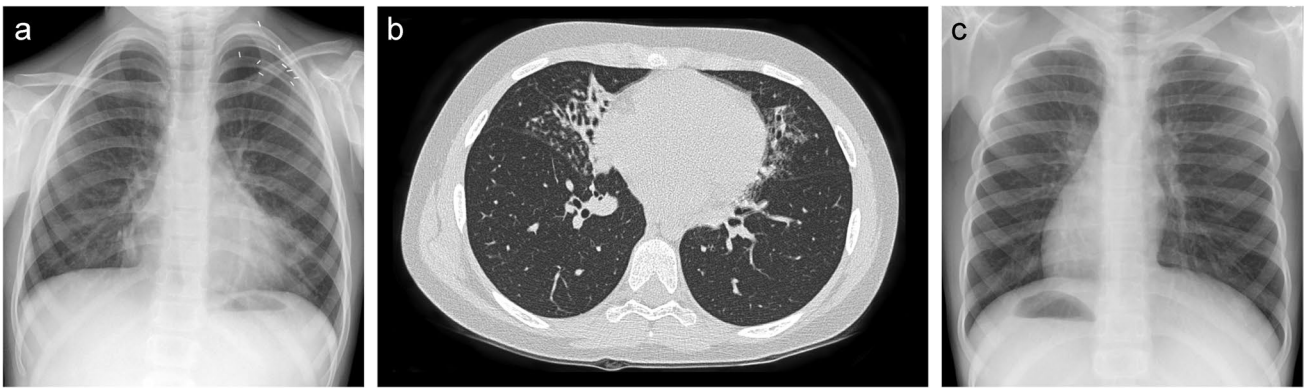

Fig. 2 A 4-year-old girl with primary ciliary dyskinesia and bronchiectasis. **a**, **b** Frontal anteroposterior chest radiograph and axial chest computed tomography show bronchial wall thickening and bronchiectasis affecting the middle lobe and lower lingula. **c** Frontal chest radiograph in the older sister at 6 years of age with situs inversus associated with Kartagener syndrome

Primary immunodeficiencies are generally categorized according to the specific type of immune defect, with certain types warranting particular attention. Their clinical manifestations often reflect the specific immune defects. For instance, complications such as bronchiectasis and lymphoproliferative change can arise as a complication of congenital deficiencies in immunoglobulin formation, while radiographically more diffuse viral infections are more commonly associated with T cell deficiencies. Selective immunoglobulin deficiencies typically lead to suppurative bacterial infections, and phagocytic or complement deficiencies predispose to infections by encapsulated bacteria [4], typically manifesting as classic air space changes at CXR or CT.

Severe combined immunodeficiency

Among primary immunodeficiencies, severe combined immunodeficiency (SCID) is considered the most severe form. SCID is a spectrum of X-linked and autosomal recessive disorders resulting in major deficiencies in both T and B cell function. Distinct subtypes of SCID occur through various deficiencies in T-cell receptors (e.g., autosomal recessive), cytokine production (e.g., X-linked SCID), and/or T-cell enzyme production (e.g., adenosine deaminase (ADA) and purine nucleoside phosphorylase). The incidence rate is estimated as high as 1:50,000 live births [5, 6]. While newborn screening has more recently been accepted in a number of countries, there is no consensus on best practices for screening and follow-up [7]. Most children present in the first year of life with varying severities of failure to thrive and pneumonia, frequently in combination with other infections such as thrush. The most common pulmonary infecting organisms are *Pneumocystis jirovecii* (PJP) and cytomegalovirus (CMV), sometimes present in combination (Fig. 3) [8]. As such, the involved infant is acutely ill and unresponsive to antibiotics. Radiographic patterns, therefore, tend to be diffuse, widespread, and severe.

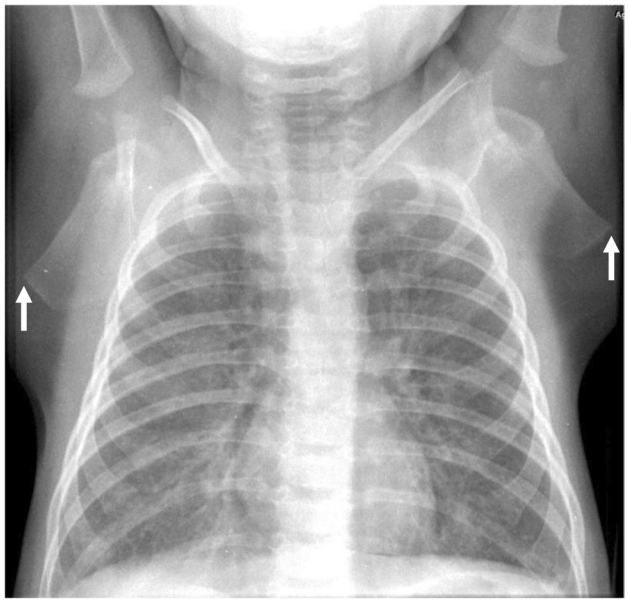

Fig. 3 Frontal anteroposterior chest radiograph in a 3-year-old boy with severe combined immunodeficiency syndrome (SCID) due to adenosine deaminase (ADA) deficiency, with mixed *Pneumocystis jirovecii* and *Cytomegalovirus* pneumonitis, demonstrates diffuse bilateral ground-glass opacities and bilateral squaring of the inferior scapular edges (*arrows*), a characteristic finding in the dysplasia associated with ADA-deficiency SCID

Immunoglobulin deficiencies

Primary immunoglobulin deficiencies are the most common type of primary, congenital immunodeficiencies, accounting for about 70% of cases [9, 10]. These deficiencies of B-cell immunity include common variable immunodeficiency (CVID), selective IgA or IgM deficiency, hyper-immunoglobulin M immunodeficiency (X-linked hyper-IgM syndrome), and X-linked agammaglobulinemia (also

known as Bruton's agammaglobulinemia), the latter of which manifests a deficiency of the enzyme tyrosine kinase within B-cells and results in a severe quantitative deficiency of serum immunoglobulins.

Common variable immunodeficiency

The prevalence of CVID is estimated to be between one in 25,000 and one in 50,000 [9, 10]. This entity is thought to be comprised of a series of disorders that result from defective cytokine formation by helper T-cells. These cytokines are responsible for the induction of B cell maturation into plasma cells. The resultant quantitative and qualitative immunoglobulin deficiencies predispose the child to recurrent sinopulmonary pyogenic infections. When left untreated, these infections can result in bronchiectasis and chronic sinusitis (Fig. 4). Bacterial infections are most important, especially those caused by *Streptococcus*, *Haemophilus*, and *Staphylococcus* species, which may lead to unusually severe illnesses. Susceptibilities to PJP pneumonia and *Mycoplasma* pneumonia can occur relatively early in life. The current use of monthly intravenous immunoglobulin therapy has significantly improved the extent and severity of lung disease, i.e., bronchiectasis [9, 10], although resulting in only variable success at preventing neoplasia.

Symptoms of CVID can occur at any age and can be indolent and variable, resulting in delayed diagnosis. In the pediatric population, symptoms tend to peak in early childhood, late childhood, and adolescence. As a result of the high variability in clinical features seen in CVID, the delay from the onset of initial symptoms to formal diagnosis averages around 5 years in developed countries [10].

Chronic granulomatous disease

Children with disorders of phagocytosis and complement are typically most vulnerable to infections caused by encapsulated organisms. Chronic granulomatous diseases (CGD) are characterized by impaired granulocytic destruction of ingested catalase positive microorganisms. The incidence is thought to be approximately one in 125,000 live births [10]. It is slightly more common in boys (approximately 60% of cases) where it is inherited as an X-linked disorder. It occurs due to a deficiency of NAPDH oxidase within phagocytic cells including macrophages, neutrophils, and eosinophils. Consequently, children with CGD are at risk of recurrent or life-threatening pyogenic or fungal infections originating in the respiratory tract. The most classically offending organisms are, therefore, *Staphylococcus*, *Pseudomonas*, and *Aspergillus*. Infections are, as in most immunodeficient children, classically difficult to treat, slow to resolve, and commonly recur. Clinically, CGD may present in early childhood with recurrent sinopulmonary infections or later with pneumonia due to one of notable unusual pathogens (Fig. 5). Pulmonary radiographic manifestations are non-specific but predominantly involve air space changes that may persist or recur, despite treatment.

Hyper-IgE syndrome

Similar to CGD, this disorder (originally named Job's syndrome) is characterized by recurrent pneumonias from *Staphylococcus* and *Candida*. This disorder is likely due to a defect in the T cell production of gamma interferon, a cytokine which normally suppresses IgE production. Serum IgE levels are extremely high in these children. The lack of gamma interferon also results in defective induction of chemotactic migration by granulocytes allowing local infections to spread more easily [4]. One classic manifestation of this disorder in children is in the propensity to form pneumatoceles in association with infections, which are notably slow to resorb [11] (Fig. 6).

Secondary immunodeficiencies

If we consider immune deficiency more globally, the population of children without a complete immune system is large. Infection associated with malnutrition remains a leading cause of death in children as malnutrition is a known cause for variable immune compromise. As well, chronic

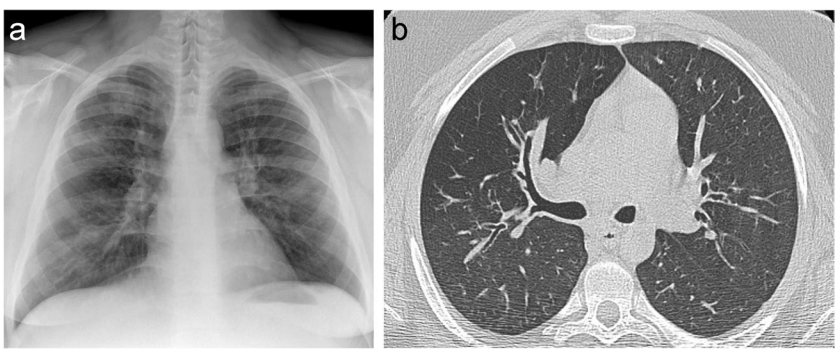

Fig. 4 A 15-year-old boy with late presentation of bronchiectasis from subsequently diagnosed common variable immune deficiency. **a** Frontal anteroposterior chest radiograph and (**b**) axial computed tomography chest demonstrate cylindrical bronchiectasis and bronchial wall thickening

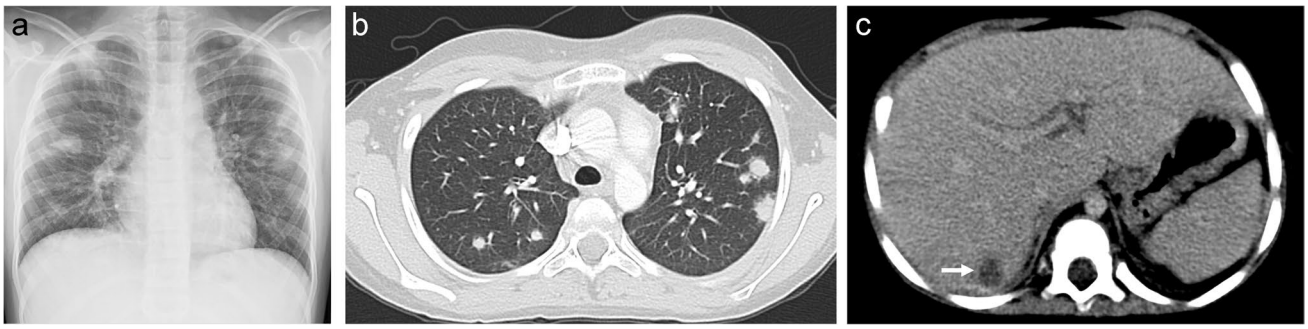

Fig. 5 A 12-year-old boy with chronic granulomatous disease and *Aspergillus* lung infection with (**a**) frontal chest radiograph and (**b**) axial computed tomography chest showing multiple bilateral lung nodules. **c** Axial contrast-enhanced computed tomography abdomen in a 21-month-old boy with chronic granulomatous disease and unexplained fever showing a subcapsular liver abscess in the right posterior liver (*arrow*)

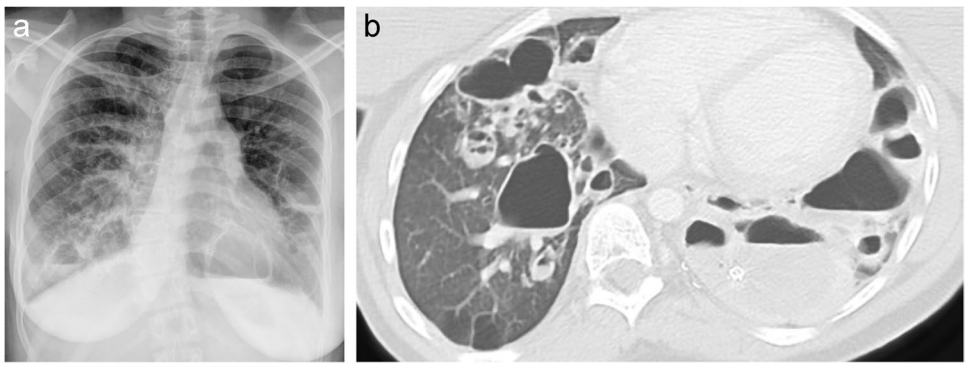

Fig. 6 A 17-year-old girl with hyper-IgE syndrome (Jobs). **a** Frontal anteroposterior chest radiograph and (**b**) axial computed tomography chest showing multiple bilateral thin-walled cavitary lesions, some containing air-fluid levels, thought to represent pneumatoceles

diseases of the heart, liver, kidneys, and other organs often cause significant generalized debilitation, which results in a decreased immune response to common pathogens making these children particularly susceptible to serious, life-threatening infections. Despite obtaining some immunity from their mothers, infants in the first few months of life are especially vulnerable to infection and can be considered as immunodeficient due to the immaturity of their immune system [12]. Complications in children with iatrogenic or secondary immunodeficiency generally also depend on the severity of the immune compromise. Milder states of immunocompromise can result from simple chronic steroid use, while more intense immune depression from immunosuppressing biologics, chemotherapies, and bone marrow ablation intuitively result in more severe susceptibilities. It is estimated that close to 50% of children who must use steroids on a chronic basis will at some point develop pneumonia [13]. Hospitalized children are most at risk for hospital-acquired gram-negative organisms, and coagulase-negative staphylococci and *Staphylococcus aureus* are often encountered, many in relation to indwelling central catheters [14].

Most children with iatrogenic immunosuppression are under the careful watch of medical teams who are cognizant of the risk for infectious complications. Many of these children are prescribed prophylactic medications to help protect against acute infection. These would include, to various degrees, the administration of pneumococcal vaccine, trimethoprim-sulfamethoxazole for PJP prophylaxis, several antifungal agents, and even ganciclovir for EBV seroconversion prophylaxis. EBV seroconversion is not only associated with acute infection, but, as we will see, is also associated with a spectrum of lymphoproliferative disorders including lymphoma. While potentially the most clinically severe, bacterial infections are generally less common due to early widespread use of broad-spectrum antibiotics at the first clinical hint of an infection. These preventative measures can diminish but not eliminate the occurrence of super-infection (Fig. 7). As such, the radiographic differential diagnoses must consider the timing of infection, the extent of pneumonia, and the radiographic pattern. The radiology literature supports the use of CT for any immunocompromised child with "prolonged" fever of undetermined origin [15]. Studies have confirmed that the early detection of radiographic changes leads to earlier interventions aimed at identification of the causative organism, which in turn leads to earlier therapy [16].

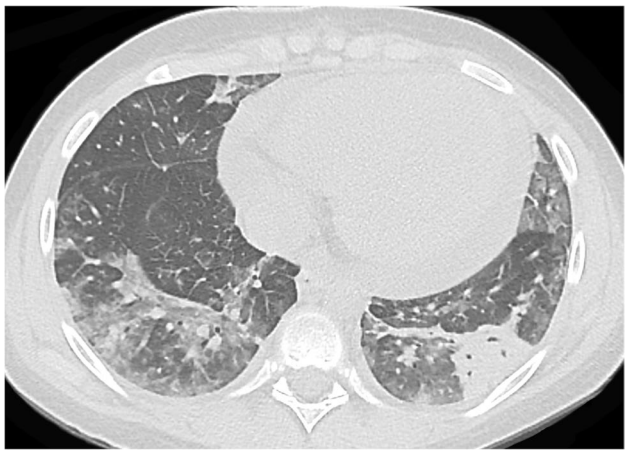

Fig. 7 A 12-year-old girl with aplastic anemia following hematopoietic stem cell transplant who developed fatal bacterial pneumonia in addition to parainfluenza infection. Non-contrast axial chest computed tomography demonstrates bilateral multifocal alveolar consolidations on a background of multifocal ground-glass opacities

Curiously, in children who have undergone organ transplantation, the most common site of bacterial infection is at, or near, the site of transplantation [14]. Urinary tract infection is said to be the most common infectious complication among renal transplant recipients. Intraabdominal infection most often complicates liver and/or intestinal transplantation, and lower respiratory tract infections (including pneumonia and lung abscess) are the most common site of infection reported in many series of pediatric heart and lung transplant recipients, especially in children who have undergone lung transplantation for cystic fibrosis, as it is difficult to eradicate the pulmonary infections(s) in the transplant recipient (Table 1).

Pneumocystis jirovecii pneumonia (PJP) is a potential problem in all immunocompromised children, yet there are particular clinical scenarios during which a child may be most susceptible. We previously mentioned the propensity for children with SCIDs and immunoglobulin deficiencies to develop infections from PJP. As well, PJP has a classic propensity to occur in children undergoing maintenance chemotherapy for acute lymphoblastic leukemia (Fig. 8). The risk level can vary according to the severity of immunosuppression induced during the induction phase of chemotherapy. More intense induction chemotherapy regimens can increase the risk of PJP pneumonia by 70% compared to milder induction chemotherapies. However, the peak incidence is said to occur between 6–12 months after induction chemotherapy [17]. PJP is also a recognized problem after solid organ or bone marrow transplantation. Following BMT, the time of onset is usually after the first month with the highest risk period in the first 6 to 12 months post-transplant [14]. Its radiographic manifestations do not seem to vary with the level of immune compromise, but the appearance of diffuse, bilateral ground-glass opacities in any of these settings should lead the radiologist to raise this etiology in the differential diagnosis.

Fungal disease, especially problematic in cases of treated acute myeloid leukemia, often presents with characteristic radiographic findings, such as those associated with aspergillosis of which most of us are acquainted. Multiple pulmonary nodular foci, especially with fungal "halo" and/or internal cavitation, are well-accepted hallmark findings of angioinvasive fungal disease (Fig. 9). In children undergoing hematopoietic stem cell transplantation (HSCT), their relative infectious complications are usually classified into early and late stages. Early complications include the more opportunistic etiologies such as fungi and PJP, as well as *Staphylococcus* and *Streptococcus* contaminants from indwelling catheters [2, 14]. Angioinvasive aspergillosis is said to occur in approximately 5% of children who have undergone HSCT, while *Candida* is said to occur in up to 10% [2].

Table 1 Immunodeficiencies predisposing to specific pulmonary infections and their most common radiological manifestations

Immunologic defect	Bacteria	Virus	Fungi
Combined B and T cell (SCIDS)		*Cytomegalovirus* (diffuse interstitial)	*Pneumocystis jirovecii* (diffuse ground glass)
B cell (immunoglobulin)	*Staphylococcus aureus*, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli* (consolidative airspace)		
T cell ("cellular")	Mycobacteria species (variable radiologic manifestation)	*Cytomegalovirus*, herpes, varicella-zoster (diffuse interstitial)	*Cytomegalovirus*, varicella-zoster (diffuse interstitial)
Phagocyte/complement	*S. aureus*, *S. pneumoniae*, *P. aeruginosa*, *E. coli* (consolidative airspace)		*Aspergillus* (consolidative airspace)

Adapted from Wilson and Dermody [4] Respiratory infections in immunocompromised children. Semin Pediatr Infect Dis 6:156–165

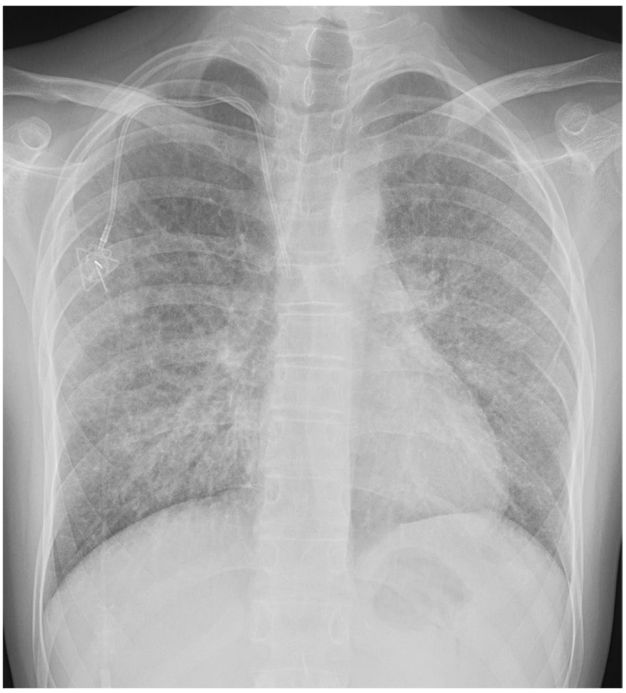

Fig. 8 Frontal postero-anterior chest radiograph in a 15-year-old boy with *Pneumocystis jirovecii* pneumonia 6 months after induction therapy for acute lymphoblastic leukemia showing a diffuse interstitial pattern

Pulmonary fluid

Pulmonary interstitial fluid can accumulate in relation to primary processes in the lung itself or as a result of damage to other organs, such as those stemming from cardiotoxicity or nephrotoxicity.

Primary pulmonary edema often results from changes in lung permeability rather than as a direct consequence of immunocompromise. It may arise from local factors, such as the edema commonly observed after lung transplantation, or from systemic conditions such as macrophage activation syndrome (MAS) and/or cytokine release syndrome, which may be related to secondary sepsis or neoplastic processes [18]. The underlying pathophysiologic mechanisms vary, sometimes being well-defined, such as lymphatic obstruction in lung transplantation, in contrast to more poorly understood pathophysiologic mechanisms such as HSCT associated engraftment syndrome. Unfortunately, radiographic evaluation is frequently non-specific, and relies on a close interrelationship between the clinical scenario and imaging findings.

In the context of HSCT, pulmonary edema typically occurs as an early complication within the first few weeks post-transplant. Mechanisms that have been attributed to the early onset of pulmonary edema in HSCT may include aggressive hydration, especially in the presence of reduced kidney function, the cardiac toxicity of induction therapy, and total body irradiation (TBI) [2]. Distinguishing between pulmonary edema, acute pulmonary hemorrhage, and post engraftment respiratory distress syndrome (PERDS) – all of which are potential early complications after HSCT – can be challenging. In the case of lung transplantation, it was initially thought that poor lymphatic drainage was the primary factor leading to edema, although it now seems that more complex changes in lymphangiogenesis may contribute [19].

Systemic issues at play in many immunocompromised children result in variable susceptibilities to the accumulation of interstitial pulmonary fluid. Direct pulmonary toxicity from chemotherapies and radiation therapies, renal compromise (usually related to various chemotherapeutic and antimicrobial agents), cardiac compromise (also usually related to chemotherapies), and cytokine release syndrome (associated with a number of immunotherapies) may all occur individually or in combination. In the pediatric setting, aggressive fluid administration is a frequent clinical adjunct in the children who have undergone transplantation, assuming a lack of confounding underlying comorbidities that are seen in the adult [18].

Radiographic manifestations are as expected and non-specific in terms of potential etiology. Rapidly developing

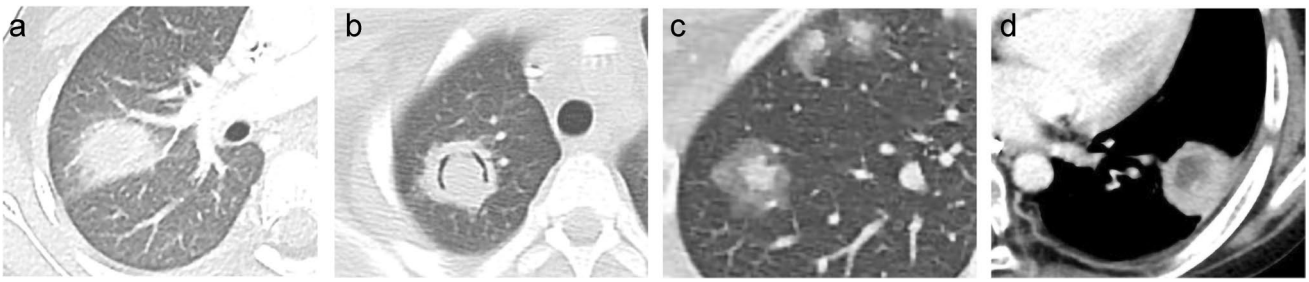

Fig. 9 Axial computed tomography chest in four children with acute invasive pulmonary aspergillosis showing different classic radiographic patterns that may represent different stages of infection. **a** Focal consolidation with ill-defined margins in a 7-year-old boy with relapsed acute lymphoblastic leukemia. **b** Nodule with a crescent-shaped rim of air along its inner margin in a 9-year-old girl. **c** Nodules with surrounding ground-glass opacity (*halo sign*) in a 5-year-old girl. **d** Subpleural nodule with a ring-enhancement pattern in an 11-year-old boy

or resolving fissural fluid, increased interstitial "markings," appearing as septal lines on both chest radiographs and CT, and pulmonary vascular plethora are well known findings (Figs. 10 and 11). Gross cardiac enlargement with vascular "redistribution" could help point toward a chemotherapy-induced toxic cardiomyopathy.

Neoplasia

It is estimated that up to 80% of children with Hodgkin lymphoma and 50% of children with non-Hodgkin lymphoma present with a mediastinal mass. These masses can be very large, impinging on both the airways and vascular structures, especially the superior vena cava (Fig. 12) [20]. In fact, over half of all pediatric mediastinal masses are symptomatic, mostly from tumor compression of vital structures [21]. Additionally, 10% to 20% of anesthetic procedures in children with a mediastinal mass result in significant perioperative complications [22]. Of all anesthesia-related complications in children with a mediastinal mass, 85–100% are associated with anterior mediastinal masses [23].

As such, children with mediastinal masses can present with an unusual pediatric symptom of orthopnea. Pretest knowledge of the presence of potential vascular return obstruction can warrant pre-emptive airway support measures, such as alternate position for initial diagnostic CT scanning [24, 25].

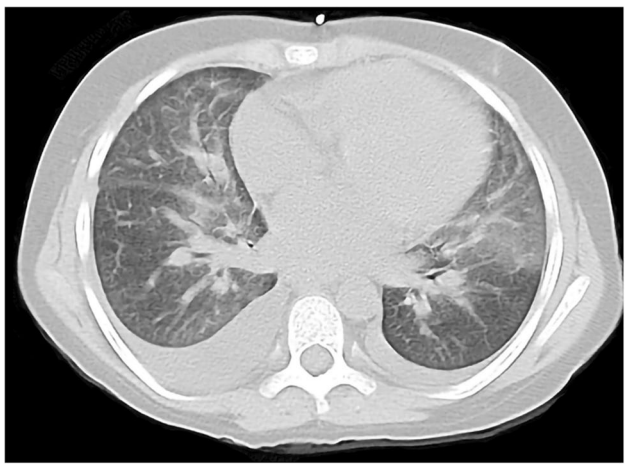

Fig. 10 An 8-year-old boy with pulmonary interstitial edema 1 week after hematopoietic stem cell transplant. Non-contrast axial chest computed tomography demonstrates smooth interlobular septal thickening, peribronchovascular thickening, ground-glass opacities in the lingula, and bilateral pleural effusions

Primary immunodeficiencies

Common variable immunodeficiency

Administration of periodic, usually monthly, immunoglobulin replacement to children with immunoglobulin deficiencies has decreased their susceptibility to infections and the subsequent potential sequelae of bronchiectasis. However, non-infectious morbidities persist. Of utmost concern is the increased susceptibility to neoplasms related to the lymphoreticular system. Lymphoproliferative diseases, with lymphoma at the extreme end of the spectrum, still occur (Fig. 13). These lymphomas are usually of the non-Hodgkin variety. Lymphoma ranks as the second leading cause of mortality among CVID patients, with an occurrence rate estimated at 2–8% [11, 26]. Overall lymphoproliferative states are more common than overt lymphoma, occurring in about 17% of cases, which include lymphadenopathy, lymphoid hyperplasia, lymphocytic inflammation, and lymphocytosis. The risk of developing lymphoma has been

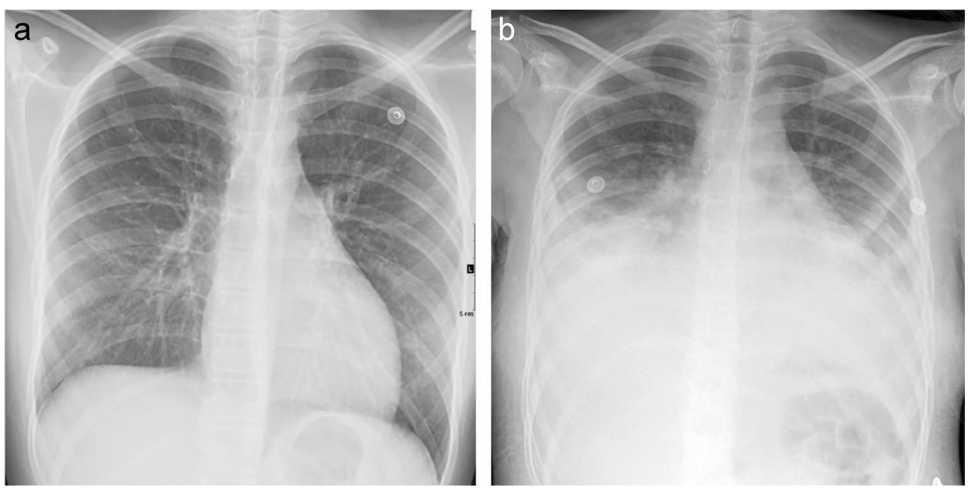

Fig. 11 Frontal chest radiographs in a 15-year-old boy with anthracycline-induced cardiomyopathy (**a**) before and (**b**) 7 days after treatment initiation show rapid development of pulmonary edema and cardiomegaly

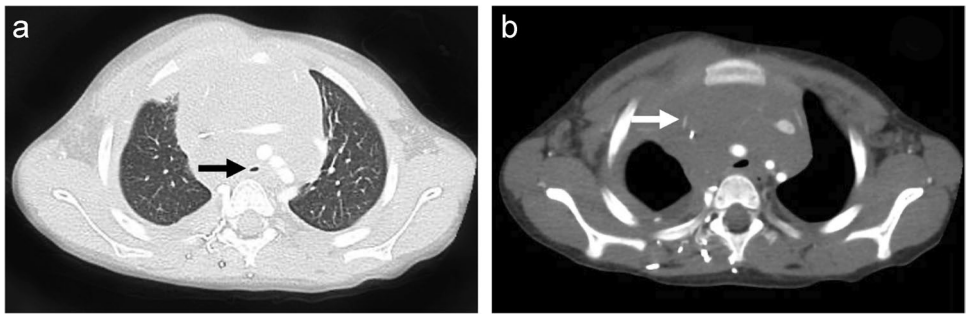

Fig. 12 A 14-year-old boy with a primary mediastinal lymphoma causing extrinsic mass effect on mediastinal structures. **a**, **b** Axial contrast-enhanced computed tomography chest in (**a**) lung window (width 2000, level 500) and (**b**) mediastinal window (width 350, level 50) demonstrates a large mediastinal mass causing severe tracheal narrowing (*black arrow*, **a**) and superior vena cava narrowing (*white arrow*, **b**)

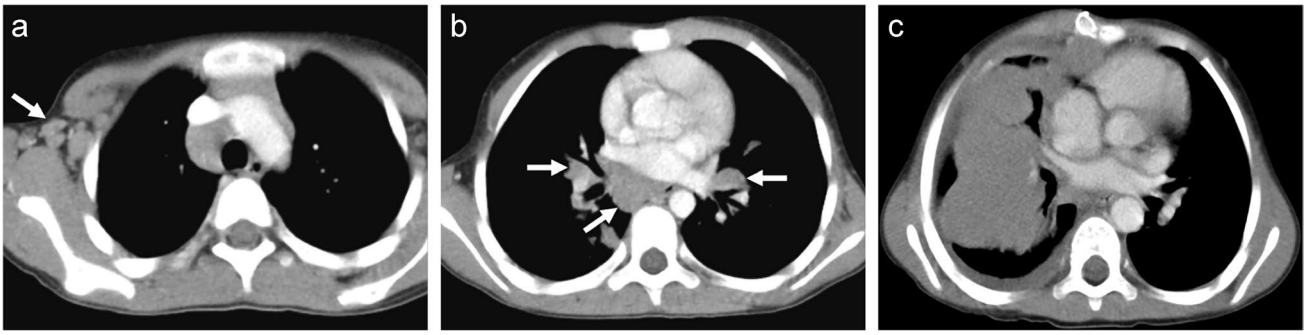

Fig. 13 A 10-year-old boy with post-transplant lymphoproliferative disorder with (**a**, **b**) axial contrast-enhanced computed tomography chest showing multiple enlarged axillary, mediastinal, and hilar lymph nodes (*arrows*). **c** Axial contrast-enhanced computed tomography chest in a boy with fulminant lymphoma following heart transplant demonstrates multiple pleural-based lobulated masses

reported to be up to 300-fold higher than normal, especially in women [27].

Less common but more classic is the incidence of lymphoreticular malignancies associated with ataxia-telangiectasia. This disorder includes part of its pathophysiology the inability to repair nucleic acid strands of DNA [28]. This problem is of particular interest in the field of radiology, where minor structural nucleic acid damage is thought to be a contributing factor to lymphoma formation. This is one of the few disorders where radiation-producing diagnostic procedures must be minimized, used only when alternate imaging modalities such as ultrasound or MRI will not be able to answer a clinical question satisfactorily (Fig. 14).

Repeated exposure to ionizing radiation is a concern in all primary immunodeficiencies, as variable degrees of radiation sensitivity and lymphoreticular induction are shared by some immunodeficiencies. Accordingly, imaging protocols should therefore minimize radiation exposure. MRI has been explored as an alternative to CT; however, scan resolution remains a challenge [10].

Secondary malignancies

Post-transplant lymphoproliferative disorder (PTLD) refers to a heterogenous group of disorders that occur as a result of immunosuppression following solid organ or bone marrow transplantation. The clinical presentation and manifestations of PTLD are highly variable, ranging from minor and somewhat inconsequential (Fig. 13) to full blown, aggressive lymphoma. Incidence rates vary, with stated incidence rates of above 50% [29, 30] although it is suggested that in children who have undergone solid organ transplantation, more than 70% of malignancies are part of the PTLD spectrum. Despite this, PTLD accounts for less than 5% of all pediatric non-Hodgkin lymphomas.

In pediatric organ transplantation, the primary risk factor for PTLD and lymphoma is Epstein-Barr virus (EBV) seroconversion. The occurrence of seroconversion at the time of, or after transplantation has a higher association with these lymphoproliferative disorders. Given that 60–80% of children who are EBV-naive will seroconvert within the first

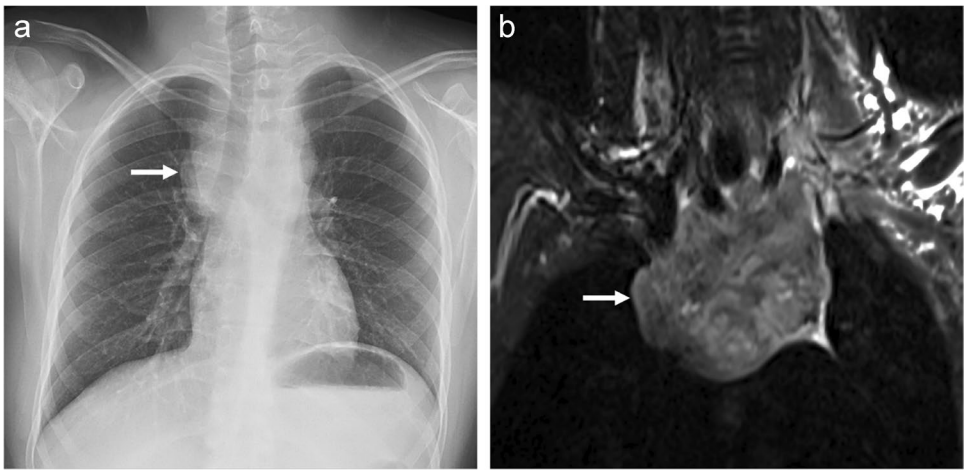

Fig. 14 A 17-year-old boy with ataxia-telangiectasia presenting with shoulder pain and tachycardia. **a** Frontal chest radiograph demonstrates large superior mediastinal mass (*arrow*). **b** Coronal chest MRI T2 HASTE sequence shows a lobulated mass with mildly increased signal intensity (*arrow*). Biopsy revealed a T-cell lymphoblastic lymphoma

3 months post-transplant, lymphoproliferative disorders are a significant concern for transplant teams [29].

The risk of PTLD varies among organ transplant recipients, with kidney recipients experiencing a 2–3% incidence rate. The risk increases for pancreas, liver, heart, and lung recipients (10%), and is highest for intestinal transplants recipients, with an incidence rate reaching up to 20% [30].

There is a suggestion from case series data that PTLD has a predilection for the transplanted organ [30, 31]. As such, pulmonary, mediastinal, and cardiac sites of PTLD occur more commonly in the transplanted lungs or heart, renal PTLD close to the transplanted kidney, gastrointestinal PTLD in transplanted bowel, etc.

Idiopathic pneumonia syndrome

Idiopathic pneumonia syndrome remains a poorly understood phenomenon of acute onset of severe and diffuse alveolar injury in recipients of stem cell marrow transplantation. It usually occurs within several weeks of transplantation. The recipient develops bilateral diffuse alveolar damage leading to acute pulmonary dysfunction and often to respiratory failure. The damage occurs without identifiable etiology, after infection, cardiac disease, renal failure, or iatrogenic pulmonary damage have been excluded. Incidence rates of 2–12% have been quoted with mortality rates as high as 50–80%. Risk factors discussed in relation to pediatric HSCT are graft vs. host disease and previous viral pneumonitis. It is thought to possibly be a non-specific result of diffuse cytokine induction [32].

Conclusion

The breadth and depth of acute lung pathologies in immunocompromised children are extensive and multifaceted, encompassing a wide range of intrathoracic conditions. This review discusses the heightened risk and complex nature of "acute" pulmonary complications that can arise in these patients, including infection, pulmonary edema, and malignancies. The importance of early and accurate diagnosis is paramount to guide prompt treatment. Effective management of lung pathologies in the immunocompromised child requires a multidisciplinary approach, including vigilant monitoring, prompt intervention, and individualized care strategies to address the unique challenges presented by their compromised immune systems.

Author contribution D Manson: manuscript writing and preparation, reference writing and preparation, editing, image processing, image interpretation, image legends. C Rutten: manuscript writing and preparation, reference writing and preparation, editing, image processing, image interpretation, image legends.

Declarations

Conflicts of interest None

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