INVITED ARTICLE

CUTANEOUS MANIFESTATIONS OF CARDIAC DISEASES

H L Chan

ABSTRACT

Many general signs familiar to physicians can be found on the skin in cardiac patients. These include (a) cyanosis, central and peripheral, (b) erythremia, flushing and erythema, (c) digital clubbing and (d) alteration in texture.

Specific cardiac conditions often have useful diagnostic cutaneous clues. Of these the association of coronary heart disease, hyperlipidemia and xanthomas is the most important. Rare syndromes such as the "leopard syndrome" often have distinctive skin signs.

Multisystemic disorders may affect the heart and skin simultaneously or in sequence. They include collagen vascular diseases, amyloidosis, sarcoidosis and relapsing polychonditis.

Finally iatrogenic disease arising from treatment of cardiac or cutaneous disease may induce changes in one or the other organ.

The heart and the skin have much in common. These manifestations help elucidate the cause, evaluate the diagnosis, and follow the treatment and progress of these diseases.

Keywords: Skin and heart disease, cutaneous and cardiac disease, skin and systemic disease, coronary artery disease and skin.

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INTRODUCTION

Many general signs familiar to practising physicians are to be found on the skin in patients suffering from cardiac diseases. These are part of the clinical picture. Specific cardiac conditions, both common and rare, often have useful diagnostic cutaneous clues. Additionally, multisystem disorders may affect heart and skin at the same or different times.

GENERAL CUTANEOUS SIGNS OF CARDIAC DISEASES

General cutaneous signs of cardiac diseases are known since the time of Hippocrates. They include changes in skin colour, abnormalities of the digits and hands[1] and alterations in skin texture.

Divison of Dermatology
National University Hospital
National University of Singapore
Lower Kent Ridge Road
Singapore 0511

H L Chan, AM, MBBS, FRCP, FRACP, Dip Derm(Lond)
Professor of Medicine

National Skin Centre
1 Mandalay Road
Singapore 1130

Visiting Consultant

Cyanosis

Central cyanosis occurs when 5 gms or more of reduced (unoxygenated) haemoglobin is present. This results in a bluish or purplish discoloration of the skin and mucous membranes (tongue, oral mucosa and conjunctiva). Central cyanosis is seen in congenital heart disease with intracardiac or intrapulmonary right to left shunting; this occurs in association with digital clubbing. Peripheral cyanosis, on the other hand, occurs in states with normal arterial oxygen saturation but reduced blood flow such as low output cardiac failure or peripheral vascular disease. Peripheral cyanosis is usually seen on the cool areas eg. nose, lips, earlobes and fingertips. Detection of cyanosis may be difficult.

Cyanosis of the fingers more intense than that of the toes suggest complete transposition of the great vessels, with either a preductal coarctation or complete interruption of the aortic arch and a reversed shunt through a PDA. If the cyanosis is more on the right than the left hand, a preductal coarctation of the aorta is more likely. Equal cyanosis of both hands suggest a postductal coarctation or complete aortic interruption. In PDA Eisenmenger's syndrome, cyanosis of the toes is more intense than that in the fingers.

Erythremia/Flushing/Erythema

Polycythemia produces the "ruddy" complexion more readily seen in white patients. A peculiar coloration termed "erythremia" may be evident. This consists of a combination of redness and cyanosis. This feature is demonstrable in the tongue, conjunctiva, nose, lips,

earlobes, fingertips and toe-tips. Erythremia resulting from an increased amount of oxygenated haemoglobin producing the redness together with an increased amount of unoxygenated haemoglobin producing cyanosis. Unlike polycythemia vera, erythremia in congenital heart disease is associated with digital clubbing.

Flushing of the face, neck and chest may occur with carcinoid tumours that have metastasized to the liver. Paroxysmal flushing from increased production of seratonin in time lead to telangiectases of the face and neck. Fibrosis of the right side of the heart may result in tricuspid stenosis and/or regurgitation and pulmonary stenosis. Pheochromocytoma may cause periodic flushing of face and forehead associated with sweating and hypertension. Generalized intense flushing may also be seen in Sipple's syndrome (multiple endocrine neoplasia II) where prostaglandin and seratonin are increased in addition to catecholamines. Flushing of the nail beds synchronous with the heart beat is a sign of severe aortic regurgitation (Quincke pulsations). Capillary "fill" at the nail beds may also be used to evalute peripheral microcirculation.

Facial erythema associated with a dusky cyanotic hue, edema of face and engorged non-pulsatile neck and chest veins would indicate superior vena cava obstruction.

Digital Clubbing

Although digital clubbing is more often seen with pulmonary diseases, gross "drum-stick" clubbing is more likely seen with congenital cyanotic heart disease. Hypertrophic osteoarthropathy with painful swollen wrists and ankles and subperiosteal new bone formation on X-ray may be found. Following corrective surgery for cyanotic heart disease. the combination of pink digits with gross clubbing form a striking feature. Infective endocarditis causes a milder degree of digital clubbing.

Texture

The texture of the skin may be dry and coarse in myxedema, "fine" and smooth in hyperthyroidism and "thick" in acromegaly. It is waxy in amyloidosis and when rubbed becomes hemorrhagic ("pinch purpura"). Systemic amyloidosis may cause cardiomyopathy and postural hypotension from autonomic neuropathy. Hyperelastic velvety skin and hyperextensible joints are characteristic of the Ehlers-Danlos and Marfan syndromes. Mitral valve prolapse and aortic dilatation and rupture may occur.

Pendulous folds and a progressive looseness of skin suggest cutis laxa. Generalized hyperelastosis may cause aortic dilatation and/or rupture. The skin is lax and yellow in pseudoxanthoma elasticum especially over the axilla and cubital flexures. The medium sized arterioles may be calcified. Claudication and angina pectoris may be present. Mitral valve prolapse may be associated[2]. In Werner's syndrome, the skin is atrophic and appear tight with loss of subcutis. Severe coronary artery disease occurs at an early age.

HEART DISEASES WITH SKIN SIGNS

Coronary Artery Disease (CAD)[3]

CAD,specifically coronary arteriosclerotic disease, is a major cause of death in developed countries.

Hyperlipoproteinemia/Xanthomas

Hperlipidemia is a major risk factor for CAD and can be primary (genetic, familial) or secondary (acquired). Therefore, examination of the patient with CAD, particularly the young patient, for cutaneous xanthomas is very important. Xanthomatosis is the deposition of lipids in skin, tendon and fascia. Xanthomas are classified according to their appearance and anatomical location. Their yellow coloration is believed to be due to carotene.

The following forms of xanthomas are recognized: plane, tendinous, palmar (crease or linear), tuberous, & eruptive.

Xanthoma planum are flat yellowish plaques seen most frequently in the eyelids above the inner canthi of the eye (xanthelasma). In about a third of these patients, lipid abnormalities may be found. Xanthelasma is also more often seen among diabetics. Xanthoma tendinosum is most commonly found in the Achilles tendon which is usually the earliest tendon involved. Other preferred sites of involvement are the extensor tendons of the hands and the feet. Tendon xanthomas usually indicate a hypercholesterolemia.

Xanthoma palmaris are seen mainly on the creases of the hands. Xanthoma tuberosum are painless tumours caused by lipid deposition in the dermis. They can be large and usually occur in the extensor aspects of the elbows and knees (Figs 1 and 2) and the buttocks.The combination of tendon and tuberous xanthomas indicate a Frederickson Type II hyperlipoproteinemia, a potent marker of premature CAD.

Fig 1
Xanthoma tuberosum: knobbly, firm swellings around the knees. This patient also had xanthoma tendinosum and was hospitalized for an acute myocardial infarction.

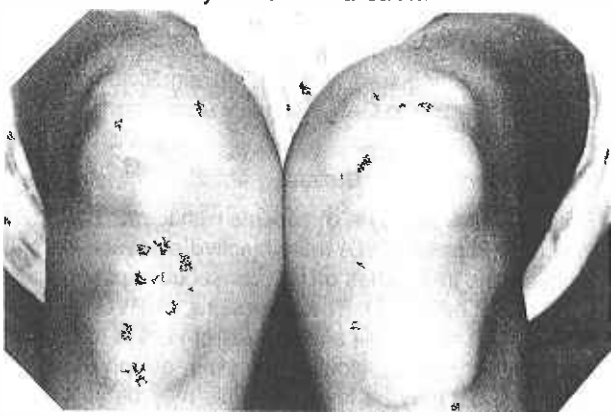
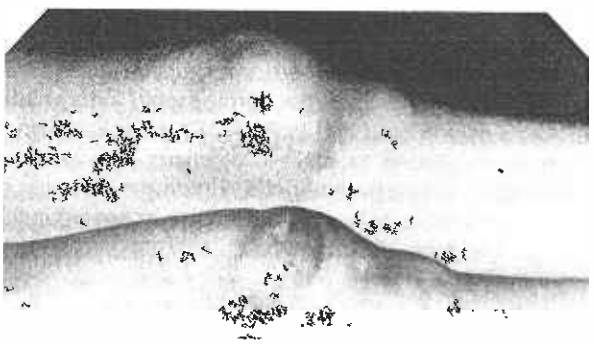


Fig 2
Xanthoma tuberosum: side view demonstrates swelling on the anterior aspects of the knees.



Xanthoma eruptivum arises as crops of yellowish papules on the buttocks, abdomen and extremities. The presence of eruptive xanthomas indicate an abrupt rise of serum triglycerides to high levels. This is seen most frequently with uncontrolled diabetes mellitus.

Hyperuricemia

Gout and hyperuricemia are minor risk factors for CAD. The characteristic skin sign of gout is tophi. These represent deposition of uric acid crystals (monosodium urate) in the subcutaneous tissue. Tophi are usually found on the helix and antihelix of the ear and in the olecranon and prepatellar bursae. Acute deposition of crystals cause inflammation. Confirmation may be obtained by aspiration of fluid to demonstrate uric acid crystals.

Cholesterol Embolization

Cholesterol crystals may microembolize to the lower extremities in patients with advanced atherosclerosis of the abdominal aorta. This occurs rarely. Systemic complaints include pains in the legs, buttocks and abdomen. On the skin, indurated plaques and nodules develop in the lower extremities[4]. Their association with livedo reticularis and ulceration mimic polyarteritis nodosa. A deep skin and muscle biopsy is required to reveal arterioles occluded by multinucleated foreign-body giant cells and fibrosis surrounding biconvex, needle-shaped forms, leaving clefts corresponding to the cholesterol crystal microemboli[5].

Earlobe Crease

A number of reports in the 1970's seen to indicate that the presence of the crease diagonally disposed along the earlobe(s) is associated with an increased risk for CAD(6). It remains unclear whether this sign represents a genetic or acquired finding. The significance of this finding in relation to CAD is equally uncertain.

Peripheral Vascular Disease

Between 46% and 61% of patients with known peripheral vascular disease (PVD) has objective evidence of CAD. Conversely, in a series of 100 consecutive patients with CAD, 62% had PVD. The skin signs of PVD are well-known. The skin in the affected extremities is usually dry and shiny. Painful ulcers and pulp atrophy may be present. Hair may be lost. The nails may be yellow and nail growth slow.

Diabetes Mellitus

Diabetes mellitus has long been known to be a risk factor for CAD. The cutaneous signs are many and have been well documented. Non-infective associations include PVD, neuropathic foot, diabetic dermopathy, necrobiotic lipoidica, scleredema and vitiligo[7]. Eruptive xanthomas have been alluded to earlier. Infections like candidial vulvovaginitis is characteristic. Epidermophytosis or furunculosis tends to be more extensive or severe in the diabetic and more difficult to treat.

Post -Coronary Artery Bypass Graft (CABG) Surgery Problems

CABG surgery is commonly performed using portions of the long saphenous vein as donor grafts. A dermatitis has been reported to occur along the saphenous vein graft scar especially in the distal parts on the medial aspect of the leg[8, 9]. This develops 2 to 6 months after the surgery. The cause is not clear, but may possibly relate to post-operative thrombophlebitis and venous stasis. The dermatitis responds to topical corticosteroids but recurrence is usual.

About 1% of patients developed post-operative infection from leg wounds at the vein graft sites. The majority has either S. aureus or gram-negative infections. A number of cases have recurrent cellulitis in the healed vein graft sites from beta-hemolytic streptococcus many months after surgery.

Kawasaki's disease

Kawasaki's disease (mucocutaneous lymph node syndrome) is a condition of unknown aetiology mainly affecting infants and children under 5 years of age. The principal features are persistent fever, indurative edema of extremities followed by membranous desquamation from finger tips, polymorphous exanthema, bilateral conjunctiva injection, strawberry tongue and cervical lymphadenopathy. Coronary arteritis leading to formation of coronary aneurysms is very characteristic and can be detected by two dimensional echocardiography or coronary angiography. Angina pectoris or myocardial infarction may result.

Coronary arteritis may also be a feature of collagen vascular disease, syphilis (coronary osteitis) and Takayasu's arteritis.

Infective Endocarditis

The cutaneous signs of infective endocarditis (IE) are important clues to its diagnosis. They include Osler's nodes, Janeway lesions, subungual splinter haemorrhages and petechiae.

Painful, red finger tips were noted by Osler to occur in the course of IE. They are tender. The cause is probably due to microembolization of infected material and/or reaction to the embolized material from the heart valves[10].

Janeway lesions are papulo-nodular in morphology but may be purpuric. They are characteristically non-tender and located on the palms and soles.

Splinter "haemorrhages" appear as linear, dark red streaks beneath the nails. They are found, among other causes such as trauma, in IE. Petechiae are common but are less specific. When they occur in the conjunctiva and the oral mucosa or as retinal haemorrhages, they may be easily missed. Gangrene from infarction of digits or extremities may occur from embolization of the large vegetations in fungal endocarditis.

Myxoma

Atrial myxomas are the commonest primary tumours of the heart. They may present a plethora of symptoms and signs and mimic many diseases[11]. Fever, weight loss, arthralgia, clubbing, a high ESR and gammaglobulin level, anaemia, leukocytosis may be part ot the constellation of this clinical condition. Emboli phenomena would be suggestive. Changing heart murmurs offer an important clue.

The cutaneous manifestation may be striking. Raynaud's phenomenon, non-blanching erythema,

vasculitic lesions, splinter haemorrhages and tender digital pads simulate collagen vascular disease or IE. A deep biopsy of lesional skin may show myxomatous emboli with large pale-staining cytoplasma and stellate nuclei along occluded blood vessels in an area of emboli infarct. Myxomas are infrequently encountered and are difficult to diagnose clinically. However, since the advent of echocardiography diagnosis is now easily made and is done earlier permitting surgical intervention. More recently, the association of atrial myxomas with lentigines, nevomelanocytic and blue nevi as well as dermal myxodematous nodules have been described as the NAME[12] (Nevi, Atrial myxoma, Myxoid neurofibromas, Ephelides) or LAMB[13] (Lentigenes, Atrial myxoma, Mucocutaneous myxomas, Blue nevi) syndromes.

Leopard Syndrome

The "Leopard syndrome"[14,15] is an autosomal dominant disorder with variable clinical expression. Each letter of the word "leopard" represents a feature of the syndrome.

Lentigenes (L) is the most characteristic (Figs. 3 & 4). These are multiple and usually present at birth but increase during puberty. The entire skin surface may be involved but the lips and oral mucosa are usually spared.

Fig 3
"Leopard" syndrome: numerous lentigenes seen on face and neck. Note significant sparing of lips.

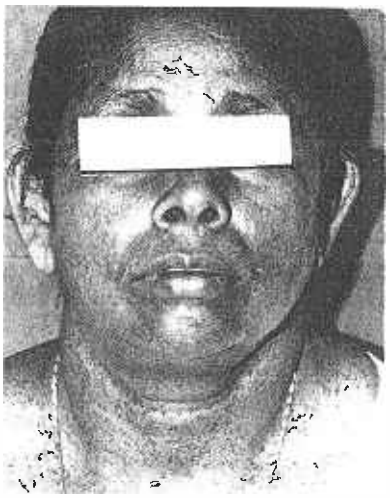
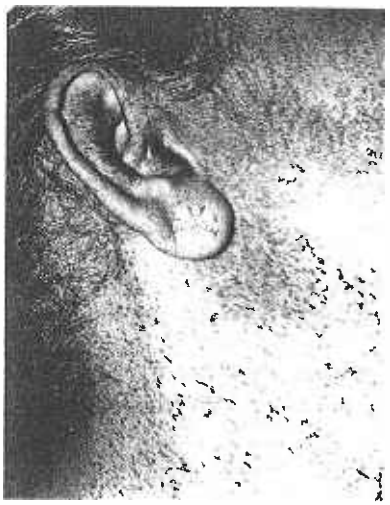


Fig 4
"Leopard" syndrome: close up of neck showing multiple lentigenes. The family history was positive.



Electrocardiographic (E) abnormalities may be present. They are axis deviation, prolonged P-R intervals, bundle branch block, left anterior hemiblock and complete heart block. Associated anatomic abnormalities include hypertropic cardiomyopathy with subaortic stenosis. Ocular (O) telorism may be a feature. Abnormal pigmentation may be found in the iris or retina. Pulmonary (P) stenosis was thought to be an associated feature but now aortic stenosis is known to be more common. Abnormalities (A) of gentialia, retardation (R) of growth and deafness (D) of the sensorineural type are other features of the syndrome.

Cardiomyopathy

Cardiomyopathies may be primary or secondary. The causes of the cardiomyopathies (dilated, hypertrophic or restrictive) are many and varied. They include genetic, infective, infiltrative and metabolic diseases. Their cutaneous manifestations are correspondingly diverse and their discussion is beyond the scope of this brief. Suffice it to say that in the occasional patient, a specific cutaneous finding may point to the correct diagnosis of the type of cardiomyopathy.

MULTISYSTEMIC DISEASES WITH CUTANEOUS AND CARDIAC SIGNS

These will be discussed briefly.

Collagen Vascular Diseases

Systemic Lupus Erythematosus

Cutaneous manifestations of systemic lupus erythematosus (SLE) appear in about 80% of patients during the course of the disease. Features citied as ARA criteria and considered more specific are the malar rash, discoid lesions. photosensitivity and mucous membrane ulcerations. Others features include vasculitis, nail fold telangiectasia, alopecia (diffuse or localized), livedo reticularis and panniculitis. Subacute cutaneous lupus erythematosus is typified by annular or psoriasiform lesions. SLE patients presenting initially with cardiac manifestations are rare. However, subclinical involvement of heart detectable by echocardiography is not uncommon. Pericarditis is possibly more common in drug-induced syndromes. Myocarditis may be associated with prolonged PR intervals and arrhythmias. Complete heart block in the neonate may be associated with the placental transfer of maternal anti-Ro (SSA) antibodies. Endocarditis of the Libmann Sacks type is best known but are often not significant clinically.

Progressive Systemic Sclerosis

Skin involvement generally follows 3 stages : edematous, fibrotic (sclerotic) and atrophic. The characteristic changes are found on the hands where Raynaud's phenomenon is often the presenting feature. Dilated tortuous capillary loops in the nail folds and mat-type telangiectasia on the palms may be found. As the disease progresses sclerodactyly becomes evident and calcinosis cutis may be a complication. Painful difficult-to-heal ulcers represent microvascular involvement.

Cor pulmonale is secondary to pulmonary artery hypertension and pulmonary fibrosis. Scleroderma heart is believed to be the result of small-vessel involvement

of the myocardium[16]. Coronary artery disease with angina also occur. Fibrosis of the conduction system causes arrhythmia and sudden death. Pericarditis, both occult or overt, are reported.

Dermatomyositis

Characteristic cutaneous changes in dermatomyositis include a heliotrope rash of eyelids associated with photosensitivity, nail fold telangiectasia with mini-infarcts of the cuticular edge, 'knuckle' plaques which heal with atrophy (Gottron's sign) and poikiloderma in the sun-exposed areas in particular.

The incidence of myocarditis and coronary artery disease may be increased in dermatomyositis.

Polarteritis Nodosa

This condition is rarely seen. Dermal nodules along the course of superficial arterioles are the characteristic lesions. Skin infarction results in painful indolent ulceration. Coronary arteritis is a known complication.

Relapsing Polychondritis

Relapsing polychondritis is caused by inflammation and destruction of cartilage and connective tissue. Auricular chondritis with painful swelling of the pinna but sparing the earlobes is characteristic. Nasal chondritis leads to saddle-nose deformity and costo-chondritis to chest deformity. Cutaneous vasculitis and panniculitis are additional features.

Cardiac involvement result in degeneration of the aortic ring, aneurysmal dilatation and aortic value regurgitation[17]. "Floppy" mitral valve syndrome also occurs.

Amyloidosis

Involvement of the heart occurs in systemic forms of amyloidosis both primary and secondary, including myeloma-associated types[18]. Infiltration of the myocardium leads to a restrictive cardiomyopathy which has distinctive echocardiographic findings. Thickening of the inter-atrial and/or inter-ventricular septa may be seen. Infiltration of the valves lead to malfunction and of the pericardium to pericardial effusion.

Cutaneous involvement occurs most often in the primary and myeloma-associated types. Translucent papules or plaques occur on the eyelids, nasolabial folds, lips, neck and upper trunk. Sclerodermoid appearance may occur with extensive infiltration. Areas of petechiae and ecchymoses (pinch purpura) occur readily due to early involvement of dermal blood vessels.

Lipoid Proteinosis

Lipoid proteinosis is a rare hereditary condition transmitted by a recessive autosomal gene. An amorphous "hyalin" substance is deposited primarily in the mucous membranes and the skin.

Hoarseness from infiltration of the larynx is usually the initial presentation in infancy and childhood. The skin abnormalities appear soon after. They consist of translucent, waxy indurated papules, nodules and plaques often on the face. A beadlike pattern on the palpebral margins and ankles of mouth is characteristic. Acneiform scars, alopecia and nail dystrophy occur. Cardiovascular involvement with conduction defects and arrhythmias have been reported.

Sarcoidosis

Sarcoidosis is a multisystemic disorder of unknown cause typified by non-caseating epithelial granulomas. The incidence is higher in the Western population. The acute forms present with bilateral hilar lymphadenopathy and erythema nodosum (Löfgren's syndrome). In the chronic form, the lung parenchyma is often affected. The skin lesions consist of firm, flesh-coloured or reddish, papules or nodules on the face or body. Large plaques may show a ringed border. Cardiac involvement may be occult. When overt, conduction disturbances and ventricular arrhythmias manifest as palpitations and syncope. Cor pulmonale is consequent on lung involvement.

OTHER ASSOCIATIONS

An erythroderma (generalised exfoliative dermatitis) may precipitate a compromised heart into cardiac failure. Drugs used in cutaneous diseases eg. acitretin in psoriasis can increase the risk to CAD by elevating the serum lipid levels. Contrariwise, cardiac drugs eg. hydrallazine or procainamide can induce SLE and calcium-channel blockers can cause severe adverse cutaneous drug reactions such as erythema multiforme or toxic epidermal necrolysis.

It can be seen from the foregoing that the heart and the skin do have much in common. These cardiocutaneous associations can certainly aid physicians in understanding the aetiologies, in the diagnostic evaluation, and in following the progress and treatment responses of this group of diseases.

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