



body. When the forehead is affected, it is called sclérodemie en coup de sabre; this spreads to the scalp, leading to alopecia (Fig. 12.13). Linear scleroderma generally penetrates to deep sites. Lilac rings are rarely seen.

Pathogenesis

The pathogenesis is unknown. The disorder may be induced by external injury. Involvement of *Borrelia* infection has been reported recently.

Pathology, Laboratory findings

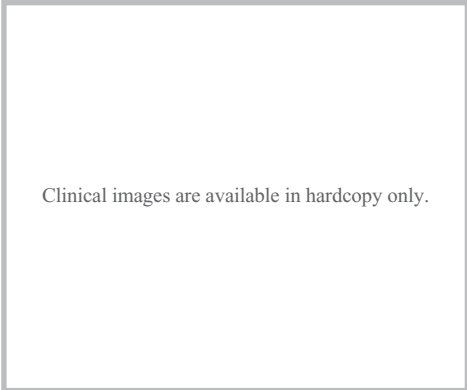
Localized scleroderma has a histopathology similar to that of SSc. The abnormal laboratory findings that are seen in SSc are not usually found in localized scleroderma. Rheumatoid factors and antinuclear antibodies may be present in generalized morphea.

Treatment

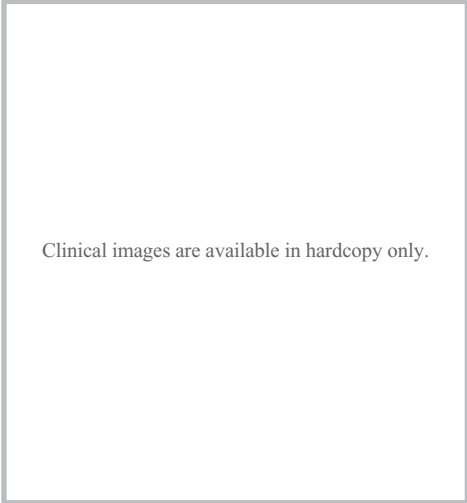
Steroids are topically applied or locally injected. Oral steroids may be administered for severe cases. If no spreading tendency is observed for a certain period of time, surgery may be considered.

Prognosis

Patients with localized scleroderma have a good life expectancy; however, the condition is usually chronic. Indurated patches gradually shrink, and abnormal pigmentation appears.



Clinical images are available in hardcopy only.



Clinical images are available in hardcopy only.

Fig. 12.13 Linear scleroderma with facial hemiatrophy.

Alopecia and sclerosis on the head. It resembles the slash of a sword. Atrophy occurs in the hypodermic scalp.

C. Other collagen diseases

1. Dermatomyositis (DM) ★ ★

Outline

- Heliotrope rash, Gottron’s sign and unique erythema and poikiloderma appear, and there is telangiectasia in the perionychia.
- Muscle weakness begins in the proximal muscles. Elevated levels of CPK, aldolase and urinary creatine reflect myositis.
- Malignant tumor commonly develops as a complication.
- Interstitial pneumonia may aggravate rapidly. The prognosis is poor.

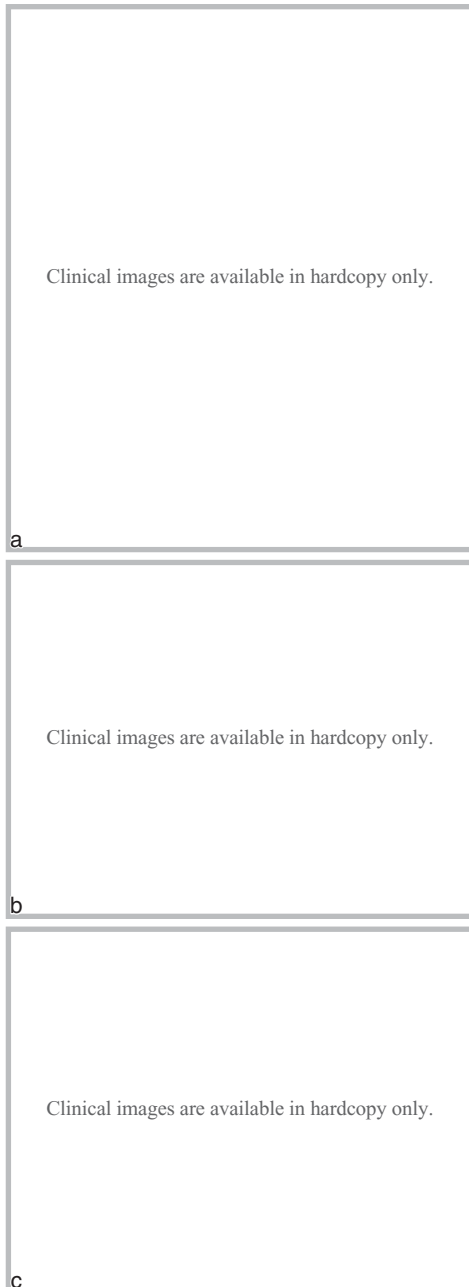


Fig. 12.14-1 Dermatomyositis (DM).

a: Diffuse, edematous erythema accompanied by itching on the trunk. b: Itchy erythema on the back. c: An atrophic, erythematous plaque on the knee.

- Steroids are the main treatment.

Epidemiology

There are fewer patients with dermatomyositis (DM) than with SLE or scleroderma. It most commonly occurs in adults aged 30 to 60 and in children, with a male to female ratio of 1 to 2. DM that does not cause cutaneous lesions is called polymyositis (PM).

Clinical features

Cutaneous symptoms: Edematous purplish-rose patches on the face, especially the eyelids (heliotrope rash), and flat elevated papules with scaling (Gottron's sign) on the extensor surface of fingers and joints are diagnostically significant (**Figs. 12.14-1** and **12.14-2**). Seborrheic dermatitis-like erythema on the cheeks and scalp often progresses to butterfly-rash-like skin lesions in children (**Fig. 12.15**). Intensely itching dermatitis-like diffuse edematous erythema appears on the neck and trunk, which sometimes shows linear distribution on the trunk and extremities (linear dermatitis). These eruptions cause abnormal pigmentation or depigmentation, skin atrophy, scaling and telangiectasia over time; they present as poikiloderma. Erythema in the perionychia and hair loss are also seen. Panniculitis resembling lupus erythematosus profundus may be produced.

Muscular symptoms: Muscle pain (spontaneous pain, tenderness, gripping pain) and weakness occur symmetrically in the trunk, the proximal regions of the extremities, and the neck. Disorder of the proximal muscles causes difficulties in ascending and descending stairs and other walking. Weakness of the pharyngeal muscle group may lead to dysphagia, dysphonia and respiratory disturbance.

Other symptoms: Raynaud's symptoms, multiple arthralgia, subcutaneous calcium deposition, pulmonary fibrosis, myocarditis and sometimes interstitial pneumonia occur.

Dermatomyositis in children: It may be caused secondarily after a vaccination or a viral or bacterial infection. Muscular symptoms are preceded by cutaneous symptoms (**Fig. 12.15**). Subcutaneous and muscular calcium deposition is found in 10% to 20% of all cases, frequently causing dyskinesia. It progresses rather chronically. Myoatrophy, articular contracture and subcutaneous calcium deposition are seen. Fever and muscular weakness may occur. The patients may die from multiple ulcers of the gastrointestinal tract.

Classification, Pathogenesis

Viral infection, autoimmunity, and allergy to malignant tumors or infection are known to be involved in DM; however, the pathogenesis is unknown.

Complications

Malignant tumor of the internal organs is found as a complication

in 30% to 40% of adult cases. The incidence is even higher when severe edema and intense itching are present. Stomach cancer, breast cancer, lung cancer and malignant lymphoma are frequently caused as complications. Malignant tumor is rarely seen as a complication in children.

Pathology

Edema in the upper dermal layer and mild thickening of the basement membranes (staining positive in PAS) are major findings in the early stages of erythematous eruptions. As the lesions progress, cutaneous atrophy, vacuolar degeneration of the basal cell layer, mucin deposition, telangiectasia, swelling of collagen fibers, lymphocytic infiltration and increase of histiocytes in the tissue are found, and these resemble the erythematous histology of SLE. Immunoglobulins and complement deposition on the skin are rarely seen. In muscle tissue biopsied from a painful site, myositis symptoms are present.

Laboratory findings

Nonspecific inflammatory reactions such as leukocytosis and

Table 12.7 Classification criteria for DM and PM.

Criteria	
1. Skin lesions	
(a) Heliotrope rash (red-purple edematous erythema on the upper palpebra)	
(b) Gottron's sign: purplish-red erythema accompanied by hyperkeratosis and atrophy on the dorsum of finger joints	
(c) Erythema on the extensor surface of extremity joints: slightly raised red-purple erythema over elbows or knees	
2. Proximal muscle weakness (upper or lower extremities and trunk)	
3. Elevated serum CK (creatine kinase) or aldolase level	
4. Muscle pain on grasping or spontaneously	
5. Myogenic changes in EMG (short-duration, polyphasic motor unit potentials with spontaneous fibrillation potentials)	
6. Positive anti-Jo-1 (histadyl tRNA synthetase) antibody	
7. Nondestructive arthritis or arthralgia	
8. Systemic inflammatory signs (fever: more than 37°C at axilla, elevated serum CRP level or accelerated ESR of more than 20 mm/h by the Westergren method)	
9. Pathological findings compatible with inflammatory myositis (inflammatory infiltration of skeletal evidence of active regeneration may be seen.)	
Diagnosis	
Dermatomyositis	Patients presenting at least one item from the first criterion and four items from the second through ninth criteria
Polymyositis	Patients presenting no items from the first criterion and at least four items from the second through ninth criteria
Differential Diagnosis	
Myositis caused by infections, drug-induced myopathy, myopathy resulting from endocrinopathy, muscular dystrophy, other congenital myopathies	

(Tanimoto K. et al. Classification criteria for polymyositis and dermatomyositis. J Rheum 1995; 22 : 668-74).

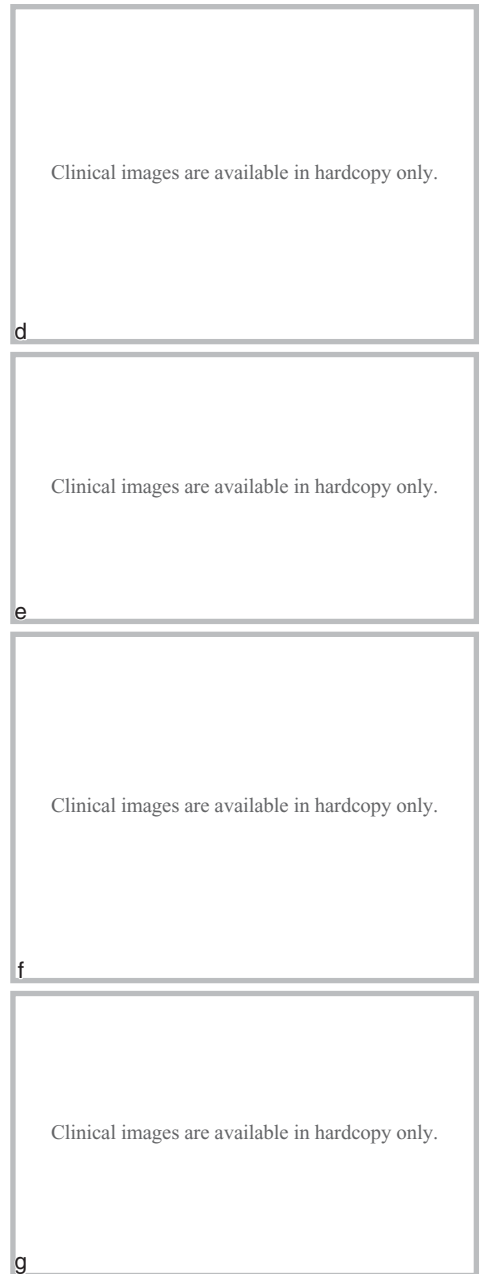


Fig. 12.14-2 Dermatomyositis (DM).

d: Poikiloderma on the neck and cheek. e: Intense edema and purplish eruptions on the eyelids (heliotrope rash). f: Multiple, scattered, sharply margined, keratotic erythema several millimeters in diameter on the extensor joints of DIP and PIP of fingers (Gottron's sign). g: Telangiectasia of nail folds.

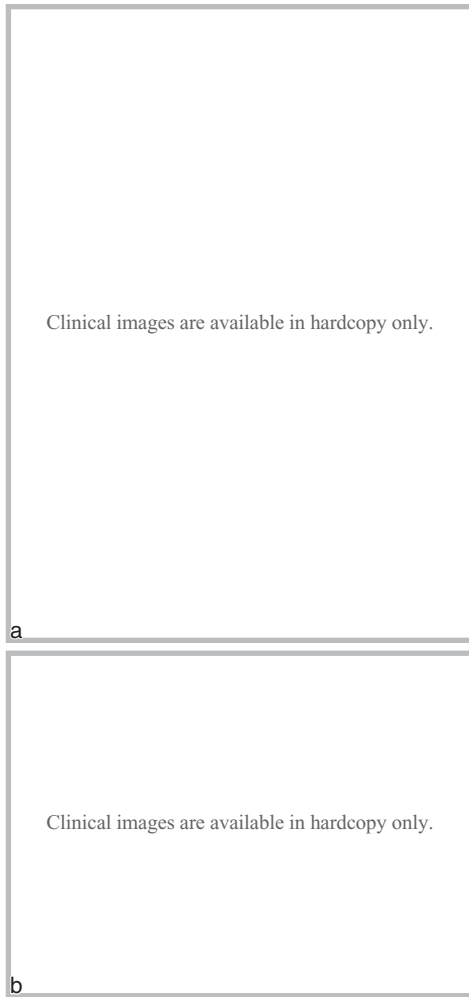


Fig. 12.15 Dermatomyositis (DM) in children.
 a: Diffuse erythema accompanied by scaling on the face and trunk. b: The cheeks are most commonly show with diffuse erythema. The skin lesion clinically resembles butterfly rash in SLE.

Amyopathic dermatomyositis



Dermatomyositis without myositis (proximal muscular weakness and laboratory evidence of myositis) but with typical cutaneous symptoms of dermatomyositis such as Gottron's sign and heliotrope rash is called amyopathic dermatomyositis (ADM). Systemic symptoms may occur rapidly; therefore, careful observation is required.

elevated erythrocyte sedimentation rate are the only symptoms in the early stages. Rheumatoid factors and antinuclear antibodies are positive in 60% to 80% of cases. Myogenic enzymes such as CPK, aldolase, GOT and LDH in serum are elevated, and creatine in urine and myoglobin are elevated by myositis. Specific antibodies such as anti-Jo-1 (histidyl tRNA synthetase) antibodies and anti-PL-7 (threonyl-tRNA synthetase) antibodies are found (**Table 12.9**). Skin and muscle biopsy findings and myogenic changes in electromyography are also important for diagnosis.

Diagnosis

DM can be easily diagnosed by the characteristic cutaneous manifestations, muscular symptoms and laboratory findings. However, in early stages it is difficult to confirm the diagnosis only by the eruptions. The major diagnostic criteria are shown in **Table 12.7**.

Treatment

If a malignant tumor is involved, it is treated primarily. Systemic steroids are the main treatment. Steroid pulse therapy is performed in severe cases. Immunosuppressants may also be administered.

Prognosis

If steroid therapy is given in the early stages, reduced muscular symptoms and decrease of serum CPK are observed in about 80% of cases, which makes a normal life possible. However, prolonged steroid treatment is required in many cases. Life expectancy depends on the severity of malignant tumors and on heart or lung complications. The mortality rate of patients with the complication of interstitial pneumonitis is particularly high. Patients whose onset is in their youth tend to have a good life expectancy.

2. Mixed connective tissue disease (MCTD) ★★

Outline

- Symptoms of SLE, SSc, and PM/DM are seen; nonetheless, it does not meet any of the diagnostic criteria of these diseases.
- Anti-U1RNP antibodies and Raynaud's syndrome are positive. Sausage-like fingers are present.
- Pulmonary hypertension may develop as a complication, and this greatly influences the prognosis.
- It is internationally controversial whether MCTD is an independent entity.

Clinical features

Mixed connective tissue disease (MCTD) most frequently

occurs in women in their 40s. The typical pathological features are Raynaud’s phenomenon, multiple arthralgia (inflammation), and swelling in the dorsal hands (sausage-like swelling). SLE-like symptoms such as erythema and fever, SSc-like symptoms such as lung fibrosis and esophageal reduction, and PM- and DM-like symptoms such as inflammatory myositis and muscular weakness are seen. Renal disorders and central nervous disorders are not usually present. From these symptoms, collagen disease may be suspected; however, most cases do not meet the diagnostic criteria of SLE, SSc or DM/PM.

Laboratory findings

MCTD is characterized by high titers of anti-U1RNP antibodies in serum. Collagen disease conditions cause positive rheumatoid factor, reduction in pulmonary diffusing capacity, elevation of myogenic enzyme, pancytopenia and hypergammaglobulinemia.

Diagnosis

There are various diagnostic criteria. Those published in 1996 by the research division of the Health and Welfare Ministry of

Table 12.8 Guidance for diagnosis of mixed connective tissue disease (MCTD).

Concept	Diagnosis
MCTD is a disease in which the symptoms and findings of SLE, SSc, and polymyositis are present. Anti-U1RNP antibodies are serologically observed.	<ol style="list-style-type: none"> 1. Positive for one or both of the common findings 2. Anti-U1RNP antibody positive 3. Positive for two or more items in A, B or C of III, and at least one item in A, B, and C <p>MCTD is diagnosed by all three items above.</p>
I. Common findings	Additional note
Raynaud’s phenomenon Swelling in fingers and dorsa of hands	
II. Immunological findings	<ol style="list-style-type: none"> 1. Anti-U1RNP antibody is detected either by double immunodiffusion (DID) or by ELISA. If DID is positive and ELISA is not, the DID result has priority. 2. Diagnosis of MCTD is carefully made when the following labeled antibodies are positive. <ol style="list-style-type: none"> 1) Anti-Sm antibody 2) High titers of anti-dsDNA antibody 3) Antitopoisomerase I antibody (anti-Scl-70 antibody) 4) Anti-Jo-1 antibody 3. Cases of pulmonary hypertension with positive anti-U1RNP antibody are likely to be diagnosed as MCTD in the future, even if other symptoms do not meet the criteria.
Anti-U1RNP antibody positive	
III. Mixed findings	
A) SLE-like findings <ol style="list-style-type: none"> 1. Thrombocytopenia 2. Lymphadenopathy 3. Erythema on the face 4. Pericarditis or pleuritis 5. Leukopenia ($\leq 4000/\mu\text{l}$) or thrombocytopenia ($\leq 10,0000/\mu\text{l}$) 	
B) SSc-like findings <ol style="list-style-type: none"> 1. Hardening of skin in the fingers 2. Pulmonary fibrosis, restrictive ventilatory defect (%VC $\leq 80\%$), or decreased pulmonary diffusing capacity (%DLco $\leq 70\%$) 3 Diminished esophageal peristalsis, or esophageal enlargement 	
C) Polymyositis-like findings <ol style="list-style-type: none"> 1. Muscle weakness 2. Increased myogenic enzyme (CK) 3. Electrographic finding of myogenic abnormality 	

(Tohjo T. A diagnostic criteria for MCTD. In: Torikai K, Kashiwagi H, Tohjo T, editors. MCTD studying group in the Ministry of Health and Welfare in Japan. A guideline for treatment of mixed connective tissue disease. 1996: 4-9).

Table 12.9 Major specific autoantibodies in collagen diseases and diseases related to collagen disease.

Disease	Autoantibody
SLE	Anti-dsDNA antibody Anti-Sm antibody
SSc	Anti-Scl-70 antibody Anti-centromere antibody (ACA) Anti-Mi-2 antibody
DM/PM	Anti-Jo-1 antibody Anti-PL-7 antibody Anti-Mi-2 antibody
MCTD	Anti-RNP antibody (Anti-U1RNP antibody)
Overlap syndrome	Anti-dsDNA antibody Anti-Sm antibody Anti-Scl-70 antibody Anti-Jo-1 antibody Anti-Ku antibody
Sjögren syndrome	Anti-SS-A antibody Anti-SS-B antibody

Japan are shown in **Table 12.8**. There is international disagreement on the diagnostic criteria of MCTD. They require further deliberation and discussion.

Treatment

Systemic steroids are fairly effective. Vasodilators such as calcium antagonists and NSAIDs are the main agents used for Raynaud's syndrome and arthralgia. Systemic steroids, oxygen inhalation, and vasodilators are helpful for pulmonary hypertension.

Prognosis

The kidneys and central nervous system are not affected, and steroids are highly effective; MCTD generally has a good prognosis. However, when pulmonary hypertension is involved as a complication, the prognosis may be poor.

3. Overlap syndrome ★ ★

Outline

- This is the name for SLE, SSc or DM/PM whose symptoms meet diagnostic criteria for 2 or more collagen diseases. The collagen diseases do not need to occur simultaneously.
- Many cases meet the diagnostic criteria of both SLE and SSc.

Clinical features

92% of patients with overlap syndrome are women. When patients have both SLE and SSc, they frequently have fever, Raynaud's phenomenon, polyarthritis, ulceration of the fingertips, and pericarditis. Vascular lesions frequently occur, resulting in poor prognosis.

Pathogenesis

The pathogenesis is unknown. Hereditary factors are thought to cause overlap syndrome, in conjunction with environmental factors; however, the influential hereditary factors are unknown. Antibodies that are detected specifically for each collagen disease (labelled antibodies) are found independently or simultaneously.

Laboratory findings

Elevated erythrocyte sedimentation rate and polyclonal hypergammaglobulinemia are seen. SLE-specific antibodies (anti-dsDNA antibodies, anti-Sm antibodies), SSc-specific antibodies (anti-Scl-70 antibodies), and PM-specific antibodies (anti-Jo-1 antibodies) are positive. Anti-Ku antibodies are positive when SSc and PM occur simultaneously (**Table 12.9**).

Diagnosis

The symptoms of overlap syndrome meet the diagnostic criteria for various collagen diseases. When anti-U1RNP antibodies are positive and the diagnostic criteria of MCTD are met, the disease is often diagnosed as MCTD.

Treatment

As a general rule, the most significant symptom is treated according to the treatment guidelines for each collagen disease.

4. Anti-phospholipid antibody syndrome (APS) ★ ★

Outline

- This disorder is caused by antibodies produced against phospholipids whose antigens are various. It tends to accompany SLE.
- Anti-phospholipid antibody is a general term that includes anti-cardiolipin antibodies and lupus anticoagulants.
- Thrombosis, habitual abortion, ischemic heart disease, distal cyanosis, ulceration in the lower legs, and livedo reticularis are caused.

Clinical features

Livedo reticularis, purpura, subcutaneous nodules, fingertip ulceration and gangrene are caused by thrombotic vasculitis in the cutaneous blood vessels (**Fig. 12.16**). Cutaneous vasculitis is pathologically seen. SLE-like symptoms (e.g., butterfly rash, DLE, photosensitivity) may appear. Thrombophlebitis is often found. In addition to cutaneous symptoms, the thrombosis can cause pulmonary embolism, transient ischemic attack, cerebral infarction, Budd-Chiari syndrome and myocardial infarction. Another typical symptom is habitual abortion. Thrombus formed in the placenta is known to cause the inadequate placental function that is frequently seen in the fifth or sixth month of pregnancy. About 20% of habitual abortions in the absence of obvious underlying disease are thought to result from anti-phospholipid antibody syndrome (APS).

Pathogenesis

Anti-phospholipid antibodies, often abbreviated as a PL, contain anti-cardiolipin antibodies (antibodies to β -2 glycoprotein I) and lupus anticoagulants. β -2 glycoprotein I plays a role in anti-coagulation, such as by inhibiting prothrombinase activity and the formation of activated X factors. Accelerated blood coagulation is thought to be caused by disruption of these functions. From recent studies it has been widely accepted that a complex of β -2 glycoproteins I and phospholipids (cardiolipin) accelerates blood coagulation by connecting with a PL.

Clinical images are available in hardcopy only.

Fig. 12.16 Anti-phospholipid antibody syndrome (APS).

Intractable skin ulcer and purpura on the lower leg of a middle-aged postmenopausal female. This ulceration results from circulatory disorder caused by angioma that is induced by anti-phospholipid antibodies.

Anti-phospholipid antibody syndrome (APS) MEMO

Lupus anticoagulant, an immunoglobulin that prolongs the activated partial thromboplastin time (APTT) without inhibiting coagulation factor activation, and biologic false positive of syphilis are frequently observed in APS. This has been recognized since the 1950s. In the 1980s, extensive examination showed that cardiolipin is the only antigen of the disease, and the name was changed to anti-cardiolipin antibody syndrome. From further examination, it has become clear that the antigens are various phospholipids; the disease is now called APS.

Clinical images are available in hardcopy only.

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Fig. 12.17 Sjögren syndrome.

It begins with elevated, edematous erythema 1 cm in diameter. The erythema gradually enlarges and becomes ring-shaped. It occurs multiply in most cases. The center of the erythema tends to heal, and there is severe infiltration at the periphery. Sjögren syndrome resembles the skin lesions seen in neonatal lupus erythematosus.

Laboratory findings

Anti-cardiolipin antibodies and lupus anticoagulants are positive. The anti-cardiolipin antibody titer increases when patients are infected with syphilis. In serological test for syphilis, the most reactive antibodies are anti-cardiolipin antibodies. Biological false positive is observed. Lupus anticoagulants inhibit phospholipid-dependent blood coagulation reactions, leading to prolongation of the APTT; however, the thrombin time is normal. Since APS has a thrombotic tendency, thrombocytopenia is often seen. Positive anti-cardiolipin antibodies in the absence of syphilis infection is biological false positive.

Treatment

Anticoagulant therapy using heparin and warfarins is effective for cases with thrombosis. Small doses of aspirin and simultaneous use of steroids are helpful in preventing abortion. It has been reported that plasmapheresis, megadoses of human immunoglobulins and megadoses of steroids are useful.

5. Sjögren syndrome



Synonym: Sicca syndrome

Outline

- This is an autoimmune disease which mainly targets exocrine glands, including the salivary glands and lacrimal glands.
- Annular erythema and purpura due to vasculitis are characteristic skin features.
- Xerostomia, keratoconjunctivitis sicca and distal renal tubular acidosis occur. Tooth decay is frequently caused by dryness of the mouth.
- Anti-SS-A antibodies and anti-SS-B antibodies are positive.
- Hashimoto's disease (chronic thyroiditis) and B-cell lymphoma occur as complications.
- Symptomatic treatments and steroid administration are the main treatments.

Classification

When there are only the characteristic symptoms of Sjögren syndrome unaccompanied by any other collagen disease, it is called primary Sjögren syndrome (sicca syndrome). Cases with other collagen diseases such as SLE are diagnosed as secondary Sjögren syndrome.

Clinical features

Sjögren syndrome most commonly occurs in adults in their 30s to 50s and affects 9 females for every 1 male. The characteristic cutaneous symptoms are annular erythema and purpura accompanying vasculitis. Punctate hypergammaglobulinemic

purpura is recurrently seen in the lower extremities. Extended macular purpura may also occur (refer to the section on clyoglobulinemic purpura in Chapter 11). Annular erythema, either edematous or urticarial, that is sharply margined and 1 cm to 5 cm in diameter is seen (**Fig. 12.17**). There is a close relationship between anti-SS-B antibodies and edematous annular erythema. Annular erythema frequently occurs multiply on the face, healing spontaneously in about 2 weeks or sometimes persisting longer. Dry skin, telangiectasia, hair loss, butterfly rash, chilblain erythema and nodular erythema also occur.

Eye symptoms: Keratoconjunctivitis sicca, photophobia, pain, itching and lacrimal disorder occur.

Oral symptoms: Dryness of the mouth, dysphagia, and sharp pain in the mouth are caused by affected salivary glands. Tooth decay, angular cheilitis and oral candidiasis occur secondarily.

Other mucosal symptoms: Lesions are found in the nasal cavity, pharynx, larynx, bronchial tubes, external genitalia and alimentary mucosa.

Other symptoms: Raynaud's phenomenon, arthralgia, fever, fatigue, myalgic pain, lymph node enlargement and interstitial pneumonia occur. When B-cell lymphoma is produced, the prognosis is adversely affected.

Pathogenesis

The pathogenesis has not been identified.

Complications

Sjögren syndrome tends to accompany SLE and rheumatoid arthritis. SSc, polyarteritis nodosa, polymyositis, idiopathic thrombocytopenic purpura, Hashimoto's disease, autoimmune hemolytic anemia, primary biliary cirrhosis, renal tubular acidosis and malignant lymphoma may occur as complications (**Table 12.10**).

Pathology

Annular erythema shows pathological features similar to those of SLE and SCLE. Typically, the secretory glands are densely infiltrated by lymphocytes and plasma cells. Labial biopsy of minor salivary glands has prognostic value. Skin biopsy of the purpura shows involvement of vasculitis in the small blood vessels. Immunoglobulin deposition may be found in the blood vessels.

Laboratory findings

Schirmer test, Rose-Bengal test and fluorescent dye test are ophthalmologically performed to identify lacrimal tear gland abnormality. Otologically, apple-tree appearance is observed by parotid gland radiography, and salivary gland dysfunction can be detected by parotid gland scintigram. Serologically, antinuclear antibodies, anti-SS-A antibodies, anti-SS-B antibodies and anti-RNP antibodies are positive. Elevated levels of immunoglobulin,

Table 12.10 Complications of Sjögren syndrome.

Other autoimmune diseases	SLE, SSc, PN, PM/DM, annular erythema, ITP
Joints	Rheumatoid arthritis
Thyroid	Hashimoto's disease
Blood and lymphatic system	Autoimmune hemolytic anemia, lymphoma, hypergammaglobulinemia, hypermacroglobulinemia
Lungs	Interstitial pneumonia
Stomach	Atrophic gastritis
Pancreas	Acute pancreatitis
Liver	Primary biliary cirrhosis
Kidneys	Renal tubular acidosis

Table 12.11 Revised version of the European classification criteria for Sjögren syndrome (2002).

I. Ocular symptoms: a positive response to at least one of the following questions: <ol style="list-style-type: none"> 1. Have you had daily, persistent, troublesome dry eyes for more than 3 months? 2. Do you have a recurrent sensation of sand or gravel in the eyes? 3. Do you use tear substitutes more than 3 times a day?
II. Oral symptoms: a positive response to at least one of the following questions: <ol style="list-style-type: none"> 1. Have you had a daily feeling of dry mouth for more than 3 months? 2. Have you had recurrently or persistently swollen salivary glands as an adult? 3. Do you frequently drink liquids to aid in swallowing dry food?
III. Ocular signs - that is, objective evidence of ocular involvement defined as a positive result for at least one of the following two tests: <ol style="list-style-type: none"> 1. Schirmer's test, performed without anaesthesia (≤ 5 mm in 5 minutes) 2. Rose bengal score or other ocular dye score (≥ 4 according to van Bijsterveld's scoring system)
IV. Histopathology: In minor salivary glands (obtained through normal-appearing mucosa) focal lymphocytic sialoadenitis, evaluated by an expert histopathologist, with a focus score ≥ 1 , defined as a number of lymphocytic foci (which are adjacent to normal-appearing mucous acini and contain more than 50 lymphocytes) per 4 mm ² of glandular tissue
V. salivary gland involvement: objective evidence of salivary gland involvement defined by a positive result for at least one of the following diagnostic tests: <ol style="list-style-type: none"> 1. Unstimulated whole salivary flow (≤ 1.5 ml in 15 minutes) 2. Parotid sialography showing the presence of diffuse sialectasias (punctate, cavitory, or destructive pattern), without evidence of obstruction in the major ducts. 3. Salivary scintigraphy showing delayed uptake, reduced concentration and/or delayed excretion of tracer
VI. Autoantibodies: presence in the serum of the following autoantibodies: <ol style="list-style-type: none"> 1. Antibodies to Ro (SSA) or La (SSB) antigens, or both

(Vitali C, et al. Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. *Ann Rheum Dis* 2002;61:554-8).

salivary amylase and rheumatoid factor may be present. Anti-SS-A antibodies tend to show high sensitivity in Sjögren syndrome, and anti-SS-B antibodies tend to show high specificity for Sjögren syndrome.

Diagnosis

Currently, Sjögren syndrome is diagnosed by clinical features according to diagnostic criteria established by European diagnostic criteria (**Table 12.11**).

Treatment

The main treatments are symptomatic therapies, because no effective pharmacologic therapy is available. Mouthwash, treatment for periodontal disease, and administration of artificial saliva and of artificial tears for protection of the cornea are the main therapies. Large doses of internal steroids and immunosuppressants are administered in severe cases in which systemic angio-pathic lesion or malignant lymphoma occurs as a complication.

D. Rheumatic diseases with arthritis

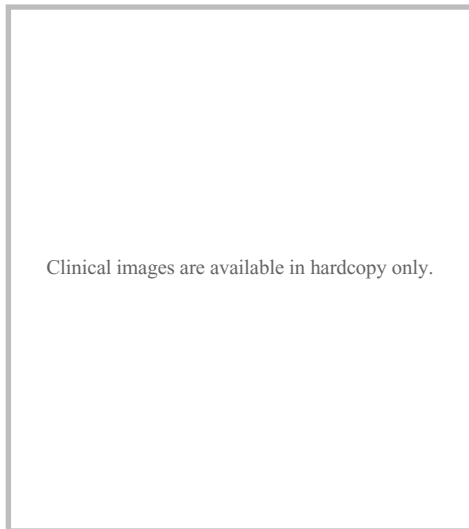


Fig. 12.18 Rheumatoid vasculitis.

1. Rheumatoid arthritis (RA) ★ ★

Outline

- This collagen disease causes sharp pain and swelling in the joints.
- Rheumatoid nodules and cutaneous lesions accompanying vasculitis are found.
- Chronic inflammation occurs in the synovial membranes of joints. The articular cartilages and bones are destroyed by synovial proliferation.
- Diseases closely related to RA include juvenile rheumatoid arthritis, adult Still disease, ankylosing spondylitis, psoriatic arthritis and Reiter syndrome.

Clinical features

The primary disease of rheumatoid arthritis (RA) is symmetrical arthritis. In dermatology, RA is characterized by rheumatoid nodules and cutaneous lesions that accompany vasculitis (**Fig. 12.18**). Rheumatoid nodules are found in 20% to 25% of patients with RA. The nodules, 0.5 cm to several centimeters in diameter, are painless, solid, subcutaneous nodules frequently produced on sites where the skin is subjected to pressure, such as the knees, hips, Achilles tendons and occipital region. They persist for a long time, sometimes rupturing and causing secondary infection. Ulceration on the fingertips and elsewhere, gangrene, purpura, blistering, and livedo accompany rheumatic vasculitis. RA is usually accompanied by extracapsular symptoms, such as pericardial