

Retrospective study of papulonodular skin lesions and their clinopathological correlation

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Abstract

Background: Papulonodular lesion of the skin is a more common variety. Various types of diseases manifested with papulonodular lesions surface, for example, infectious diseases, benign neoplastic diseases, and malignant tumors as well as metastatic tumors. Therefore, a brief idea about the clinical history, age, sex, and various sites of lesion is important.

Objectives: To evaluate the incidence of different infectious, benign, and malignant diseases manifested with papulonodular lesions. To study the various papulonodular lesions of skin in relation to different age group, sex, and location. To compare our observation with that of other authors and to correlate clinical data with that of histopathological study.

Materials and Methods: In the present study, from November 2007 to November 2009, total 75 cases of papulonodular lesions were taken for study from Department of Dermatology and Department of Pathology, BJ Medical College and Civil Hospital, Ahmedabad, Gujarat, India. All lesions were studied with respect to clinical history, physical examination, histopathological examination of biopsy material on HE stain and also on special stains when required.

Results: In the present study, 69% of papulonodular lesions of skin were of infectious origin followed by 24% as benign origin and 7% as malignant origin. In infectious lesions, most common is leprosy with incidence of 22.67%, erythema nodosum leprosum 20%, and cutaneous tuberculosis mostly scrofuloderma 8% and Prurigo Nodularis 6.67%. In benign lesions, trichoepithelioma has incidence of 8% and syringoma 5.33%. In malignant lesions, Basal cell carcinoma has incidence of 4% and metastatic carcinoma 2.67%. Clinically, most of infectious lesions are diagnosed and are confirmed by histopathology. In leprosy, clinopathological correlation is 94.12% and in erythema nodosum leprosum, it is 93.33%, while in cutaneous tuberculosis, actinomycosis, and epidermoid cyst, clinopathological correlation is 100% with histopathological diagnosis.

Conclusion: Papulonodular lesion of skin is clinically well diagnosed and better correlated with histopathological examination.

KEY WORDS: Cutaneous tuberculosis, leprosy, papulonodular lesions, trichoepithelioma

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Introduction

Papulonodular lesion of the skin is a more common variety. Different kinds of infectious diseases, benign neoplastic diseases, and malignant tumors as well as metastatic tumor are also manifested with papulonodular lesions. So a brief idea about the clinical history, age, sex, and various sites of lesion is important. In past few years, various advances in

pathology made diagnosis easier, but still it is a challenging job for the histopathologist to find out right diagnosis by using H&E stain with addition to various special stains, as well as immunohistochemistry.

A papule is defined as a solid raised lesion that has distinct borders and is less than 1 cm in diameter. Papules may have a variety of shapes in profile (domed, flat-topped, umbilicated) and may be associated with secondary features such as crusts or scales. A nodule is defined as a raised solid lesion more than 1 cm and may be in the epidermis, dermis, or subcutaneous tissue.

The lesions which are maximally diagnosed in our study are leprosy, erythema nodosum leprosum, cutaneous tuberculosis, trichoepithelioma, Prurigo Nodularis, actinomycosis, granuloma annulare, epidermoid cyst, syringoma, Jessener lymphocytic infiltrate, basal cell carcinoma (BCC), and metastatic carcinoma.

Leprosy is caused by mycobacterium leprae and predominantly affects the skin and peripheral nerves. The mode of transmission is probably inhalation of bacilli. Clinically, lepromatous leprosy presents as papulonodular lesion. Initially, it has cutaneous and mucosal lesion. Clinical types are macular type, infiltrative nodular type, and diffuse type. Histologically, it exhibits an extensive cellular infiltrate that is separated from the flattened epidermis by a narrow grenz zone of normal collagen. The infiltrate causes the destruction of the cutaneous appendages and extends into subcutaneous fat. In florid early lesion, the macrophages have abundant eosinophilic cytoplasm and contain a mixed population of solid and fragmented bacilli. If solid, macrophages may be packed like cigar on fitefarraco staining in endothelial cells. Lepra cells or Virchow cells- macrophage having vacuolated or foamy cytoplasm with degerated bacilli.^[1] The most frequently used special stain is a polyclonal anti BCG- antibody.^[2]

Erythema nodosum leprosum is an acute inflammatory reaction seen in a patient with lepromatous leprosy. It is Type-2 lepra reaction, which is an antigen antibody-mediated immune complex reaction.^[3] Usually 15%–50% of lepromatous leprosy patients develop this reactions within the first year of therapy.^[4] Clinically it is tender, red plaques or nodules together with areas of erythema. The eruption is wide spread and is accompanied by fever, malaise, arthralgia, and leukocytosis.^[1] Histologically, there are foci of acute inflammation superimposed on chronic muitibacillary leprosy. Polymorph neutrophils may be scanty or so abundant as to form a dermal abscess with ulceration.^[4] Foamy macrophages containing fragmented bacilli are seen as a granular pink hue on Wade-Fite staining, including mycobacterial debris. Immunohistochemically, anti-BCG will indicate abundant antigen.^[5]

Cutaneous tuberculosis is infection of the skin, and subcutis caused by mycobacterium tuberculosis occurs by three routes^[1]—direct inoculation, hematogenous spread and direct extension from underlying tuberculous lymph node (causing scrofuloderma). Scrofuloderma is the most common form of cutaneous tuberculosis in children. It results as a direct extension from an underlying TB focus, such as a regional lymph node or infected bone or joint, to the overlying skin. Clinically,

it present as firm, painless, subcutaneous, red-brown nodules overlying an infected focus, which gradually enlarge and suppurate forming ulcers and sinus tracts that drain watery, purulent, or caseous material.^[1] Histologically, skin biopsy reveals tuberculoid granuloma surrounding areas of wedge-shaped necrosis.

Trichoepithelioma is also known as Brooke's tumor. In most instances, the first lesions appear in childhood and gradually increase in number.^[6] Clinically, it appears as round, skin colored, firm, papule, or nodules usually between 2 and 8 mm sizes. It is located mainly over face in nasolabial fold but also on nose, forehead, and upper lip. Histologically, it appears as a well-circumscribed, small, and symmetrical lesion. Horn cysts are more common. "Basalioma cells" characterized by fully keratinized center surrounded by basophilic cells, lack of high-grade atypia, and mitoses. The keratinization is abrupt and complete in the same manner as so-called trichilemmal keratinization.^[1] Special stains using a panel of monoclonal anti-keratin antibodies suggest that trichoepithelioma differentiates toward the outer root sheath.^[7] It is also difficult to differentiate it from keratotic basal cell carcinoma on histologic grounds, so the need for clinical data has been stressed.^[8]

Prurigo Nodularis is a chronic dermatitis. The cause remain unknown but local trauma, insect bites, atomic background, and metabolic or systemic disease have been implicated as predisposing factors in some cases.^[9] Clinically, it presents as discrete, raised, firm hyper-keratotic papulo nodules, usually 5–12 mm in diameter but occasionally larger. It occurs chiefly on extensor surfaces of extremities and intensely pruritic. The disease usually begins in middle age and more common in female. Histologically, pronounced hyperkeratosis and irregular acanthosis are observed. There may be papillomatosis and irregular downward proliferation of epidermis and adnexal epithelium^[10] approaching pseudo-epitheliomatous hyperplasia.^[11] The papillary dermis shows a predominantly lymphocytic inflammatory infiltrate and vertically oriented collagen bundles. Many nerve fibers are demonstrable with immunostains for S-100 protein.^[12]

Actinomycosis is a rare, chronic infection caused by bacteria known as Actinomyces Israeli, which is a gram-positive, branching, filamentous bacterium.^[13] Actinomycosis causes tissue damage and the formation of multiple pus-filled swellings, known as abscesses. Actinomycosis is a rare type of infection. Actinomycosis can occur in most areas of the body; most commonly reported sites are face and neck (50%–70%), chest (15%–20%), abdomen, and pelvis.

Clinically, it presents as chest wall-draining sore with minimal or no pain, on face or upper neck-hard red to purple papule or nodule with sinus formation and discharge of sulfur granules.^[14] Histologically, it is typically a chronic abscess with polymorphs, surrounding the granulation tissue, and fibrosis. The organism is usually tangled together in a matted colony, forming a granule or grain. These grains commonly, termed "sulfur granules," may be 20 μ m to 4 mm in diameter.

Granuloma annulare is a chronic degenerative skin disorder. In addition to the localized form, there are four less

common forms: generalized or disseminated, linear, perforating, and subcutaneous. Clinically, it is characterized by the presence of small, firm, red, or yellow colored nodules or papules that appear arranged in a ring on the skin. In most cases, the sizes of the lesions range from 1–5 cm. The most commonly affected sites include the feet, hands, and fingers. Females are affected more commonly.^[15–17] Histologically, it shows an infiltrate of histocytes and a perivascular infiltrate of lymphocytes that is usually sparse. The histocytes may be present in an interstitial pattern without apparent organization or in palisades, surrounding areas with prominent mucin. Increase mucin is the hallmark of granuloma annulare. It appears a faint blue material with stringy, finely granular appearance.^[18] Stains such as colloidal iron and alcian blue can be used to highlight mucin if it is not clearly apparent.^[1] A sparse infiltrate of eosinophils is seen in approximately half of cases and occasional biopsies show abundant eosinophils. The histiocytic infiltrate most commonly multinucleated form is usually present throughout the full thickness of the dermis or the middle and upper dermis, but occasionally just the superficial or the deep dermis is involved.^[19] On immunoperoxidase study of the histiocytic population showed staining for lysozyme, but not for other macrophage markers such as HAM 56 or CD68.^[20]

Epidermoid cysts are subcutaneous cysts that usually are present at birth.^[1] Clinically, they occur most commonly on the head, mainly around the eyes, and occasionally on neck. Usually, they measure between 1 and 4 cm in diameter.^[1] Histologically, they are lined by epidermis that possesses various epidermal appendages which are usually fully matured. Hair follicles containing hairs that project into the lumen of the cyst are often present. In addition, the dermis of epidermoid cyst usually contains sebaceous glands, often eccrine glands, and in about 20% of the cases, apocrine glands that have matured.^[21] It represents an adenoma of intraepidermaleccrine ducts. It is more common in women, mostly at puberty and later in life.^[1] Clinically, solitary or multiple small, skin colored or slightly yellow, soft papules usually 1–2 mm in diameter. In many cases, the lesion is limited to the lower eyelids. Other sites of predilection are the cheeks, thighs, axillae, abdomen, and vulva.^[22,23] Histologically, numerous small ducts are embedded in a fibrous stroma, the walls of which are usually lined by two rows of epithelial cells. In most instances, these cells are flat. The lumina of the ducts contain amorphous debris. Some of the ducts possess small, comma-like tails of epithelial cells, giving them the appearance of tadpoles. In addition, there are solid strands of basophilic epithelial cells independent of the ducts. Near the epidermis, there may be cystic ductal lumina filled with keratin and lined by cells containing keratohyline granules.^[24] Syringoma may be confused with fibrosing basal cell carcinoma. However, fibrosing basal cell carcinoma lacks ductal structures containing amorphous material.^[1]

Jessner lymphocytic infiltrate is commonly asymptomatic, non-scaly, erythematous papules, or plaques on the face and neck of several months duration.^[25] Some patients report burning or pruritic sensation. Histologically, the epidermis may be normal but often appears slightly flattened. In the dermis,

there are moderately dense perivascular and diffuse infiltrates composed of small, mature lymphocytes admixed with occasional histiocytes and plasma cells.^[1]

Immunohistochemical cell marker studies indicate that the predominant component of lymphocytic infiltration of the skin is mature T lymphocytes. The histologic differential diagnosis of lymphocytic infiltration of the skin includes the other four of the five “L’s”: lupus erythematosus, polymorphous slight eruption, lymphocyte cutis, and lymphoma.^[25]

Basal cell carcinoma (BCC) is the most common form of skin cancer. The reason for this rise might be that people are receiving more unprotected exposure to the harmful ultraviolet (UV) rays of the sun. Risk of developing this skin cancer increases significantly with age. And almost twice as often in men.^[1] Clinically, most commonly involved sites are head, neck, trunk, and legs, but BCC can appear anywhere on the body. Noduloulcerative basal cell carcinoma begins as a small, waxy nodule that often shows a few small telangiectatic vessels on its surface. The nodule usually increases slowly in size and often undergoes central ulceration. A typical lesion then consists of a slowly enlarging ulcer surrounded by a pearly, rolled border. This represents the so-called rodent ulcer.^[1] Histologically, the characteristic cells of basal cell carcinoma, referred as a basaloma cells, have a large, oval, or elongated nucleus and relatively little cytoplasm. From a histological point of view, basal cell carcinoma can be divided into two groups: undifferentiated and differentiated. Those of latter group show a slight degree of differentiation toward the cutaneous appendages of hair, sebaceous glands, apocrine glands, or eccrine glands.^[1]

Metastatic tumors to the skin may occasionally be the first manifestation of a cancer. Unfortunately, when this occurs, the cancer is usually advanced. The incidence and type of metastases varies by age, sex, and tumor type.^[1] Skin metastases were the initial presenting manifestation of the cancer in 0.8%.^[26] In male, most common sources are from^[15,26] lung (25%), large bowel, skin, and kidney; and in female, from breast (69%), lung, skin, and kidney. Clinically, cutaneous metastases present themselves in a variety of clinical patterns and tend to be manifested as indurate papules/nodules/tumors. Most common sites in descending order are: chest and abdomen, head and neck, and extremities (rare). Grossly multiple, firm nonulcerated nodules are present. Microscopically, different lesions have different appearances as primary lesion, correctly diagnosed by nuclear atypia.

Materials and Methods

In the present study, from November 2007 to November 2009, total 75 cases of papulonodular lesions were taken for study from Department of Dermatology and Department of Pathology, BJ Medical College and Civil Hospital, Ahmedabad, Gujarat, India. Approval from Institutional Ethical Committee was taken before commencing study. All patients signed their consent form, which includes information regarding their name, age, sex, name of hospital, name of clinician, date and

type of procedure, and site of lesions and their symptoms. Relevant history like duration of lesion, family history of same lesion, any exposure to radiation or chemicals, past history of same lesions, any treatment taken, and history of diabetes mellitus were also collected from all subjects. As acne is most common papulonodular lesion of skin, but no histopathological examination is done for that, so we have excluded it from our study.

In all these cases, 4 mm punch biopsy was taken and fixed in 10% neutral buffered formalin for 24 h. These fixed tissues then processed through ascending grade of alcohols and xylene in automated tissue processor and finally tissues were embedded in melted paraffin wax to make paraffin block. Then thin sections were taken using standard microtome by expert trained technicians. Then all slides were stained by standard haematoxylin and then by eosin. Then slides were studied under light microscopes. Different special stains were also done as and when required.

Results

In the present study, from November 2007 to November 2009, 69% of papulonodular lesions of skin were of infectious origin followed by 24% as benign origin and 7% as malignant origin.

The overall incidence of papulonodular lesions of skin is leprosy (22.67%), erythema nodosum leprosum (20%), cutaneous tuberculosis and trichoepithelioma (8% each), Prurigo Nodularis, actinomycosis and epidermoid cyst (6.67% each), syringoma and granuloma Annulare (5.33% each), basal cell carcinoma and Jessner lymphocytic infiltrate (4% each), and metastatic carcinoma (2.67%).

Lesions like leprosy, erythema nodosum leprosum, trichoepithelioma, Metastatic carcinoma were more common in males, while Prurigo Nodularis and granuloma annulare were more common in females.

In the present study of total 75 cases, clinical diagnoses of 67 (89.33%) cases were confirmed by histopathological examination. Clinical correlation with histopathology report was best achieved (100%) in cutaneous tuberculosis, actinomycosis, epidermoid cyst, syringoma, and metastatic carcinoma cases. Trichoepithelioma was the only lesion which was least correlated (66.67%) with histopathological examination.

Discussion

In the present study, it was noted that incidence-wise papulonodular lesions of skin are leprosy (22.67%), erythema nodosum leprosum (20%), cutaneous tuberculosis and trichoepithelioma (8% each), Prurigo Nodularis, actinomycosis and epidermoid cyst (6.67% each), syringoma and granuloma annulare (5.33% each), basal cell carcinoma and Jessner lymphocytic infiltrate (4% each), and metastatic carcinoma (2.67%).

In case of leprosy, overall incidence is 22.67% and M/F ratio is 2.4:1, which is very much comparable with study

of Gill *et al.*,^[27] which is 20% and 3:1, respectively. In case of cutaneous tuberculosis, overall incidence is 32% and M:F ratio is 2:1, which is very much comparable with study of Acharya and Ranpara^[3] showing 28% and 1.5:1, respectively. In case of trichoepithelioma, overall incidence is 6.67% and M:F ratio is 2:1, which is very much comparable with study of Samaila,^[28] which is 5.8% and 2:1, respectively. In case of Prurigo Nodularis, overall incidence is 6.67% and M:F ratio is 1:1.5, which is very much comparable with study of Kim and Ahn,^[29] which is 5.2% and 1:2.4, respectively. In case of actinomycosis, overall incidence is 6.67% and M:F ratio is 4:1, which is very much comparable with study of Chakravarty and Hodarkar.^[30] showing 6% and 3:1, respectively. In case of syringoma, overall incidence is 4% and M:F ratio is 1:1, which is very much comparable with study of Reddy *et al.*^[31] showing 3.53% and 1:2, respectively. In case of basal cell carcinoma, overall incidence is 4%, which is very much comparable with study of Chuang *et al.*^[32] showing 3%. In case of metastatic carcinoma, overall incidence is 2.67%, which is very much comparable with study of Wesche *et al.*^[33] showing 2%. But in case of erythema nodosum leprosum, overall incidence is 8%, which is not much comparable with study of Pocaterra *et al.*^[13] showing 24%.

In the present study of papulonodular lesions of skin, findings and results of leprosy, cutaneous tuberculosis, trichoepithelioma, Prurigo Nodularis, actinomycosis, syringoma, basal cell carcinoma, and metastatic carcinoma are very much consistent with study of different authors.

Conclusion

In this study, 69% of papulonodular lesions of skin were of infectious origin followed by 24% as benign origin and 7% as malignant origin. The most common diagnosis of papulonodular lesions of skin is leprosy, which is followed by erythema nodosum leprosum. Lesions like leprosy, erythema nodosum leprosum, trichoepithelioma, and metastatic carcinoma were more common in males, whereas Prurigo Nodularis and granuloma annulare were more common in females.

This study reveals clinical correlation with histopathology report was best achieved (100%) in cutaneous tuberculosis, actinomycosis, epidermoid cyst, syringoma, and metastatic carcinoma cases. Findings and results of leprosy, cutaneous tuberculosis, trichoepithelioma, Prurigo Nodularis, actinomycosis, syringoma, basal cell carcinoma, and metastatic carcinoma are very much consistent with study of different authors. So, papulonodular lesions of skin are clinically well diagnosed and better correlated with histopathological examination.

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