Ward Rounds in DERMATOLOGY
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Bela J Shah  MD
Professor and Head
Department of Dermatology,
Sexually Transmitted Infection (STI) and Leprosy
BJ Medical College and Civil Hospital
Ahmedabad, Gujarat, India

Santosh Rathod  MD (Skin and VD) DNB
Associate Professor
Department of Dermatology
Smt Nathiba Hargovandas Lakhmichand (NHL)
Municipal Medical College and VS Hospital
Ahmedabad, Gujarat, India

Foreword
Sudhir Pujara

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Dedicated to
My father, Late Sree Jaswantlal Shah; my mother, Vanlila J Shah; my husband, Ushir Mashruwala; and my son, Soham Mashruwala

—Bela J Shah

Three lovely ladies of my life: My mother, Manjula; my wife, Archana; and my daughter, Kanvi

—Santosh Rathod
Ward Rounds in Dermatology by Bela J Shah and Santosh Rathod, provides a refreshing view of several clinical presentations that generally require admission, and discusses all the diagnostic aspects and management in great details.

Dedicated chapters on immunosuppressives, corticosteroids, antibiotics and signs in dermatology make reading interesting. Discussion on recent aspects (e.g. in relation to autoimmune-blu**stering disorders) improves the already rich value of the book.

The book contains practically everything one would want to know about common, and some not-so-common clinical situations. It elaborates the theoretical discussions (which one would have anyway read elsewhere to build up the conceptual framework) and provides enough practical details.

This work by two accomplished dermatologists would serve as a quick-reference source to recapitulate what one has already learned earlier; but it is not just a compilation of facts, it is much more.

Dr Santosh Rathod has been known to me as a well-read doctor. I had a pleasure of being Dr Bela's postgraduate examiner for MD degree. She had already demonstrated her potential then. I have also worked with her on some projects. I have always appreciated her dedication while working with her.

Sudhir Pujara  
MD DVD DDV (Bom)  
Formerly, Professor and Head  
Department of Dermatology  
Smt Nathiba Hargovandas Lakhmichand (NHL)  
Municipal Medical College  
Ahmedabad, Gujarat, India
Preface

Dermatology is a branch of medicine which caters mainly to outdoor patients. Compared to outdoor patients, dermatologists have less workload as far as indoor patients are concerned. The management of indoor patients takes a backseat many a times.

Patients with skin failure need to be monitored round the clock. We have been using dexamethasone cyclophosphamide pulse (DCP) therapy and biologics. This requires admission of the patients in the ward.

Every morning for every admitted patient, we have to have our own checklist which will help us to manage the indoor patients effectively.

We have included all the aspects of history-taking in dermatology in the book. This book is a culmination of knowledge gathered from standard textbooks/journals and authors’ own experience. The information has been produced in the form of questions and answers to guide the residents in their postgraduate examinations. The chapter on the drugs is a concise synopsis for a quick revision. At the end, a chapter on frequently asked questions (FAQs) in examinations is included in the complete question-answer format.

Ward Rounds in Dermatology is essentially designed and aimed to help the beginners and the practitioners alike.

We hope that you all will appreciate our hard work, and the book makes reading enjoyable.

Bela J Shah
Santosh Rathod
The book is an amalgamation of the experience gained in clinical practice for over the last 28 years (Dr Bela J Shah), and of an extensive study. We are grateful to a number of people, who have helped us during preparation of the script, without whom this journey would have been impossible.

First and foremost, I (Bela J Shah) thank my revered teacher Dr Bharat H Shah, who has been a great guide, philosopher and teacher par excellence. With his blessings only I am able to pen down this book.

We would like to acknowledge the efforts of our postgraduates who were involved at every stage. We thank our residents, Drs Uzzaif Mansuri, Ankan Gupta, Sonal Patel, Suyog Dhamale, Darshan Karia and Sonal Tibrewal for their untiring efforts. We would also like to acknowledge the efforts made by the residents of LG Hospital, Ahmedabad, Gujarat, India, especially Dr Shikha Shivhare.

We are grateful to M/s Jaypee Brothers Medical Publishers (P) Ltd, New Delhi, India, for their continued support in publishing this book.

Lastly, we are thankful to the Almighty who helped us at every step.
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PYODERMA GANGRENOSUM

CHIEF COMPLAINTS
- History of recurrent ulcerations since past 8 years
- Episodes of blood in stool off and on since past 4–5 years
- Aggravation of complaints with new lesions since past 15 days.

HISTORY OF PRESENT ILLNESS
A 21-year-old male presented with history of recurrent painful erythematous nodules on his right foot which ulcerated and rapidly enlarged associated with pus discharge 8 years back. Few more nodules appeared on left leg which also ulcerated and healed with scarring 4–5 years back. At present, the patient came with complaint of lesions with similar morphology since past 15 days developed over left buttock, pubic region, left forearm and face.

Patient had history of loose motions with blood and mucus off and on since past 4–5 years.

History of fever, mild grade off and on not associated with chills and rigors or evening rise and relieved by medications. No history of:
- Joint pain
- Weight loss
- Abdominal pain
- Photosensitivity
- Pedal edema
- Dryness of mouth or eyes.

Treatment History
The patient was admitted previously for the similar complaint 4 years back when he was given steroids and capsule cyclosporine 100 mg twice daily. He was then maintained on tablet dapsone 100 mg at night for 3 years and was symptom free. He stopped treatment thereafter and after 1 year he relapsed with new ulcers and was admitted for the same once again.

There was no response to treatment with various antibiotics and low doses of steroids taken from outside before getting admitted.

No history of smoking or alcohol addiction. No history of diabetes mellitus (DM), hypertension (HTN), tuberculosis (TB) or any other major surgical or medical illness. Family history was not significant.

PHYSICAL EXAMINATION
Cutaneous examination showed multiple ulcers, varying in size from 4 to 15 cm and present on left cheek, left forearm and left buttocks and mons pubis region (Figs 14.1 to 14.3). Borders were well defined, elevated,
Fig. 14.1  Crusted lesion with scarring in the edges in pyoderma gangrenosum

Fig. 14.2  Necrotic ulcer with surrounding erythema over left thigh

Fig. 14.3  Single pustular lesion with ulceration in the center and surrounding erythema. Cribriform scarring from ulceration in the past
violaceous and edges were undermined. Floor was covered with slough and bloody discharge. Single fixed, tender swelling overlying the right parotid region was also noted.

Systemic examination was normal.

Investigations revealed Hb of 11 g%, total leukocyte count (TLC)-24000/cu.mL, differential leukocyte count-normal range (DLC-N) 69%, L 31% and erythrocyte sedimentation rate (ESR) 72 mm in first hour. Fasting blood sugar was 76 mg%. Total serum protein and serum albumin were 5.6 g% and 2.0 g respectively. Serum bilirubin was 1.0 mg%, serum glutamate oxaloacetic transaminase (SGOT)-34 IU/mL, serum glutamate pyruvate transaminase (SGPT)-45 IU/mL. Screen for human immunodeficiency virus (HIV) and hepatitis was negative.

Mantoux and pathergy tests were negative.

Rheumatoid factor was also negative.

Chest X-ray was normal. Pus and stool culture were sterile.

Skin biopsy from the edge of the ulcer showed lymphocytic vasculitis, extravasation of RBCs and abscess formation in the dermis consistent with pyoderma gangrenosum (PG). Colonoscopy revealed red colonic mucosa with multiple diffuse ulcerations and erosions. There were multiple pseudopolyps over upper rectum and lower sigmoid colon.

Colonic biopsy was not done.

Q.1. How will you investigate a case of pyoderma gangrenosum?

Ans. Pyoderma gangrenosum is a diagnosis of exclusion because no specific criteria have been determined to confirm the diagnosis. All other potential causes of similar lesions must be excluded prior to making the diagnosis.

Q.2. How will you manage a case of pyoderma gangrenosum?

Ans. Patient was started on treatment with dexamethasone 1.5 cc IV once in the morning, ranitidine 150 mg bid and dapsone 100 mg along with antibiotics. Local care of ulcers included potassium permanganate soaks and dressings with topical antimicrobial agents.

The ulcers started healing within 4 weeks of starting treatment. The dose of steroid was gradually tapered and shifted to oral prednisolone and all other drugs were continued in the same dosage. All the ulcers completely healed 3 months after starting the treatment (Figs 14.4 and 14.5).

The treatment of PG is mostly unsatisfactory. The aim is to treat the underlying disease.

Numerous modes of treatment have been tried with varying outcomes.

More frequently used treatments include:
- Topical, intralesional oral, and pulse steroid therapy
- Cyclophosphamide
- Azathioprine
- Antibiotics
- Sulpha drugs
- Dapsone
- Clofazimine
- Minocycline

Fig. 14.4 Two weeks post-treatment
• Cyclosporine
• And intensive local treatment
• Cyclosporine has been reported as a very effective drug for PG in the dose of 6–10 mg/kg/day with healing in 1–3 months.

Q.3. Which systemic conditions are associated with pyoderma gangrenosum frequently?
Ans. Associated systemic diseases reported are:
• Ulcerative colitis
• Crohn’s disease
• Rheumatoid arthritis
• Seronegative arthritis
• Hematologic malignancies
• Collagen vascular diseases
• Monoclonal gammopathy
• Hepatic and pancreatic diseases
• Wegener’s granulomatosis and
• Other neutrophilic dermatosis.

Q.4. What is the prevalence of PG with ulcerative colitis?
Ans. The prevalence of PG associated with ulcerative colitis has been reported to range from 30 to 60%.
Symptoms of ulcerative colitis may precede, follow or be concomitant with PG.
Q.5. Which differential diagnosis to be considered in a case suspected with pyoderma gangrenosum?

Ans.
- Antiphospholipid antibody syndrome
- Anthrax
- Arterial insufficiency
- Acute febrile neutrophilic dermatosis (Sweet syndrome)
- Blastomycosis
- Factitial dermatitis
- Traumatic ulceration
- Tuberculosis gumma
- Hidradenitis suppurativa
- Insect bites
- PAPA syndrome
- Sporotrichosis
- Squamous cell carcinoma
- Venous insufficiency
- Verrucous carcinoma
- Wegener granulomatosis
- Atypical mycobacterial infections.

ANTIPHOSPHOLIPID ANTIBODY SYNDROME

A 33-year-old female presented with blackish discoloration of fingers, toes and lower leg since 1 month. It started as multiple flat reddish lesions over the finger tips and gradually progressed to become confluent. Then fingers, toes, feet and even lower legs were involved. Patient had history of fever since 8 months. Five months ago, she had transient loss of vision that lasted for two days. She had a history of three consecutive miscarriages all in her first trimester. There was no history of any precipitating factor like drug intake, smoking, use of oral contraceptives, any chronic disease or peripheral vascular disease.

PHYSICAL EXAMINATION

Her general condition was poor with temperature 101°F, pulse rate 90/minute and blood pressure 122/78 mm Hg. Some of her nails showed subungual hemorrhages.

CUTANEOUS EXAMINATION

Blackish discoloration of all fingers, toes, soles in a pattern of socks (Figs 14.6 and 14.7).

Fig. 14.6 Symmetrical gangrenous changes on fingers and toes
Laboratory Investigations

Investigations revealed anemia, elevated total leukocyte count, platelet count and erythrocyte sedimentation rate. Activated partial thromboplastin time and prothrombin time were also mildly elevated. Peripheral smear revealed neutrophilic leukocytosis with marked thrombocytosis. Serum electrolytes, renal function tests, chest radiography, ultrasound abdomen, blood culture, fundus examination and echocardiography were normal. Antinuclear antibody profile was negative. Skin biopsy revealed vascular thrombosis, dermal hemorrhage, obliterating endarteritis and epidermal necrosis. Anticardiolipin antibody IgG, IgM were positive in high titers. The lupus anticoagulant test was positive. In view of the clinical and laboratory findings, a final diagnosis of APS was made.

Q.6. What is antiphospholipid antibody syndrome?

Ans. Antiphospholipid syndrome or APS is an autoimmune condition which is characterized by recurrent arterial or venous thrombosis and/or poor pregnancy outcomes in the persistent presence of circulating antiphospholipid antibodies (aPL). Based on the presence or absence of underlying etiology, it can be primary or secondary APS.

Conditions associated with APS

<table>
<thead>
<tr>
<th>Immunosuppressive/Anti-inflammatory</th>
<th>Antiproliferative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common autoimmune or rheumatic diseases with aPL</td>
<td>SLE, Sjögren syndrome, rheumatoid arthritis, autoimmune thrombocytopenic purpura, autoimmune hemolytic anemia, psoriatic arthritis, systemic sclerosis, mixed connective-tissue disease, polymyalgia rheumatic, giant cell arteritis, Behçet syndrome.</td>
</tr>
<tr>
<td>Infections</td>
<td>Syphilis, hepatitis C infection, HIV infection, human T-cell lymphotrophic virus type 1 infection, malaria, bacterial sepsis.</td>
</tr>
<tr>
<td>Drugs</td>
<td>Cardiac—procainamide, quinidine, propranolol, hydralazine. Neuroleptic or psychiatric—phenytoin, chlorpromazine. Other—interferon alfa, quinine, amoxicillin</td>
</tr>
</tbody>
</table>

Q.7. What are the clinical manifestations of antiphospholipid syndrome?

Ans.

- **Venous or arterial thrombosis**: Involving the cerebrovascular system, coronary arteries, pulmonary emboli or thromboses, hepatic or renal veins, ocular veins or arteries
- **Recurrent abortions or premature births or even pre-eclampsia in pregnancy**
- **Skin disorders**: Livedo reticularis, splinter hemorrhages, leg ulcers, superficial thrombophlebitis, blue toe syndrome, vasculitis involving medium-sized and small vessels (Fig. 14.8)
- **Neurological defects**: Migraine headaches, seizures, multi-infarct dementia
- **Cardiac abnormalities**: Heart murmur, cardiac valve vegetations
- **Blood abnormalities**: Thrombocytopenia, hemolytic anemia
Q.8. What are the cutaneous manifestations of APS?

Ans.
- Livedo reticularis
- Sneddon’s syndrome
- Skin ulcers
- Necrotizing vasculitis
- Livedoid vasculitis (Figs 14.9A and B)
- Cutaneous gangrene
- Superficial thrombophlebitis
- Pseudovasculitic lesions: Nodules, papules, pustules, palmar–plantar erythema
- Subungual bleeding
- Anetoderma

Q.9. What are the diagnostic criteria for APS?

Ans. In 1999 an International Workshop issued the first Consensus Statement on preliminary classification criteria for definite APS. The classification criteria were revised in 2006 (revised Sapporo criteria) and definite APS was the presence of at least one of the clinical and one of the laboratory criteria as outlined in table below.

<table>
<thead>
<tr>
<th>Clinical Criteria</th>
<th>Laboratory Criteria</th>
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<tbody>
<tr>
<td>Vascular Thrombosis</td>
<td>1. Lupus anticoagulant present in plasma, on two or more occasions, at least 12 weeks apart, detected according to the guidelines of the International Society on Thrombosis and Hemostasis (Subcommittee on Lupus Anticoagulants/Antiphospholipid Antibodies).</td>
</tr>
<tr>
<td>Pregnancy Morbidity</td>
<td>2. aCL of IgG and/or IgM isotype in serum plasma, present in medium or high titer on two or more occasions, at least 12 weeks apart, measured by a standardized ELISA.</td>
</tr>
<tr>
<td></td>
<td>3. Anti-β2GPI of IgG and/or IgM isotype in serum or plasma (titer &gt;99th percentile) on two or more occasions, at least 12 weeks apart, measured by a standardized ELISA according to recommended procedures.</td>
</tr>
</tbody>
</table>
Q.10. What is the treatment of antiphospholipid syndrome?
Ans. Risk factors for thrombosis should be identified and removed or corrected, for example, smoking, oral contraceptives, high blood pressure or elevated blood fats.

Treatment involves primary thromboprophylaxis and secondary management of thromboembolism.
1. Primary thromboprophylaxis with low dose aspirin is given in all patients with APS and no thrombotic events.7
2. Secondary thromboprophylaxis is the treatment started after any thrombotic episode to prevent further attacks. Lifelong warfarin keeping the INR between 2 and 3 to avoid hemorrhagic complications is the current recommendation. During pregnancy, low-molecular weight heparin is used.8 Other antiplatelet agents like dipyridamole, ticlopidine or clopidogrel9 and even intravenous immunoglobulin10 have been used for secondary thromboprophylaxis.

POLYARTERITIS NODOSA

CHIEF COMPLAINTS

- Multiple raw areas in both the lower limbs for four months
- Blackish discoloration of the left index finger for two-months and
- Constitutional symptoms like fever, malaise and multiple joint pains for two months.
HISTORY OF PRESENT ILLNESS

A twenty six-year-old female presented with history of fever, multiple joint pains along with few painful subcutaneous nodules with ulcerations in both the lower limbs for four months, and blackish discoloration of the left index finger for two-month duration. There was no history of purpura, Raynaud’s phenomenon, recurrent oral ulcers, hair loss, malar rash. No history of jaundice or tuberculosis in past.

GENERAL PHYSICAL EXAMINATION

Her vitals were within normal limits.

CUTANEOUS EXAMINATION

Few punched out ulcerations with surrounding livedo reticularis predominantly over both the legs and dorsum of feet and bluish black discoloration of distal phalanx of the left index finger.

LABORATORY INVESTIGATIONS

Complete blood count showed leukocytosis. The renal function and liver function tests were normal. Anti-streptolysin O (ASLO) titer, ESR and CRP were raised. Other immunological tests including ANA, ANCA, APLA, lupus anticoagulant, rheumatoid factor, HIV, HBsAg and HCV were negative. The throat and urine culture showed no growth of bacteria. The echocardiography and ultrasonography of the abdomen and pelvis were normal. The deep skin biopsy taken from the subcutaneous nodule showed leukocytoclasic vasculitis of the dermal vessels suggestive of cutaneous PAN. The patient was treated with methyl prednisolone (three pulses doses of 750 mg/day) followed by oral prednisolone of 1 mg/kg/day. She also received a course of oral penicillin for antecedent streptococcal throat infection. The skin lesions completely healed over a period of five months with scarring, and patient is on regular follow up since then.

Q.11. What is polyarteritis nodosa (PAN)?

- Polyarteritis nodosa (cPAN) is a necrotizing inflammation of medium to small vessels leading to microaneurysm formation, aneurysmal rupture with hemorrhage, thrombosis, and, ultimately, organ ischemia or infarction.
- PAN, like other vasculitides, affects multiple systems and has multiple manifestations, although it most commonly affects skin, joints, peripheral nerves, the gut, and the kidney.\(^\text{11}\)
- Cutaneous PAN is usually said to be PAN affecting the skin with no major organ involvement but in which mild fever, muscle, joint and peripheral involvement may also occur.\(^\text{12-14}\)
- Classic PAN or systemic PAN patients have multi-organ involvement along with constitutional symptoms like fever and weight loss.

Q.12. What is the etiology of PAN?

- The exact etiology of CPAN is not known, but immune complex mediated disease plays a role in etiopathogenesis.
- Various infections like Streptococcus, Parvovirus B19, Mycobacterium, hepatitis viruses B and C and noninfectious conditions like connective tissue diseases (systemic lupus erythematosus, rheumatoid arthritis), Wegener’s granulomatosis and Churg-Strauss syndrome have been associated both with initiation and relapse of the disease.\(^\text{15-17}\)

Q.13. What are the clinical features of cutaneous polyarteritis nodosa?

- Clinical features in PAN are due to inflammation of small and medium sized vessels causing thrombosis and finally vascular occlusion. This process occurs in several organs including skin. The disease has periods of activity and remission.
- Vasculitic lesions are most often found on the legs and feet. Other areas that may be affected include the arms, trunk, buttocks, and head and neck. They are most likely on pressure points such as the knees, back of the foot and lower leg.
- The most common findings are:
  - Palpable purpura
  - Livedo racemosa
  - Retiform purpura and
  - Punched-out ulcers.
- Painful subcutaneous nodules, digital infarcts and gangrene are less commonly seen in classic PAN.
Q.14. How is cutaneous polyarteritis nodosa diagnosed?
• There are no specific clinical and laboratory findings.
• A deep incisional biopsy, including subcutaneous tissue, is required for the definitive diagnosis of the disease. The characteristic pathologic feature is a leukocytoclastic vasculitis in the small to medium sized arterioles of the deep dermis or hypodermis with or without associated fibrinoid necrosis.18
• Immunological testing does not help in confirming the diagnosis of cPAN, however, they help to rule out other severe forms of vasculitis.

Q.15. What is the differential diagnosis of PAN?
• Cryoglobulinemic vasculitis
• Autoimmune connective tissue disease
• MPA
• Wegener’s granulomatosis
• Churg-Strauss syndrome
• Fibromuscular dysplasia
• Atherosclerosis
• SLE
• Cholesterol emboli
• Neurofibromatosis
• Ehlers–Danlos syndrome
• Emboli from infective endocarditis and
• Left atrial myxoma
• Cholesterol emboli
• Antiphospholipid syndrome.

Q.16. What is the treatment for cutaneous polyarteritis nodosa?
• Milder cases of cPAN are treated symptomatically with NSAIDs and a course of antibiotic for antecedent streptococcal infection.
• Severe cases definitely require systemic steroids and even immunosuppressives like cyclophosphamide, methotrexate or azathiprine.
• Intravenous immunoglobulins and biologics (etanercept, infliximab and rituximab) have been tried with good results.10,19
• For hepatitis B–related PAN, treatment consists corticosteroids with antiviral agents and plasmapheresis.

GRANULOMATOSIS WITH POLYANGIITIS (GPA)/WEGENER’S GRANULOMATOSIS

A 55-year-old man presented with bloody discharge from the nose with nasal obstruction and pain, and a reddish swelling near the right nostril for four months. The disease started insidiously with a gradually increasing obstruction of the right side of nasal cavity and a scanty blood-stained serous discharge followed by crusting. Subsequently, the patient developed redness and swelling inside the oral cavity over the hard palate which was causing discomfort while swallowing food. He had history of fever which was associated with weakness since past few months. No complaint of any specific symptoms referable to other systems apart from recurrent upper respiratory tract infections. No family history of a similar or related illness was reported. No history of smoking or alcohol addiction. No history of diabetes mellitus (DM), hypertension (HTN), tuberculosis (TB) or any other major surgical or medical illness. Not significant (Figs 14.10 to 14.12).

Q.17. How to take relevant history of a case of Wegener’s granulomatosis?
Ans. Wegener’s granulomatosis has a spectrum of clinical presentations that includes recurrent respiratory infection in adults and upper and lower respiratory tract involvement in children. In addition, patients may report the following chronic, nonspecific constitutional complaints:
• Fever, night sweats
• Fatigue, lethargy
• Loss of appetite
• Weight loss.

Ophthalmic manifestations
• Conjunctivitis
• Episcleritis
Fig. 14.10 Nodule on the right nostril

Fig. 14.11 Polypoid growth over the palate

Fig. 14.12 Palatal perforation in case of Wegener's granulomatosis
• Uveitis
• Optic nerve vasculitis
• Retinal artery occlusion
• Nasolacrimal duct occlusion
• Proptosis.

_Ear, nose, and throat manifestations_
Chronic sinusitis is the most common initial complaint, occurring in 67% of cases; failure to respond to conventional treatment is suggestive. Other ENT manifestations are as follows:
• Rhinitis (22%)\(^{20}\)
• Epistaxis (11%)\(^{20}\)
• Collapse of nasal support, resulting in saddle nose deformity (common)
• Serous otitis media and hearing loss
• So-called strawberry gingival hyperplasia
• Stridor, possibly leading to respiratory compromise, from tracheal or subglottic granulomatous masses.

**PULMONARY**
Pulmonary involvement in GPA can be asymptomatic, insidious in onset, or severe and fulminant. Pulmonary disease may cause any of the following:
• Pulmonary infiltrates (71%)
• Cough (34%)
• Hemoptyis (18%)
• Chest discomfort (8%)\(^{20}\)
• Dyspnea (7%)\(^{20}\)
• Diffuse alveolar hemorrhage due to alveolar capillaritis (5–45%)\(^{21}\)
• Atelectasis, with dullness on percussion, decreased breath sounds, and crackles on auscultation.

**Musculoskeletal Manifestations**
• Myalgias
• Arthralgias, usually polyarticular and symmetrical, affecting small and medium joints
• Arthritis, typically affecting large joints, but rarely deforming.

**Renal Manifestations**
• Crescentic necrotizing glomerulonephritis characterized by urinary sediment with more than 5 RBCs per HPF or erythrocyte casts
• Renal disease is present in 17% of patients at initial diagnosis and is usually asymptomatic\(^{22}\)
• Renal failure occurs in 11% at presentation.\(^{20}\)

**Nervous System Manifestations**
Peripheral nervous system (PNS) involvement may occur in as many as 67% of patients, typically later in the disease course, and includes the following:
• Mononeuritis multiplex
• Sensorimotor polyneuropathy
• Cranial nerve palsies.
The CNS manifestations include vasculitis of small to medium-sized vessels of the brain or spinal cord and granulomatous masses that involve the orbit, optic nerve, meninges, or brain.\(^{23}\)

**Cutaneous Manifestations**
• Cutaneous findings are variable and nonspecific and usually affect the lower extremities
• Palpable purpura or skin ulcers (45%);\(^{20}\) ulcerations may resemble pyoderma gangrenosum
• Petechiae, vesicles, pustules, hemorrhagic bullae, livedo reticularis, digital necrosis, subungual splinter hemorrhages, and genital ulcers resembling squamous cell carcinoma have been reported.
Additional systemic findings:
- Cardiac: Pericardial rub, myocardial infarction, or sudden death
- Gastrointestinal: Abdominal pain may be present with splanchnic vasculitis.

Physical Examination

Pulmonary/Respiratory System

Atelectasis: May be present, with examination findings of dullness on percussion, decreased breath sounds, and cracks on auscultation.

Lower respiratory tract involvement: May also produce signs of pulmonary consolidation and/or pleural effusion.

Tracheobronchial disease: May manifest as hoarseness, cough, dyspnea, stridor, and wheezing.

Subglottic or tracheal stenosis: May also manifest as stridor; stenosis may prove fatal if untreated.

Hemoptysis—may result from cavitated pulmonary parenchymal lesions, DAH, or bronchiectasis.

Cutaneous Examination

Cutaneous findings are variable and nonspecific and usually affect the lower extremities. Palpable purpura, papules, subcutaneous nodules, and ulcerations are the most common findings. Ulcerations may resemble pyoderma gangrenosum.

Petechiae, vesicles, pustules, hemorrhagic bullae, livedo reticularis, digital necrosis, subungual splinter hemorrhages, and ulcers resembling squamous cell carcinoma have been reported.

General examination: Patients may be febrile and appear ill.

Cardiovascular system: Pericardial rub may occur with pericarditis.

Gastrointestinal system: Abdominal pain may be present with splanchnic vasculitis.

Musculoskeletal examination: Large- and medium-joint arthritis; polyarticular, symmetrical small- and medium-joint arthropaligias; and myalgias may be appreciated.

Nervous system: Examination of the nervous system may confirm a pattern of mononeuritis multiplex, polyneuropathy, or cranial nerve paralysis.

Q.18. How to investigate a suspected case of Wegener’s granulomatosis?
Ans. Routine laboratory tests are nonspecific in granulomatosis with polyangiitis (GPA). Elevated blood urea nitrogen (BUN) and creatinine levels may signal renal involvement.

ESR and C-reactive protein (CRP) levels are elevated in 90% of patients with active and generalized disease. They may decrease in response to treatment.

Q.19. What is ANCA?
Ans. Anti-neutrophil cytoplasmic antibodies (ANCAs) are a group of autoantibodies, mainly of the IgG type, against antigens in the cytoplasm of neutrophil granulocytes (the most common type of white blood cell) and monocytes.

The discovery of ANCA within neutrophils in the majority of patients with GPA suggested the role of humoral autoimmunity. GPA is usually associated with the presence of diffuse staining cytoplasmic ANCA (c-ANCA) directed against serine proteinase 3 antigen (PR3-ANCA), the so-called Wegener autoantigen.

The other ANCA associated vasculitis (AAVs) include microscopic polyangiitis, renal-limited vasculitis, and Churg Strauss syndrome (allergic granulomatous angiitis), which are more commonly associated with perinuclear-staining ANCA (p-ANCA) directed against myeloperoxidase (MPO-ANCA).

A pathogenic role for PR3-ANCA in GPA has been proposed, because PR3-ANCA is strongly associated with the disease; over 90% of GPA patients have been reported to have ANCA positivity during active disease. Longitudinal observations have indicated that relapse is sometimes heralded by a rise in PR3-ANCA titers, although other studies could not confirm these results.

The sensitivity of c-ANCA test was found to be 67% by immunofluorescence and 60% by ELISA for patients with active local or regional symptomatology. Hence, although a positive c-ANCA test is adjunctive evidence for the diagnosis of Wegener granulomatosis, the result must be viewed in the context of the patient’s clinical picture and disease activity.
CT scan: Findings on chest radiography are abnormal in two thirds of adults with GPA. The most common radiologic findings are single or multiple nodules and masses. Nodules are typically diffuse, and approximately 50% are cavitated.

Diffuse alveolar opacities due to diffuse alveolar hemorrhage (DAH), atelectasis, and obstructive pneumonia caused by bronchial stenosis may also be seen. Findings on computed tomography (CT) scans and high-resolution CT (HRCT) scans include consolidation, patchy or diffuse ground-glass opacities, or both.

Additional CT scan findings include stenoses of the larynx or tracheobronchial tree, bronchial wall thickening, bronchiectasis, pleural thickening or effusion, and lymphadenopathy.

Sinus CT scanning and radiography can be done for further evaluation.

Histopathological examination of biopsy: stained with H & E stain showed features of granulomatous infiltration with foci of necrosis. Evidence of vasculitis with fibrinoid degeneration was also noted in some sections.

The diagnosis of GPA is generally confirmed with tissue biopsy from a site of active disease and renal and lung biopsies are most specific for GPA. However, sampling error may occur, and histopathologic findings can be nonspecific. Tissue diagnosis may not be required if the clinical gestalt is convincing and a site for biopsy is not apparent or would be too invasive to obtain. Renal biopsy may be easier to perform than lung biopsy.

Q.20. What other differentials should be considered?
Ans. Other conditions to consider in the differential diagnosis of GPA include the following:

- Cocaine abuse
- Acute glomerulonephritis
- Crescentic glomerulonephritis
- Diffuse proliferative glomerulonephritis
- Membranoproliferative glomerulonephritis
- Membranous glomerulonephritis
- Poststreptococcal glomerulonephritis
- Rapidly progressive glomerulonephritis
- Lymphomatoid granulomatosis
- Malignancy
- Microscopic polyangiitis
- Pneumocystis jiroveci pneumonia
- Bacterial pneumonia
- Fungal pneumonia
- Polymyalgia nodosa
- Polychondritis
- Nasal-type primary NK/T-cell lymphoma (formerly known as lethal midline granuloma)
- Pyoderma gangrenosum
- Rhinoscleroma
- Sarcoidosis
- Systemic lupus erythematosus.

Q.21. What is granulomatosis with polyangiitis?
Ans. Granulomatosis with polyangiitis (GPA), formerly known as Wegener granulomatosis, is a rare multisystem autoimmune disease of unknown etiology. Its hallmark features include necrotizing granulomatous inflammation and pauci-immune vasculitis in small- and medium-sized blood vessels.

Q.22. How will you manage a case of GPA?
Ans. The mainstay of treatment for granulomatosis with polyangiitis (GPA) is a combination of corticosteroids and cytotoxic agents. Treatment should be tailored to appropriately treat GPA manifestations while minimizing long-term toxicities to the patient. Initial high-dose glucocorticoids (1 mg/kg/day) should be continued for at least 1 month. Doses should not be reduced to less than 15 mg/day within the first 3 months. The dose should then be slowly tapered to a maintenance dose of 10 mg/day or less during remission.

Approximately 90% of patients with GPA respond to cyclophosphamide, with approximately 75% experiencing complete remission. However, 30–50% of those who initially respond experience at least one relapse, requiring another course of therapy. Cyclophosphamide is given in combination with steroids.
The recommended daily oral dose of cyclophosphamide is 2 mg/kg/day (not to exceed 200 mg/day). Pulsed (intravenous) cyclophosphamide (15 mg/kg every 2 weeks for the first 3 pulses, then every 3 weeks for the next 3–6 pulses) is an alternative to daily oral cyclophosphamide; it results in less cumulative exposure to cyclophosphamide and, therefore, theoretically causes fewer adverse effects.

In 2011, however, the US Food and Drug Administration (FDA) approved the use of rituximab (a monoclonal antibody that targets B cells), in combination with glucocorticoids, as an alternative to cyclophosphamide for induction of remission in AAV (GPA and microscopic polyangiitis).29

Plasma exchange may be considered in patients with rapidly progressive renal disease (serum creatinine level >5.65 mg/dL) in order to preserve renal function.30

**SUBCUTANEOUS ZYGOMYCOSIS**

**CHIEF COMPLAINTS**

- Lesion in nasal cavity since 18 months
- Swelling over lip and face since 3 months
- Aggravation of swelling since 2 months.

**HISTORY OF PRESENT ILLNESS**

A 55-year-old male patient had history of trauma in the left side nasal cavity one and half year back by vegetative material. Following this the patient developed small papular non tender lesion at the site of trauma. The lesion progressed in size very slowly. No complaint of bleeding, discharge, respiratory symptoms were associated (Figs 14.13 and 14.14).

Patient did not give any history of prior surgery, any radiation treatment, or history/symptom of cellulitis. Patient had undergone excision for nasal lesion twice previously from various practitioners along with debridement.

**PHYSICAL EXAMINATION**

- Cervical lymphadenopathy was present.
- Systemic examination was normal.
- **Head and neck examination:** Facial swelling mainly involving forehead, nose, upper lip and malar region with small pox scars.
- Nasal septal perforation was present.

**Q.23. What is zygomycoses?**

**Ans.** The terms mucormycosis and zygomycosis are used interchangeably. Mucormycosis is an infection caused by fungi in the orders Mucorales and Entomophthorales. Previously, the term zygomycosis was

![Fig. 14.13 Pre-treatment—grotesque appearance of face in case of phaeohyphomycosis]
used to denote invasive fungal infections (IFIs) caused by the fungi belonging to the phylum Zygomycota, class Zygomyces, orders Mucorales and Entomophthorales. The Mucorales order contains 2 families—Mucoraceae and Cunninghamellaceae. Since the majority of human infections are caused by Mucorales fungi, the term Mucormycosis is now used to designate this infection.

Q.24. How to investigate a case of deep fungal infection?
Ans. Diagnosis requires deep skin biopsy from the subcutaneous mass for histopathology and for microscopy and fungal culture.

Culture reveals fast growing fungi characterized by primitive mostly aseptate hyphae. Culture at 30°C confirms which organism is involved: Conidiobolus sp. will grow white to grey waxy colonies and Basidiobolus sp. will grow cream or yellow waxy colonies.

Care needs to be taken during the biopsy not to damage the fungi because non-viable organisms result in a negative culture result.

Chest and abdominal X-ray to see dissemination is helpful.

CT scans with contrast, MRI and nasal endoscopy to see the extent of disease is also advisable.

Bronchoscopy with bronchoalveolar lavage and transbronchial biopsy provides adequate tissue to diagnose pulmonary mucormycosis.

CT-guided percutaneous lung biopsy may also be beneficial. Histology: Fixed tissue can be stained with hematoxylin and eosin (H & E). Fungal hyphae may be demonstrated with Grocott methenamine-silver stain or periodic acid-Schiff (PAS) staining. The typical appearance demonstrates the fungus as broad, nonseptate hyphae with acute right-angle branching.

Q.25. Enumerate the various types of mucormycosis?
Ans.
- Rhinocerebral mucormycosis
- Pulmonary mucormycosis
- Gastrointestinal mucormycosis
- Cutaneous mucormycosis
- Disseminated mucormycosis.

Q.26. What are the risk factors that can be associated with zygomycosis?
Ans. Most persons who develop mucormycosis are immunocompromised, although 15–20% of patients have no evidence of any underlying condition at the time of the diagnosis. The most common risk factors include the following:
- Stem cell transplantation
- Poorly controlled diabetes mellitus, either type 1 or type 2
- Hematologic malignancy (e.g. leukemias, lymphomas)
- Solid organ transplants
- Steroid use
- Metabolic acidosis
- Deferoxamine therapy
- Severe and prolonged neutropenia
- Intravenous drug use
- Renal failure
- Peritoneal dialysis
- Burns
- Penetrating trauma (rare).

Q.27. What differentials should be kept in mind when diagnosing a case of zygomycosis?

Ans.
- Actinomycosis
- Aspergillosis
- Brain abscess
- Cryptococcosis
- Nocardiosis
- Peptic ulcer disease
- Toxoplasmosis.

Q.29. Management of a case of zygomycosis?

Management of zygomycosis is described below:

Q.28. What are the other effective treatment measures?

Ans.
- Itraconazole: 400 mg/day for 8–12 weeks
- Oral KF: 500 mg TID for 6–12 weeks
- Fluconazole
- Hyperbaric oxygen therapy
- Combination of antifungals.

Q.30. What is the mortality rate of zygomycosis?

Ans. The overall mortality rate associated with zygomycosis is approximately 50% and has remained at this level for the past 50 years. Rhinocerebral zygomycosis carries a mortality rate of approximately 85%. Mortality rates are very high because, by the time zygomycosis is suspected and diagnosed, it has frequently spread diffusely and caused extensive tissue destruction. However, the risk of mortality varies depending on the characteristics of the host, the type of infection, the site of infection, and the use of surgical intervention. In general, antifungal therapy and surgical management independently decrease the likelihood of death.
REFERENCES


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