Diseases with Skin and Lung Involvement: Pulmonologist’s Perspective

Vishnu Sharma Moleyar1, Anupama Noojibail2

1Department of Respiratory Medicine, A J Institute of Medical Sciences, Mangalore, Manipal Academy of Higher Education, Manipal, Karnataka, India
2Department of Physiology, Kasturba Medical College, Mangalore, Manipal Academy of Higher Education, Manipal, Karnataka, India

INTRODUCTION

Dermatological changes are easily visible on physical examination. Often, skin is a mirror of many internal diseases. Hence, careful examination of skin from head to toe is essential in all patients.

A variety of conditions/diseases can involve skin and lungs together. Knowledge about these conditions and the skin and respiratory manifestations in these conditions will lead to early diagnosis and proper management. Some of the dermatological manifestations may be very classical where the diagnosis will be obvious at a glance. Many a times, dermatological manifestations may narrow the differential diagnoses. In some cases, dermatological manifestations may indicate the severity/stage of the disease and prognosis. In some diseases with dermatological manifestations, where no obvious respiratory symptoms or signs are evident, screening for the underlying lung disease may be indicated. Some dermatological manifestations may indicate the underlying lung or other systemic diseases where further evaluation may be warranted even in the absence of other symptoms or signs.

DISEASES WITH SKIN AND LUNG INVOLVEMENT

Diseases with skin and lung involvement can be classified into the following categories:

1. Congenital/developmental disorders with cutaneous and pulmonary manifestations
2. Primary dermatological diseases with pulmonary manifestations
3. Primary pulmonary diseases with cutaneous manifestations
4. Miscellaneous conditions involving skin and lungs

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Moleyar VS, Noojibail A. Diseases with skin and lung involvement: Pulmonologist’s perspective. Med J DY Patil Vidyapeeth 2020;13:106-12.
5. Skin changes due to drugs used to treat respiratory diseases.

**Congenital/developmental disorders with cutaneous–pulmonary manifestations**

- Neurofibromatosis
- Hereditary hemorrhagic telangiectasia (HHT)
- Yellow nail syndrome
- Birt–Hogg–Dubé syndrome
- Ehlers–Danlos syndrome
- Marfan’s syndrome
- Generalized elastolysis (Cutis laxa).

**Pulmonary manifestation in neurofibromatosis**

In neurofibromatosis, cysts/bulla can occur in the lungs which predominantly involve the upper lobes.\(^1\) Pulmonary fibrosis and honeycombing can occur in a small subset of patients, which usually involves the lower lobes.\(^2\) Increased incidence of schwannoma in the posterior mediastinum [Figures 1 and 2], lung cancer, and pulmonary hypertension has also been reported in patients with neurofibromatosis.\(^1\)

**Pulmonary manifestation in hereditary hemorrhagic telangiectasia**

More than 70% of pulmonary arteriovenous malformations (PAVM) are associated with HHT.\(^2\) PAVM increases the risk of cerebral abscess, ischemic stroke, transient ischemic attack, and cerebral infarction.\(^2\) HHT is characterized by mucocutaneous telangiectases and arteriovenous malformations in various organs. The most common presentation is recurrent epistaxis of varying severity. PAVM should be considered as a differential diagnosis in any patient with HHT having respiratory symptoms/abnormal chest radiograph.

**Yellow nail syndrome**

This rare condition is associated with lymphedema, yellow dystrophic nail, pleural effusion, and bronchiectasis/chronic sinusitis.\(^3\)

**Birt–Hogg–Dubé syndrome**

This is a rare congenital syndrome associated with an increased incidence of renal cancer and cysts in the
kidneys and lungs. These cysts in the lung can rupture leading to pneumothorax. Hence, these patients may present with recurrent pneumothorax. A noncancerous tumor of the hair follicles, called fibrofolliculoma, is the characteristic skin manifestation in this condition. Hence, any patient with recurrent pneumothorax should be evaluated for Birt–Hogg–Dubé syndrome.

**Ehlers–Danlos syndrome**
Ehlers–Danlos syndrome is characterized by loose joints, stretchy skin, and abnormal scar formation. Intrathoracic manifestations are aortic dissection, scoliosis, emphysematous bulla, and pneumothorax.

**Marfan’s syndrome**
Patients with Marfan’s syndrome may develop emphysema and bulla in the lungs and have an increased

![Figure 5: Skin tuberculosis](image)

![Figure 6: Skin tuberculosis](image)

![Figure 7: Skin tuberculosis](image)

![Figure 8: Cutaneous secondary](image)

![Figure 9: Chest X-ray showing mass lesion which was proved as bronchogenic carcinoma in the above patient with cutaneous secondary](image)

![Figure 10: Bronchogenic carcinoma with superior vena cava obstruction and cutaneous secondary](image)
incidence of pneumothorax and chest wall abnormalities such as pectus excavatum and kyphoscoliosis.[6]

**Generalized elastolysis (cutis laxa)**
Cutis laxa is a connective tissue disorder which affects all the connective tissues in the body, characterized by sagging and inelastic skin.[7] The skin hangs in loose folds usually more evident on the neck, armpits, and groin.

These patients develop progressive emphysema leading to cor pulmonale and death due to chronic respiratory failure.[7]

**Primary dermatological diseases with pulmonary manifestations**
*Staphylococcus aureus* skin infection can lead to pneumonia by hematogenous spread of infection.[8] Septic vasculitis can lead to pneumonia and septic pulmonary emboli.[8] Malignant melanoma in the skin (common skin cancer) can metastasize to lung parenchyma, endobronchial secondary, or malignant pleural effusion.[9] Kaposi sarcoma can have a multifocal origin in skin and lungs or can lead to pleural effusion.[9]

Immunocompromised/immunosuppressed patients and HIV-infected patients can have a variety of skin manifestations, both infective and noninfective skin conditions.[9] These patients are prone to develop a variety of lung diseases, both infective and noninfective conditions, which may or may not be related to the skin disease.[9]

**Primary pulmonary diseases with cutaneous manifestations**
- Tuberculosis (TB)
- *Pseudomonas pneumonia*
- *Mycoplasma pneumonia*
- Lung cancer.

Herpes labialis can occur in patients with pneumonia [Figures 3 and 4].

**Cutaneous tuberculosis**
Cutaneous TB is uncommon despite the high and increasing prevalence of pulmonary TB worldwide. *Mycobacterium tuberculosis, Mycobacterium bovis,* and
bacille Calmette–Guérin vaccine can cause cutaneous TB. \( ^{[10]} \) Cutaneous TB can be acquired exogenously or endogenously. Diagnosis of these skin lesions can be often difficult, as they resemble many other common dermatological conditions. Definitive diagnosis often requires skin biopsy with histological analysis and special staining methods for identification of acid-fast bacilli. Sometimes, tubercular empyema can track through the chest wall as empyema necessitans.

**Exogenous tuberculosis of skin**
- Tuberculous chancre
- TB verrucosa cutis
- Lupus vulgaris.

**Endogenous contiguous skin tuberculosis**
- Scrofuloderma [Figures 5-7]
- Orificial TB
- Lymphatic TB: Lupus vulgaris.

**Hematogenous skin tuberculosis**
- Acute miliary TB
- Metastatic TB abscess (gummatous TB)
- Papulonecrotic tuberculid
- Lupus vulgaris.

**Pseudomonas aeruginosa**

Pseudomonas skin infection includes cellulitis, folliculitis, pustules, small papules and plaques, erythema gangrenosum, and subcutaneous nodules. \( ^{[10]} \) In healthy individuals, apocrine folliculitis can occur. All the other skin infections due to pseudomonas occur in immunocompromised patients and neutropenic patients. They have associated \( P. \) pneumonia.

**Mycoplasma pneumoniae**

\( M. \) pneumoniae which causes atypical pneumonia can lead to Stevens–Johnson syndrome, erythema multiforme, and toxic epidermal necrolysis. \( ^{[10]} \) \( M. \) pneumoniae is the most common infectious agent associated with Stevens–Johnson syndrome. It can also cause urticaria, toxic epidermal necrolysis, and pityriasis rosea.

**Skin changes in lung cancer**

A variety of dermatologic changes can occur in lung cancer. In some cases, these skin changes may be obvious before the symptoms or signs of lung cancer. Skin manifestations in lung cancer include acanthosis nigricans, erythema gyratum repens, necrolytic migratory erythema, triple palms, dermatomyositis, migratory superficial thrombophlebitis, acquired ichthyosis, and acquired hypertrichosis lanuginosa. \( ^{[11]} \)

Lung cancer is one of the common causes for clubbing, hypertrophic osteoarthropathy, and superior vena cava obstruction. \( ^{[12,13]} \) Bronchogenic carcinoma is the most common primary malignancy to cause cutaneous secondary. \( ^{[13]} \) Sometimes, bronchogenic carcinoma and chest wall, rib, and pleural tumors can grow outward to cause chest wall swelling [Figures 8-12].

**Systemic diseases which affect both skin and lungs**

A variety of autoimmune diseases can affect lungs and skin. In majority of these conditions, skin involvement occurs first. Lung involvement occurs in varying proportions of these patients. Rarely, lung involvement may precede skin manifestations in these conditions. These conditions include the following: \( ^{[14,15]} \)

- Progressive systemic sclerosis [Figure 13]
- Systemic lupus erythematosus
- Granulomatosis with polyangiitis (Wegener granulomatosis)
- Eosinophilic granulomatosis with polyangiitis (Churg–Strauss syndrome)
- Sarcoïdosis
- Rheumatoid arthritis
- Relapsing polychondritis
- Sjögren’s syndrome
- Mixed connective tissue disease
- Undifferentiated connective tissue disease.

**Autoimmune diseases can involve the following intrathoracic structures**
- Airways
- Intrathoracic blood vessels
- Lung parenchyma
- Pleura
- Respiratory muscles
- Heart and pericardium
- Bony cage of thorax.
Dermatological manifestations in granulomatosis with polyangiitis

- Necrotic ulcers – usually on the lower extremities
- Palpable purpura (raised dark spots due to small-vessel vasculitis) usually on the lower extremities\(^\text{[16]}\)
- Nodules, papules, and vesicles
- Pyoderma gangrenosum (rare)
- Reynaud’s phenomenon (rare)
- Mouth ulcers and gingivitis.

Dermatological manifestations in eosinophilic granulomatosis with polyangiitis

- Palpable purpura (most often seen on the lower extremities)\(^\text{[17]}\)
- Subcutaneous nodules (often on the limbs or scalp)
- Urticaria and urticaria-like rashes
- Livedo reticularis.

Respiratory manifestations in eosinophilic granulomatosis with polyangiitis

Most of these patients present with asthma, often with onset during adulthood. Asthma is often severe in these patients. Other respiratory manifestations include sinusitis; hemoptysis and transient patchy infiltrates may be seen in chest X-ray.\(^\text{[17]}\)

Dermatological manifestations specific to sarcoidosis

- Lupus pernio
- Macular sarcoidosis
- Plaque sarcoidosis
- Subcutaneous nodular sarcoidosis (Darier–Roussy sarcoid).\(^\text{[18]}\)

Nonspecific dermatological manifestations in sarcoidosis

- Erythema nodosum (EN) (particularly in the early stages of sarcoidosis)\(^\text{[18]}\)
- Nummular eczema
- Erythema multiforme
- Calcinosus cutis
- Pruritus.

Miscellaneous conditions involving skin and lungs

- Anaphylaxis/hypersensitivity reactions
- Drug reactions – Skin lesions and bronchospasm/ Stevens–Johnson syndrome
- Asthma–eczema–urticaria–atopic dermatitis can co-exist in varying combinations
- Viral exanthematous fever with viral pneumonia
- Fat embolism – petechial rash
- Alpha-1 antitrypsin deficiency – Panniculitis.

Erythema nodosum

EN is characterized by painful red, rounded lumps which most commonly appear on the shins and around the ankles. The common causes include streptococcal sore throat, sarcoidosis, fungal diseases, viral infections, sulfa drugs, and TB [Figures 14 and 15].

Skin changes due to drugs used to treat respiratory diseases

Antibiotics used to treat respiratory infection can lead to skin rashes as a manifestation of drug allergy, the most common drug being penicillin group.\(^\text{[19]}\)

Antitubercular drugs can lead to skin rashes, purpura due to thrombocytopenia, and other hypersensitivity manifestations in the skin.\(^\text{[19]}\)

Immunosuppressant drugs used to treat autoimmune diseases, antimalignancy drugs, and long-term use of systemic steroids can lead to fungal or bacterial skin infections. Long-term use of systemic steroids can lead to the typical appearance of Cushing’s syndrome which can be diagnosed at a glance. Fluoroquinolones, tetracycline, and epidermal growth factor receptor inhibitors can lead to drug-induced photosensitivity.

Skin and soft-tissue swellings in the chest wall may lead to abnormal chest radiograph. Physical examination will confirm the cause in these cases.

Conclusions

A variety of conditions/diseases can manifest with skin and lung involvement. Knowledge regarding these conditions will help in early diagnosis and treatment which may improve the outcome.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Reviron-Rabec L, Girerd B, Seferian A, Campbell K, Brosseau S, Bergot E, et al. Pulmonary complications of Type 1 neurofibromatosis. Rev Mal Respir 2016;33:460-73.
2. Dupuis-Girod S, Cottin V, Shovlin CL. The lung in hereditary hemorrhagic telangiectasia. Respiration 2017;94:315-30.
3. Maldonado F, Tazelaar HD, Wang CW, Ryu JH. Yellow nail syndrome: Analysis of 41 consecutive patients. Chest 2008;134:375-81.
4. Happle R. Hornstein-Birt-Hogg-Dubé syndrome: A renaming and reconsideration. Am J Med Genet A 2012;158A: 1247-51.
5. Pyeritz RE. Ehlers-Danlos syndrome. N Engl J Med 2000;342:730-2.
6. Corsico AG, Grossa A, Tripol B, Albicini F, Gini E, Mazzetta A, et al. Pulmonary involvement in patients with Marfan syndrome. Panminerva Med 2014;56:177-82.
7. Chhabra SK, Gupta RK, Singh T. Cutis laxa and pulmonary emphysema. Indian J Chest Disease Allied Sci 2001;43:237.
8. Rullán J, Seijo-Montes E, Vaillant A. Cutaneous manifestations of pulmonary disease. In: Sánchez N, editor. Atlas of Dermatology in Internal Medicine. New York: Springer; 2012. p. 19-29.
9. Weller R. Clinical Dermatology. 5th ed.. Oxford: John Wiley and Sons; 2015.
10. Habif T, Clinical Dermatology: A Colour Guide to Diagnosis and Therapy. 6th ed.. St Louis: Saunders; 2016.
11. Owen CE. Cutaneous manifestations of lung cancer. Semin Oncol 2016;43:366-9.
12. Martínez-Lavin M. Exploring the cause of the most ancient clinical sign of medicine: Finger clubbing. Semin Arthritis Rheum 2007;36:380-5.
13. Dreizen S, Dhirgra HM, Chiuten DF, Umsawasdi T, Valdivieso M. Cutaneous and subcutaneous metastases of lung cancer. Clinical characteristics. Postgrad Med 1986;80:111-6.
14. Rigopoulos D, Larios G, Katsambas A. Skin signs of systemic diseases. Clin Dermatol 2011;29:531-40.
15. Cojocaru M, Cojocaru IM, Silosi I, Vrabie CD. Pulmonary manifestations of systemic autoimmune diseases. Maedica (Buchar) 2011;6:224-9.
16. Francès C, Du LT, Piette JC, Saada V, Boisnic S, Wechsler B, et al. Wegener’s granulomatosis. Dermatological manifestations in 75 cases with clinicopathologic correlation. Arch Dermatol 1994;130:861-7.
17. Schwartz RA, Churg J. Churg-Strauss syndrome. Br J Dermatol 1992;127:199-204.
18. Tchernev G. Cutaneous sarcoidosis: The “great imitator”: Etiopathogenesis, morphology, differential diagnosis, and clinical management. Am J Clin Dermatol 2006;7:375-82.
19. Abrams EM, Khan DA. Diagnosing and managing drug allergy. CMAJ 2018;190:E532-8.