

PediatricsⁱⁿReview[®]

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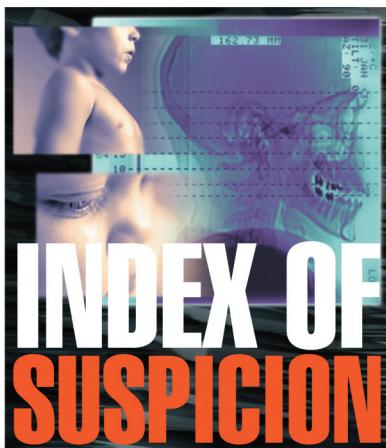
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The reader is encouraged to write possible diagnoses for each case before turning to the discussion.

The editors and staff of *Pediatrics in Review* find themselves in the fortunate position of having too many submissions for the Index of Suspicion column. Our publication slots for Index of Suspicion are filled through 2013. Because we do not think it is fair to delay publication longer than that, we have decided not to accept new cases for the present. We will make an announcement in *Pediatrics in Review* when we resume accepting new cases. We apologize for having to take this step, but we wish to be fair to all authors. We are grateful for your interest in the journal.

Author Disclosure

Drs Balma-Mena, Weinstein, Rosenthal, Henry, Gahzarian, Miller, Maul, McGuirl, and Moorthy have disclosed no financial relationships relevant to these cases. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

Case 1: Pruritic, Erythematous, Papular, and Papulovesicular Rash in an 8-year-old

Case 2: Cough With Green Phlegm in an 8-year-old

Case 3: Polyarthritis, Raynaud Phenomenon, Hoarseness, Tapering Fingers, and Digital Ulcers in a 6-year-old

Case 1 Presentation

An 8-year-old boy presents with a 3-week history of red, itchy, raised lesions that developed vesicles and black crust. The lesions started on the neck and inguinal region but became generalized within a few days. He was diagnosed as having varicella and sent home with symptomatic management. A few days later, he was seen in the ED because of fever and persistence of the eruption. He was prescribed oral cephalexin for a possible secondary infection of the varicella. He has not improved and is finally admitted to a regional hospital for further evaluation.

Physical examination shows a generalized eruption of erythematous papules, most of which have a dark crust in the center, as well as a few papulovesicles on the extremities, including the palms and soles (Fig. 1). He has enlarged inguinal

nodes and complains of intense pruritus. The differential diagnosis includes varicella, herpesvirus infection, and vasculitis.

Results of laboratory studies include:

- WBC count: $4.0 \times 10^3/\mu\text{L}$ ($4.0 \times 10^9/\text{L}$) with normal percentages and absolute numbers of lymphocytes and neutrophils
- Hgb: 12.9 g/dL (129 g/L)
- Platelet count: $349 \times 10^3/\mu\text{L}$ ($349 \times 10^9/\text{L}$)
- Creatinine: 0.5 mg/dL (44.2 $\mu\text{mol}/\text{L}$)
- BUN: 8 mg/dL (2.9 mmol/L)
- ALT: 9 U/L (normal, 0 to 41 U/L)
- Alkaline phosphatase: 200 U/L (normal, <300 U/L)
- C-reactive protein: 0.7 mg/dL (normal, <1 mg/dL)



Figure 1. Eruption consisting of erythematous papules, most of which have a dark crust in the center, and a few papulovesicles on the right lower extremity.

- ESR: 22 mm/hr (normal, 0 to 10 mm/hr)

Urinalysis is negative for protein and erythrocytes and a urine culture is sterile. Results of bacterial culture and polymerase chain reaction testing for herpes group viruses from the skin lesions are negative. Additional evaluation leads to the diagnosis.

Case 2 Presentation

An 8-year-old boy who has a history of recurrent pneumonia, CHARGE association, repaired tetralogy of Fallot, gastroesophageal reflux disease, and severe kyphoscoliosis presents with the production of green sputum and increasing work of breathing for 5 days. He is afebrile but is coughing and has tachypnea and copious rhinorrhea. His family denies other symptoms or sick contacts. He has a 5-year history of recurrent pneumonia, which has occurred more frequently over the past 6 months. He has been treated with

multiple courses of oral and parenteral antibiotics.

Physical examination reveals a temperature of 37.0°C, heart rate of 140 beats/min, respiratory rate of 40 breaths/min, blood pressure of 110/74 mm Hg, and pulse oximetry reading of 94% in room air. He does not appear toxic and has copious thick nasal secretions. Auscultation reveals clear right lung fields and bronchial breath sounds and rhonchi on the left, especially over the lower lobe of the lung. Upper and lower extremities appear acyanotic with digital clubbing.

Results of his CBC and metabolic panel are normal. His C-reactive protein measures 1.1 mg/dL. Chest radiography reveals a clear right lung with nearly complete opacification of the left hemithorax, an unchanged dextroscoliosis, and no mediastinal shift. Bronchoscopy demonstrates normal anatomy with diffuse tracheobronchitis and mucus plugging of bronchi in the left lung. An additional imaging study helps establish the diagnosis.

distress. She has tapering fingers with skin tightening; periorbital telangiectasias; round healing ulcers on her second finger tip and second, third, and fourth proximal interphalangeal (PIP) and metacarpophalangeal (MCP) joints; and nailfold capillary changes. She has calcinosis over her left arm and right knee and tightening of the skin over her hands and knees bilaterally. Subcutaneous nodules are apparent over her left elbow and right knee. She has polyarthritis involving both knees, hips, wrists, and PIP and MCP joints.

Laboratory studies reveal:

- Hgb: 10.4 g/dL (104 g/L)
- Antinuclear antibody (ANA) titer: 1:640
- Rheumatoid factor (RF) titer: 34
- Antiribonucleoprotein (RNP) antibody: positive
- Lactate dehydrogenase: 439 U/L (7.3 μ kat/L)
- Creatine kinase: 58 U/L (0.96 μ kat/L)
- Aldolase: 12.5 U/L (0.21 μ kat/L)
- ESR: 85 mm/hr

Serum complement concentrations, WBC count, platelet count, complete metabolic panel, and urinalysis findings are within normal limits. Antidouble-stranded DNA, anti-Smith, anti-Jo, anti-SSB, anti-Scl-70, and anti-centromere antibody determinations are negative. Echocardiography shows a resolving pericardial effusion, and ECG findings are within normal limits. Pulmonary function tests reveal a decrease in diffusion lung capacity (DLCO).

Case 1 Discussion

Three skin biopsies were sent for histopathologic examination. Two biopsies from the knee and one from the elbow showed similar findings consistent with a diagnosis of pityriasis lichenoides et varioliformis acuta

Frequently Used Abbreviations

ALT:	alanine aminotransferase
AST:	aspartate aminotransferase
BUN:	blood urea nitrogen
CBC:	complete blood count
CNS:	central nervous system
CSF:	cerebrospinal fluid
CT:	computed tomography
ECG:	electrocardiography
ED:	emergency department
EEG:	electroencephalography
ESR:	erythrocyte sedimentation rate
GI:	gastrointestinal
GU:	genitourinary
Hct:	hematocrit
Hgb:	hemoglobin
MRI:	magnetic resonance imaging
WBC:	white blood cell

Case 3 Presentation

A 6-year-old African American girl who has been suffering from polyarthritis for the past 2 years presents with the recent onset of increasing fatigue, new-onset Raynaud phenomenon, hoarseness, worsening arthritis, tapering fingers, digital ulcers, and tightening of the skin over her fingers. She has had minimal response to nonsteroidal anti-inflammatory agents (NSAIDs), methotrexate, and etanercept in the treatment of her arthritis. She reports an episode of fever and pericardial effusion a few months earlier that responded to a course of corticosteroids.

Physical examination reveals a tired-appearing, thin girl in no acute

(PLEVA). The boy was started on an 8-week course of oral erythromycin and was followed in the dermatology clinic, where his skin showed considerable improvement (Fig. 2). He has had no recurrence.

The Condition

PLEVA is an uncommon dermatologic condition of unknown cause that was described initially by Neisser and Jadassohn in 1894. (1)(2) It can affect both children and adults and has been reported to be associated with infectious triggers, immune complexes, and lymphoproliferative processes.

The two clinical forms described are PLEVA and pityriasis lichenoides chronica (PLC). This classification is based on the duration of the episode and different clinical presentations. PLEVA is characterized as papular or vesicular lesions with central necrosis, while PLC has thinner papules with scale that leave behind characteristic white macules. PLC has no central necrosis or vesicles and is a more chronic eruption. Some authors argue that PLEVA and PLC represent a clinicopathologic spectrum rather than independent diseases.

PLEVA is characterized clinically by the acute onset of erythematous papulovesicles with ulceronecrotic centers. These lesions can result in varioliform scars and postinflammatory hypo- or hyperpigmentation. The eruption is polymorphous and presents more frequently on the extremities and flexural areas. Affected patients complain of pruritus and a burning sensation. The differential diagnosis of PLEVA includes varicella, arthropod bites, viral exanthems, lymphomatoid papulosis, and vasculitis.

The histopathologic features of PLEVA consist of a perivascular and often wedge-shaped interstitial lymphocytic infiltrate with interface dermatitis features of exocytosis and basal cell vacuolation. Other findings include red blood cell extravasation, variable keratinocyte necrosis, and overlying parakeratosis, with crust formation possible.

Management

PLEVA generally is considered a benign process that has a self-limited course of several weeks. Different treatments have been described, including topical corticosteroids and topical tacrolimus, which evoke a good response. Oral antibiotics that have anti-inflammatory properties, such as erythromycin, tetracycline, and azithromycin, administered for 8 weeks also have produced good responses. For cases of extensive involvement, ultraviolet B phototherapy is effective in children.



Figure 2. Considerable improvement of the skin after an 8-week course of oral erythromycin.

The prognosis of PLEVA is good, with a more benign course occurring in children than in adults. A few reports in the literature show progression to cutaneous T-cell lymphoma, which is why close monitoring is recommended.

Lessons for the Clinician

- PLEVA should be considered in the differential diagnosis of vesicular, papular, and papulovesicular eruptions in children.
- For a patient who has vesicular lesions and systemic symptoms, other conditions such as varicella and herpes infection should be ruled out.
- A skin biopsy is needed to confirm the diagnosis of PLEVA and to rule out other entities.
- Management includes an 8-week

course of anti-inflammatory antibiotics, which produces a good response. The prognosis in the pediatric population usually is good.

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References

1. Neisser A. Zur frage der lichenoiden eruptionen. *Verh Dtsch Dermatol Ges.* 1894; 4:495–506
2. Jadassohn J. Über ein eigenartiges psoriasisiformes und lichenoides exanthem. *Verh Dtsch Dermatol Ges.* 1894;4:524–535

Case 2 Discussion

Noncontrast, high-resolution computed tomography (HRCT) scan of the chest revealed marked bronchiectatic changes of the entire left lung (Fig. 3). The boy underwent left pneumonectomy, and pathologic examination showed massive bronchiectasis in the upper and lower lobes, with a very small amount of normal intervening parenchyma within the left lung.

The Condition

Bronchiectasis is caused by destruction of the bronchial wall. Loss of integrity of the muscular and elastic layers of the bronchial wall results in an easily collapsible airway and obstructed sections of the bronchial tree. The first stages of change include mucosal wall thickening and mild airway dilation, referred to as cylindrical bronchiectasis. If the underlying cause can be treated effectively in the early stages, the degree of bronchiectasis may be controlled.

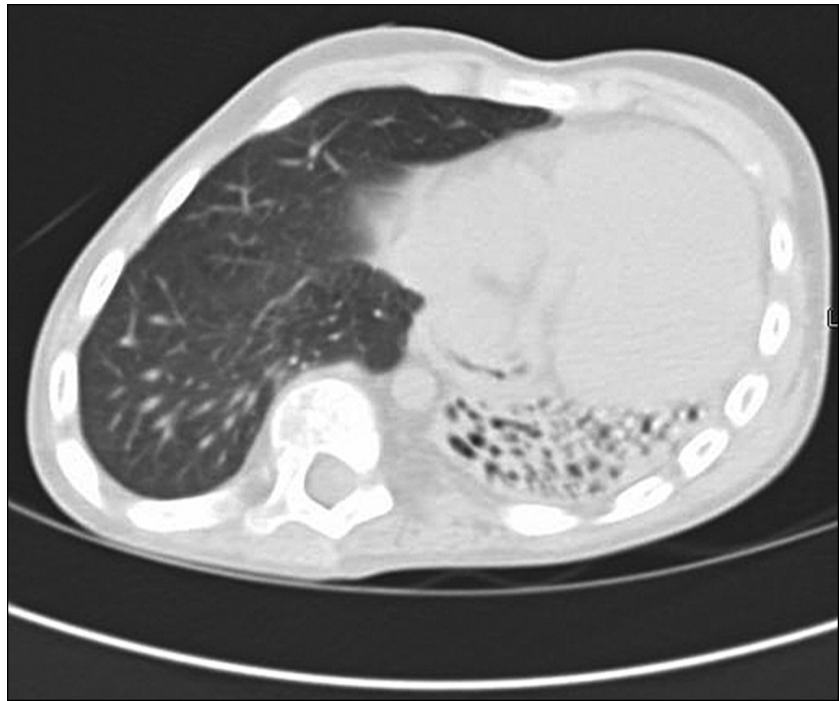


Figure 3. Noncontrast, high-resolution computed tomography scan of the chest shows diffuse saccular bronchiectasis of the left lung with a mediastinal shift to the left.

Once the disease progresses, the bronchi become tortuous and ballooned, a condition known as saccular bronchiectasis, which is considered irreversible.

Although cystic fibrosis (CF) is the most common cause of bronchiectasis in children in the United States, several other conditions must be considered. These can be divided into disorders causing fixed obstruction, diseases affecting the integrity of bronchial wall and mucus clearance, and infections.

Airway obstruction compromising mobilization of secretions from the tracheobronchial tree can be a source of bronchiectasis. Airway obstruction can result from severe kyphoscoliosis; a retained foreign body, intraluminal tumor, or other mass; lymphadenopathy; vascular anomaly; or cardiac pathology that results in airway impingement.

If mucociliary clearance is com-

promised, even in the absence of airway obstruction, bronchiectasis can result. In patients who have CF, the tenacity of the secretions and the relatively diminished amount of fluid in the airway lining makes mobilization of secretions from the lower airways difficult. Similarly, diseases in which muscle strength is compromised, such as muscular dystrophy or spinal muscular atrophy, can result in bronchiectasis from compromised mobilization of lower airway secretions. Children who have compromised ciliary function, such as occurs in primary ciliary dyskinesias, generally are unable to mobilize secretions from the lower airways and may develop bronchiectasis.

Infection of the secretions in the airway distal to either the anatomic or functional obstruction plays a critical etiologic role. Hence, disease states that entail immunodeficiencies or abnormalities in neutrophil func-

tion can lead to bronchiectasis. Among the most frequent causes of bronchiectasis in children are disorders such as hypogammaglobulinemia, abnormalities of the respiratory burst in neutrophils, complement deficiencies, selective immunoglobulin deficiencies, and acquired immunodeficiency syndrome.

Regardless of the primary cause, infection is the final factor in the development of bronchiectasis, and the likelihood of developing bronchiectasis increases with prolonged and untreated infections. The pathogens causing bronchiectasis generally are bacteria such as *Pseudomonas aeruginosa*, *Mycobacterium tuberculosis*, *Mycoplasma pneumoniae*, or *Streptococcus pneumoniae*. However, the infection may be viral, most commonly adenovirus and influenza, or even fungal.

Allergic bronchopulmonary aspergillosis, a hypersensitivity pneumonitis that is associated most commonly with CF, results in central sacular bronchiectasis.

In children, it may be difficult to identify the cause of bronchiectasis, but every attempt must be made to do so to allow institution of appropriate management.

Clinical Manifestations

Cough and sputum production are the most common symptoms of bronchiectasis; dyspnea, rhinosinusitis, and hemoptysis are less common. Affected patients frequently have received the diagnosis of recurrent pneumonia. Physical examination findings of bronchiectasis include crackles, wheezing, and rhonchi; digital clubbing also may be present.

Diagnosis

Diagnosis relies predominantly on imaging. Laboratory studies, such as CBC, quantitative immunoglobu-

lins, and sputum culture, may help determine the cause but are nondiagnostic alone. Chest radiograph may reveal airway dilation, increased pulmonary markings with tram tracking (thickening of the bronchial walls), and areas of atelectasis. HRCT is the gold standard for diagnosis and reveals detailed anatomy of the bronchial tree: lack of airway tapering with luminal dilation, bronchial wall thickening, honeycombing, and mucus plugging.

Treatment and Prognosis

Management should focus on identifying and treating the underlying cause of the bronchiectasis. Establishing the primary cause is of critical importance and is undertaken best under the direction of a pediatric pulmonologist. Following determination of the cause, optimal management often involves a multidisciplinary team, including primary care physicians, pulmonologists, and respiratory therapists.

Decreasing acute exacerbations by employing a regimented daily therapy may slow disease progression. Mucus clearance may be enhanced with hypertonic saline nebulization, inhaled mucolytics, and chest physiotherapy. Inhaled corticosteroids can reduce airway obstruction. Chronic macrolide therapy also has been found to be beneficial. In addition to antimicrobial properties, macrolides have anti-inflammatory properties. Aggressive treatment of pseudomonal and *Staphylococcus aureus* infections is indicated, but antimicrobial therapy should be targeted to specific pathogens. Lobectomy is a last resort in refractory cases.

The efficacy of different treatment modalities for non-CF-associated bronchiectasis is largely unknown at this point and remains an area of active research. The prognosis for non-CF bronchiectasis depends on

the cause and the patient's access to medical care. Regular access to a multidisciplinary team facilitates aggressive treatment of exacerbations, emphasizes prevention, and allows for teaching self-management as well as for monitoring and early intervention for comorbid conditions.

Lessons for the Clinician

- Although primarily seen in patients who have CF, bronchiectasis is a condition that clinicians may need to consider when evaluating a child who has a chronic cough.
- HRCT is vital to making the diagnosis.
- Treatment protocols and therapies are fairly well established for CF patients but not for non-CF bronchiectasis.
- A multidisciplinary approach, including the primary care clinician, pulmonologist, and allied health clinicians, is crucial for management.

(Jillian Miller, MD, Erich Maul, DO, Kentucky Children's Hospital, Lexington, KY)

Case 3 Discussion

This young girl's disease process was consistent with mixed connective tissue disease (MCTD). MCTD is considered an overlap syndrome that includes clinical features of juvenile rheumatoid arthritis, scleroderma, systemic lupus erythematosus (SLE), and dermatomyositis (DM) occurring in conjunction with high antibody titers to an extractable nuclear antigen. Children who have MCTD may progress to SLE-like or scleroderma-like disease. The tightening of the skin, digital ulcers, Raynaud phenomenon, calcinosis, hoarseness, and decrease in DLCO suggest that this girl's condition is

evolving into systemic scleroderma, also known as systemic sclerosis.

She was treated with hydroxychloroquine, methotrexate, cyclosporine, pentoxifylline, and corticosteroids. She was followed closely with frequent physical examinations, swallow studies, pulmonary and cardiac assessments, and laboratory evaluations. Currently she has persistent symptoms of decreased joint mobility, increasing calcinosis, and increased reflux suggestive of an early CREST syndrome (calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasias) that also is referred to as limited cutaneous systemic scleroderma.

The Condition

MCTD is one of the least common connective tissue diseases. The mean age of onset is 11 years, but the condition occurs in children between the ages of 4 and 16 years and is more frequent in girls. Common clinical manifestations include polyarthritis and Raynaud phenomenon, nailfold capillary changes, and cutaneous changes that may be suggestive of SLE, DM, or scleroderma. Cardio-

pulmonary disease and esophageal dysmotility are reported infrequently but may result in significant morbidity. Nephritis is less common and less severe than that seen in SLE. The sclerodermatous skin changes are slow to develop but often become the most prominent feature of the disease late in the course.

As with the clinical manifestations, the laboratory findings of MCTD and systemic sclerosis evolve over time. Most patients have positive ANA, RNP antibody, and RF.

Treatment

The treatment of MCTD is guided by strategies used in rheumatologic diseases such as SLE, scleroderma, and DM. Therapy often is based on the individual's disease course and specific organ involvement. Treatment options include corticosteroids, NSAIDs, hydroxychloroquine, methotrexate, vasodilators, and cytotoxic agents. All of these agents have been used with varying degrees of success. Overall, most patients who have MCTD survive into adulthood after the diagnosis is established. Morbidity and mortality are greatest in those who develop

either renal or pulmonary manifestations.

Lessons for the Clinician

- MCTD is an evolving disease that must be monitored closely.
- Not all polyarthritis is juvenile idiopathic arthritis; other diagnoses should be considered when the disease does not respond to standard medications.
- Systemic sclerosis is insidious in onset and often presents diagnostic challenges, mandating close observation and follow-up evaluation.
- Rheumatic diseases can have significant overlap in clinical manifestations, necessitating careful evaluation to determine that the correct disease process is being treated.

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