

Connective Tissue Disorders and Pregnancy

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Connective tissue disorders are immune mediated multisystem disorders of wide variety. Based on the presence or absence of autoantibody the disorder is broadly classified as seropositive and seronegative spondyloarthropathies, respectively^{1,2} (Table 34.1). Of these, systemic lupus erythematosus (SLE), rheumatoid arthritis and scleroderma which belong to the seropositive category are the common varieties and may be encountered by an obstetrician during clinical practice. Ehler-Danlos disease and Marfan's syndrome are categorically different from above mentioned and are due to genetic errors.

ETIOLOGY

What incites autoantibody formation/immune reaction is not clearly known. Bacterial/viral or environmental insult (ultraviolet rays inciting SLE flares³ or silica dust or polyvinyl chloride as a cause

for scleroderma⁴) in a genetically predisposed individual may trigger the immune mediated tissue destruction. Microchimerism, which is immune reaction against fetal cells in maternal blood/tissues, is hypothesized to be the cause behind systemic sclerosis.⁵

PATHOPHYSIOLOGY^{1,5}

Major histocompatibility complex (MHC) is the gene complex responsible for distinguishing self from nonself antigens. The nonself antigens are normally destroyed by complex interaction between T cells, B cells and complement system. In connective tissue disorders, self antigens are wrongly identified as foreign and the immune response results in their destruction. A deficiency of T suppressor cells is believed to result in unchecked autoantibody production. The systems commonly affected in

Table 34.1: Connective tissue disorders

Immune mediated	Seropositive	<ul style="list-style-type: none"> • Systemic lupus erythematosus • Rheumatoid arthritis • Systemic sclerosis • Mixed connective tissue disease • Dermatomyositis, polymyositis • Vasculitis syndromes
	Seronegative	<ul style="list-style-type: none"> • Ankylosing spondylitis • Psoriatic arthritis • Reiter's disease • Arthritis associated with Crohn disease, ulcerative colitis
Genetic errors		<ul style="list-style-type: none"> • Ehler-Danlos disease • Marfan's syndrome

connective tissue disorders are musculoskeletal system, kidneys, cardiovascular system and skin.

The destruction of the susceptible tissues may be by two mechanisms. They are *cytotoxic* immune response and immune complex mechanism. In the first, antibody attached to the surface antigens on the cell surface directly causes cell damage. In the immune complex response, antigen- antibody complex attached to the tissue incites a complement cascade that results in release of chemotactic agents which attract polymorphonuclear cells. These cells in turn phagocytose the affected cells.

The disease behavior in pregnancy varies in different connective tissue disorders. In SLE and systemic sclerosis, especially with active disease during pregnancy, the 'flares' and complications are higher.⁷⁻⁹ On the contrary, majority of the studies have shown the beneficial role of estrogen in pregnancy on disease activity in rheumatoid arthritis.¹⁰⁻¹² This difference is because of the differing immune response in these subsets. SLE and scleroderma are predominantly humoral immune response mediated disorders whereas in rheumatoid arthritis, the immune reaction is predominantly cell-mediated.¹³ Pregnancy induced immune alterations may modulate connective tissue disorders. As cell-mediated immunity is low in pregnancy, the disorders such as rheumatoid arthritis which are cell-mediated, may remain quiescent in pregnancy.

SYSTEMIC LUPUS ERYTHEMATOSUS

Systemic lupus erythematosus (SLE) is a multisystem connective tissue disease characterized by presence of numerous antibodies, circulating immune complexes resulting in wide spread immunologically determined tissue damage. The course of SLE is characterized by chronic exacerbations and remissions. There are several autoantibodies detected in SLE which are of obstetric significance.^{3,14} Some are associated with clinical activity and some indicate fetal cardiac block, neonatal lupus or recurrent pregnancy loss. There are few antibodies whose presence suggests nephritis or an association with pre-eclampsia (Table 34.2).

Estimation of autoantibodies with increasingly sensitive and specific laboratory tests and revised criteria for classification¹⁵ (Table 34.3) should aid in diagnosis.

Table 34.2: Autoantibodies of obstetric significance in systemic lupus erythematosus^{3,14}

Antibody	Incidence(%)	Clinical association
Antinuclear (ANA)	95	Repeated negative test makes lupus unlikely
Anti-ds DMA	70	Nephritis and clinical activity
Anti-SSA (Ro)	30	Fetal congenital heart block, neonatal lupus
Anti-SSB (La)	10	Always with anti-SSA (Ro)
ACA and LA	15-20	Recurrent pregnancy loss, early pre-eclampsia
Anti-KJ*	10	Pericarditis

*Anti-Ki itself does not have any direct obstetric significance but most maternal mortality is associated with cardiac complications, hence is advisable to assess it.

Table 34.3: Revised criteria accepted by American Rheumatism Association for diagnosis of SLE¹⁵

- Malar rash
- Discoid rash
- Photosensitivity
- Oral ulcers, usually painless
- Arthritis, non-erosive, involving two or more peripheral joints
- Serositis—pleuritis or pericarditis
- Renal disorder—persistent proteinuria > 0.5 gm/day or > 3 by dipstick or cellular casts
- Neurological disorders—seizures or psychosis
- Hematological disorders—hemolytic anemia, leucopenia < 4000/cmm, lymphopenia < 1500/cmm, thrombocytopenia < 100000/cmm
- Immunological disorders—Anti-dsDNA or anti-Sm antibodies or false positive VDRL, IgM or IgG anticardiolipin antibodies or lupus anticoagulant
- Antinuclear antibodies in abnormal titers

If four criteria are present at any time during course of disease, SLE can be diagnosed with 98 percent specificity and 97 percent sensitivity

Effect of Pregnancy on SLE

Pregnancy does not appear to affect or alter the long-term prognosis of patients with SLE. Several studies, however, have documented increased flares of SLE during pregnancy, i.e. three times during first half, 1.5 times during second half and six fold increase during puerperium.

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Clinically, flares may mimic pre-eclampsia. It is important to differentiate between these two, as treatment for pre-eclampsia will be termination of pregnancy, whereas during flares increasing dose of glucocorticoids can be started and pregnancy need not be terminated.^{14,17}

These two conditions can be differentiated by serial estimation of serum C3, C4 and CH50 (total hemolytic component) levels. During normal pregnancy or pre-eclampsia, complement level increases whereas in lupus flare it decreases.^{17,18}

Effect of SLE on Pregnancy

SLE affects pregnancy in varied ways and in varied frequencies. Fertility as such is not impaired.¹⁹ SLE is known to cause recurrent pregnancy loss (40%), hypertension (40%), fetal growth restriction (FGR, 10-50%), prelabor rupture of membranes (40%) and preterm delivery (10-50%).¹⁹⁻²¹

Effect of SLE on Neonates

Newborns of mothers with SLE may develop erythematous skin lesions, which usually disappear by 12 months of age.²² More than 80 percent of mothers with anti-SSA (Ro) positive antibody may have newborns with complete heart block.²³

Antenatal Care

Preconceptional counseling should be carried out in all patients with SLE. In view of increased chances of complications, all obstetricians should maintain close maternal and fetal follow up. Patients should be advised to have regular antenatal check up, i.e. once in 2 weeks till 32 weeks of gestation and thereafter, weekly. During each visit careful monitoring of blood pressure and weight gain is done.¹⁷ Complete blood picture, liver function, BUN-renal function, 24 hour urine protein and creatinine clearance should be evaluated every month.^{14,24} All patients on long-term glucocorticoids should undergo 1 hour 50 gm oral glucose challenge test at 20, 28 and 32 weeks of gestation.²⁵ Glucose tolerance test is done when screening test is abnormal or if there is evidence of fetal macrosomia. Serum C3 and C4 complement levels are estimated once in 6 weeks. Because of the chances of FGR, serial ultrasound examination is done once in first visit (1st trimester) for accurate gestational dating, next at 18 to 20 weeks of gestation to rule out fetal anomaly and for any early evidence fetal heart block,

and thereafter once in 4 weeks. Fetal echocardiography at 20 to 24 weeks if there is evidence of fetal heart block (fetal heart rate < 60/min with poor beat-to-beat variability) can be performed.¹⁴ Doppler blood flow velocimetry is done if there is suspicion of FGR in 3rd trimester.^{22,26,27}

Timing and Mode of Delivery

SLE in pregnancy itself is not an indication for termination of pregnancy. The timing and mode of delivery should be as directed by obstetric indications.

When in labor, stress doses of glucocorticoids (Hydrocortisone 100 mg intravenously 6 hourly) are indicated and should be continued for 48 hours postnatally. Steroids should be tapered slowly and with great care in the postpartum period to prevent exacerbation of SLE.^{18,28}

Prognostic Factors

Various favorable and unfavorable factors have been observed affecting maternal and fetal outcome. Previous pregnancy outcome is the best predictor.² It is found that SLE which is quiescent for at least 6 months prior to conception favors the pregnancy outcome.³⁰ When SLE is active during any phase of pregnancy, the chances for live birth are reduced. The prognosis markedly worsens in presence of hypertension or in presence of Lupus nephritis. Lupus nephritis is diagnosed by presence of serum creatinine > 1.5 mg/dL, BUN > 50 mg/dL, creatinine clearance < 50 ml/min, urine proteins > 500 mg/24 hr and/or presence of urine sediments.^{30,31} In cases where more than 2 drugs are required to control hypertension and when prednisolone requirement is more than 20 mg/day, the prognosis is poor. Presence of abnormal serum complement levels and high antibody titers are associated with poor prognosis.^{17,18} Likewise, presence of hemolytic anemia with reticulocytosis, leucopenia < 4000/cm, lymphopenia < 1500/cmm and/or thrombocytopenia < 100000/cmm affect the outcome of pregnancy.³²

Potential Causes of Maternal Deaths in SLE Complicating Pregnancy

Maternal mortality in SLE are mostly due to cardiopulmonary complications such as pulmonary hemorrhage, lupus pneumonitis, pulmonary vasculitis

with pulmonary hypertension, cardiac tamponade and opportunistic infection secondary to immunosuppression.^{26,33-36}

Treatment Options

The standard therapy for exacerbation of SLE during pregnancy is administration of glucocorticoids. The dose of corticosteroids varies, depending on the organ system involved and the severity of the illness. Indications for steroid treatment include pericarditis, myocarditis, pleuritis, hemolytic anemia, clotting abnormalities, severe myositis, central nervous system involvement and lupus nephritis. A dose of 40 to 60 mg/day of prednisone for 2 to 3 weeks until improvement occurs is usually necessary. Therapy can then be tapered to a minimal dose. 'Stress doses' of steroids are indicated in peripartum period as discussed earlier. The use of steroids in the postpartum period is however controversial. Most recommend following the patient closely and treating her as indicated for exacerbation on a clinical basis.²⁴

Although cleft lip and cleft palate have been found after in utero exposure to glucocorticoids, these anomalies have not been observed in the large cohorts of human fetuses studied.^{37,38} Neonatal adrenal suppression is a theoretical possibility and is rarely reported.¹⁴ Opportunistic infections and gestational diabetes are definitely a distinct possibility.

The prophylactic use of low dose aspirin (60 mg/day)³⁹ and/or low molecular weight heparin (10000-20,000 IU/day)⁴⁰ has also been advocated.

Long-term antibody-based immunoabsorption has been used in pregnancy for removal of autoantibodies and lipoproteins in women with serious complications not responding to conventional therapy.⁴¹

Various other drugs such as hydroxychloroquine,⁴² danazol (600 mg/day),⁴³ bromocriptine (2.5 mg/day),⁴⁴ azathioprine (1-2 mg/kg/day),⁴⁵ thalidomide (25-100 mg/day)⁴⁶ have also been tried in resistant cases. These drugs are better avoided in pregnancy unless life threatening complications develop.

Breastfeeding and SLE

Breastfeeding in SLE is an issue for debate. Data regarding breastfeeding in SLE are limited. Currently, breastfeeding can not be recommended while mother is on cytotoxic drugs.²⁴ The glucocorticoids in breast

milk do not appear to pose danger to the infant unless the mother is taking more than 40 mg of prednisolone per day.⁴⁷ Breastfeeding can be recommended if the mother is not having active disease as determined by antibody titers.

Contraception in Women with SLE

Counseling of patients with SLE with regard to childbearing should emphasize the maternal and perinatal risks associated with active disease. Contraception is best achieved by barrier methods until such time as sterilization, preferably vasectomy is chosen.²⁴ Tubal sterilization can be carried out whenever disease is quiescent.¹ Progestin implants provide good contraception with no known effects on lupus flare. Oral contraceptives are contraindicated in patients with active SLE and should be used with caution if desired.^{1,14} Intrauterine devices are contraindicated in patients receiving immunosuppressive therapy because of risk of pelvic infection¹ and associated lupus flares.

RHEUMATOID ARTHRITIS

Rheumatoid arthritis is a chronic inflammatory synovitis involving the peripheral joints. The disease prevalence is 2 to 3 times higher in females than males.

Cellular and humoral immunity as well as genetic preponderance have the role in pathogenesis of rheumatoid arthritis. There is significant association of rheumatoid arthritis with HLA DR4, a class II MHC molecule. The disease mainly manifests as arthritis involving the peripheral joints (small and medium sized joints) symmetrically. The gradual bony erosions and cartilage destruction result in deformities. Extra-articular manifestations are due to vasculitis or lymphoid infiltration and are associated with severe disease. It diagnosis is streamlined (Table 34.4).

Several authors have confirmed the protective effect of pregnancy hormones on the disease.^{10,11,49,50} On the contrary there is a higher chance of new disease onset in the first three months postpartum¹¹ or there may be a flare after delivery, especially if the woman is breastfeeding⁵¹. Though this is the way the disease behaves in most of the pregnant women, some women develop the disease during pregnancy, and others become worse.⁵² Amelioration of the disease during pregnancy is reported to be due to the disparity in

Table 34.4: The 1987 revised criteria for classification of RA⁴⁸

1. Guidelines for classification
 - a. Four of seven criteria are required to classify a patient as having RA
 - b. Patients with two or more clinical diagnoses are not excluded.
2. Criteria*
 - a. Morning stiffness
 - b. Arthritis of one or more joint areas; observed simultaneously, have soft tissue swellings or joint effusions. The 14 possible joint areas are: right or left proximal interphalangeal, metacarpophalangeal, wrist, elbow, knee, ankle, and metatarsophalangeal joints
 - c. Arthritis of hand joints
 - d. Symmetric arthritis
 - e. Rheumatoid nodules- subcutaneous nodules over bony prominences, extensor surfaces or juxtaarticular regions
 - f. Serum rheumatoid factor positive
 - g. Radiographic changes: Posteroanterior hand and wrist radiographs showing erosions or unequivocal bony decalcification

Criteria b-d must be present at least for 6 weeks. Criteria b-e must be observed by a physician

HLA class II antigens between mother and the fetus. The Th2 response to paternal HLA antigens, thereby suppressing cellular immunity plays a role in remission of arthritis.

Management

Symptomatic treatment with aspirin and nonsteroidal antiinflammatory drugs, taking into consideration their effect on pregnancy is all that may be required. Corticosteroids may rarely be indicated in pregnancy. Before delivery range of joint motions should be assessed so that care could be taken not to force the affected joints to move beyond the disease imposed constraints while conducting delivery or for analgesia/ anaesthesia.

Contraception

As the sex hormones offer a beneficial effect on the disease progress, combined hormonal contraception is the preferred contraception in women with rheumatoid arthritis.¹²

SCLERODERMA

Scleroderma is a chronic multisystem disorder of unknown etiology involving the connective tissues and characteristically involving the skin and viscera such as gastrointestinal tract, lungs, kidneys and heart.

The disease may be *localized* involving the skin over particular part of the body or may be *systemic sclerosis* where in addition to extensive cutaneous disease, visceral involvement will be present. Besides, there are chemical (e.g., polyvinyl chloride, epoxy resins, bleomycin, pentazocine) induced scleroderma-like disorders and other disorders simulating scleroderma (e.g., scleromyxedema, chronic graft versus host reaction, amyloidosis, digital sclerosis in diabetes). Systemic sclerosis could be grouped into three main varieties as diffuse, limited cutaneous and sine scleroderma (Table 34.5).⁴

Table 34.5: Varieties of systemic sclerosis

Varieties	Characteristics
Diffuse cutaneous disease	Rapid development of symmetric skin thickening over extremities, face and trunk followed by early visceral involvement
Limited cutaneous disease	The skin over face and distal extremities is involved, usually with features of CREST syndrome (calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly and telangiectasia) and late visceral involvement
Sine scleroderma	Visceral disease in the absence of cutaneous involvement

American College of Rheumatology has developed the criteria for diagnosis and classification. Presence of the major criterion or two or more minor criteria establishes the diagnosis (Table 34.6).⁴

Pathophysiology

The exact etiology is not fully understood. Genetic predisposition, abnormal immunologic responses or environmental insinuations could be some of the factors responsible for the disease.⁴ Overproduction and accumulation of collagen and other connective

Table 34.6: Criteria for diagnosis of Scleroderma* (American College of Rheumatology)⁴

Criterion	Description
Major criterion	Sclerodermatous skin changes of fingers of both hands with involvement of skin in any location proximal to metacarpophalangeal joints or metatarsophalangeal joints; may be entire extremity/face/neck/trunk
Major criteria	<ol style="list-style-type: none"> 1. Sclerodactyly 2. Digital pitting scars or tissue loss of volar pads of fingertips 3. Bibasilar pulmonary fibrosis

*Presence of the major criterion or two or more minor criteria establishes the diagnosis.

tissue matrix proteins in skin and viscera is the key event in the pathogenesis. To begin with there will be an immune mediated endothelial damage involving small vessels (small arteries, arterioles and capillaries) followed by intimal thickening and narrowing of the vessel lumen resulting in chronic ischemia. There will be dilatation and tortuosity of remaining capillaries that may result in telangiectasia.

Endothelial injury triggers complex immune response with an intricate interaction between activated platelets, T cells, macrophages, endothelial cells, cytokines, growth factors and several other humoral factors, that stimulate perivascular fibrosis.

Clinical Features **K. M. C. LIBRARY**

Raynaud's phenomenon is the first symptom noticed in systemic scleroderma. Further along the course, there may be gastrointestinal symptoms such as reflux esophagitis or evidence of skin involvement in the form of white patches over involved area or loss of tissue pads under the fingertips. The rapidity of visceral involvement depends on the type of scleroderma. Respiratory distress due to pulmonary fibrosis; hypertension, oliguria, fatigue due to renal scleroderma; edema, congestive cardiac failure, pericardial effusion as features of cardiac involvement; malabsorption, aspiration pneumonia due to gastrointestinal involvement are the visceral manifestations that may follow (Table 34.7).

Pulmonary hypertension or renal failure may be the terminal events preceding death.^{4,53}

Table 34.7: Clinical features of systemic sclerosis

System involvement	Pathology	Clinical presentation
Vascular	Episodic vasoconstriction of small arteries and arterioles	Raynaud's phenomenon
Skin	Edematous phase Indurative phase	Edema begins distally and advances proximally. Firm thickened taut skin, flexion contractures, ulcers, loss of volar pads, pitting scars finally leading to resorption of terminal phalanges, hyper/hypopigmentation, loss of hair, calcific deposits.
Gastrointestinal tract	Atrophy of muscularis, fibrosis of sphincters, reflux esophagitis, large intestinal diverticula	Regurgitation, retrosternal burning pain, dysphagia, constipation/diarrhea, malabsorption
Respiratory system	Diffuse interstitial fibrosis, peribronchial/pleural fibrosis	Dyspnea, pulmonary hypertension
Cardiovascular system	Degeneration of myocardial fibers interstitial fibrosis, pericarditis	Conduction defects, arrhythmias, failure, pericardial effusion
Renal	Renal vascular involvement, Glomerulosclerosis	Hypertension, failure
Genitourinary	Fibrosis	Dyspareunia, sexual dysfunction
Endocrine	Autoimmune thyroiditis fibrosis	Hypothyroidism

Prognosis

In the initial phases, it is difficult to classify the disease and to prognosticate since the disease has a variable course. The prognosis is obviously worse in diffuse cutaneous type and the death may be due to pulmonary, cardiac or renal involvement. The 5 year cumulative survival rate in diffuse cutaneous type is 70 percent and the 10 year is 55 percent. In limited cutaneous disease, it is 90 percent and 75 percent, respectively.⁴

Management

The management involves general supportive care, treatment of clinical manifestations of organ system involvement and drug therapy to modulate the disease progression.

Patients should be kept warm; smoking and external stress should be avoided. Glucocorticoids, D-Penicillamine and other cytotoxic drugs like methotrexate, azathioprine and cyclophosphamide and even interferons are being used with the purpose of disease modulation. But, no therapy has clearly shown to suppress or reverse the disease process.

*Scleroderma and pregnancy*⁵⁴ The association of scleroderma and pregnancy is a rarity. This is mainly due to later age preponderance of the disease. Of late, with pregnancies in third and 4th decade becoming commoner, clinicians may come across the problem more frequently. There is insufficient data available regarding the prognosis and management of such cases.

The available reports about the outcome of pregnancy with scleroderma are conflicting. Overall it is said that the course of the disease is unpredictable. It has been observed that in the first three years after the onset, the disease remains active and conception during this period may end with serious complications. Also women who already have evidence of pulmonary/cardiac/renal involvement, the outcome is obviously poor. Whether this is the result of natural course of the disease or should be attributed to pregnancy is debatable.⁵⁵ Hence, it is suggested that women with known scleroderma should be counseled against pregnancy during the early active years of the disease (3-5 years from onset of symptoms) and also when they have extensive visceral scleroderma.^{5,6}

Effect of Pregnancy on Disease Manifestation

Women without active disease may pass through pregnancy without any manifestation/complication. Reynaud's phenomenon, one of the early findings in scleroderma may improve because of pregnancy associated vasodilatation. Vomiting may get exaggerated in women with gastrointestinal involvement. Constipation may be a problem because of decreased colonic motility compounded by progesterone induced intestinal smooth muscle hyporesponsiveness. The pulmonary/cardiac complications or renal crisis that may occur during pregnancy seem to be part of the natural course of the disease rather than pregnancy aggravated problems. It is true that pregnancy may make the diagnosis and management of such complications more complex.

Effect of the Disease on Pregnancy

Increased miscarriages are noted in several studies^{54,55} and probably women with long-standing diffuse scleroderma are the ones at higher risk for miscarriages.⁵⁶ Preterm labor is consistently reported to be higher, around 30 percent.⁵⁵⁻⁵⁷

Association may be drawn between scleroderma and fetal growth restriction, as it happens in any disease with endotheliosis. Disease related placental insufficiency compounded by malnutrition caused by gastrointestinal involvement may result in significant fetal growth restriction. However, reports do not reveal increased occurrence of fetal growth restriction or stillbirths in these women.^{56,58} Women with scleroderma are at higher risk for developing pre-eclampsia specially if there is renal involvement.⁵⁷ In fact it is difficult to differentiate renal crisis due to the disease from severe pre-eclampsia. Prognosis is guarded in such cases and aggressive maternal management is indicated.

In general, maternal mortality does not seem to be increased in women with scleroderma.⁵⁶ However, the prognosis is influenced by the type of the disease, duration of the disease and disease activity during pregnancy. The maternal mortality noted so far is highest in those who had renal involvement prior to or during pregnancy.⁵⁴

Whether the unyielding abdominal wall hinders the uterine enlargement was a concern. But it was observed that the growing uterus could be well

accommodated. It may be difficult, however, to feel the fetal parts by abdominal examination. Wound healing is another concern which appears unaffected by the disease.

Unyielding cervix poses a problem during labor. There may be cervical scleroderma responsible for cervical dystocia in laboring woman.⁵⁹ Postoperative infective morbidity is higher in women with scleroderma. It is very important to minimize the avoidable risk factors for sepsis such as repeated vaginal examinations, prolonged rupture of membranes and protracted labor. Babies born to mothers with any of the forms of scleroderma do not manifest the stigmata of maternal disease.⁶⁰

Medications for Treating the Disease in Pregnancy

The medications are mostly symptom directed like nonsteroidal anti-inflammatory drugs (NSAIDs). Disease modifiers such as corticosteroids or D-Penicillamine are rarely prescribed in pregnancy. The use of common NSAIDs such as aspirin/indomethacin do not cause much concern except that they are better avoided after 32 weeks. The steroid treatment may be prescribed only in severe active disease. D-Penicillamine and cytotoxic drugs are contraindicated in pregnancy.

If woman develops renal involvement during pregnancy, angiotensin-converting-enzyme inhibitors will be necessary to save the lives of the mother and infant despite the concerns about its use in pregnancy.⁵⁶

Challenges in the Management

It may be difficult to get a venous access due to peripheral vasoconstriction and fibrosis of skin. It is suggested to avoid puncturing peripheral vessels for it may result in spasm and subsequent necrosis.⁶¹ The women should be kept in warm environment to minimize Reynaud's phenomenon. The ones with esophageal, pulmonary and cardiac involvement certainly pose problems of difficult intubations, aspiration and increased risk of complications at general anesthesia. Besides, if the disease is involving the spine, regional anesthesia would call for expertise.

POLYMYOSITIS AND DERMATOMYOSITIS¹

These are uncommon inflammatory diseases involving the skin and muscle. The disease may be acute, subacute or chronic. In dermatomyositis, a characteristic rash precedes or accompanies muscle weakness. The disease may be isolated myositis or may overlap with systemic sclerosis or mixed connective tissue disorders. About 15 percent of adults having dermatomyositis have an associated malignancy. Abnormal electromyogram, increased muscle enzymes and biopsy confirm the diagnosis. Pregnancy outcome is overall poor.

VASCULITIS SYNDROMES^{1,2,5}

Vasculitis syndromes are disorders due to inflammation and injury to the blood vessels. They include polyarteritis nodosa, Wegener's granulomatosis, aortoarteritis of Takayushu and various hypersensitivity arteritis including Henoch-Schonlein purpura.

The clinical brief of various vasculitis syndromes is summarized in Table 34.8.

SERONEGATIVE SPONDYLOARTHROPATHIES⁵

These are the Spondyloarthropathies with strong familial aggregation, characterized by the absence of rheumatoid factor. The group includes Ankylosing spondylitis, psoriatic arthritis, Reiter's disease, arthritis associated with Crohn disease and ulcerative colitis. There are articular and extraarticular manifestations. The common articular manifestations are sacroiliitis, spondylitis, seronegative polyarthritis and dactylitis. The extra-articular manifestations are ocular inflammation in the form of uveitis, buccal and genitourinary ulcerations and psoriasisiform rash and nail changes.

There is apparently no adverse effect of the disease on pregnancy. Postural and breathing exercises are important for the pregnant women with this condition.

INHERITED CONNECTIVE TISSUE DISORDERS¹

Marfan's Syndrome

Marfan's syndrome is an autosomal dominant disorder involving the FBNI gene mutation that is on the long arm of chromosome 15. The disease severely

Table 34.8: Vasculitis syndromes

Vasculitis syndrome	Pathology	Clinical presentation	Diagnosis	Diseases in pregnancy
Polyarteritis nodosa	Systemic necrotizing vasculitis involving small and medium sized vessels	Fever, weight loss, myalgia, arthralgia, hypertension, renal failure	Biopsy	Prognosis poor in active disease
Wegener's granulomatosis	Necrotizing granulomatous vasculitis involving upper and lower respiratory tract and kidneys	Sinusitis, nasal disease, pulmonary symptoms, glomerulonephritis, musculoskeletal involvement	Biopsy	Rare in pregnancy because affects individuals above 50 years
Takayasu arteritis (pulseless disease)	Chronic inflammation of large vessels mainly of upper extremity (upper aorta and its main branches)	Young women Absent radial pulse, claudication, renovascular hypertension, aortic insufficiency, pulmonary hypertension, transient ischemic cerebral symptoms	Aortography, CT, MRI imaging, biopsy	Reports indicate better prognosis in pregnancy

Temporal arteritis (age above 55 years), cutaneous or hypersensitivity arteritis, Henoch-Schönlein purpura are few other arteries.

may vary from subclinical disease to severe involvement resulting in aortic dilatation/dissecting aneurysm. Death in severe cases maybe due to valvular insufficiency and congestive heart failure or rupture aneurysm.

Increased frequency of dissecting and ruptured aneurysms in pregnancy, especially in the last trimester is the concern. Elective cesarean delivery is indicated in these women to avoid Valsalva maneuver and rupture aneurysm.

EHLER DANLOS SYNDROME

This syndrome maybe autosomal dominant/recessive/sex linked. The disease is characterized by hyperelasticity of skin associated with changes in connective tissue. In severe forms, there can be manifestations of arterial rupture and internal hemorrhages. Increased frequency of prelabor rupture of membranes, preterm labor, antepartum and postpartum hemorrhage, uterine rupture, difficulty in suturing the episiotomy/cesarean incisions and defective wound healing are the concerns when the disease is encountered in pregnancy.

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