Pityriasis Rosea - Literature Review

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ABSTRACT

Pityriasis rosea (PR) is a common papulosquamous disorder. It is seen mostly in children and young adults. The underlying cause of PR is unclear but a viral aetiology has been postulated. It is characterized by scaly papules and plaques distributed mainly on the trunk parallel to Langer's skin lines in a Christmas tree pattern. The generalized eruptions are often preceded by the appearance of a single larger lesion known as the herald patch. Prodromal symptoms of fever, sore throat or arthralgia may occur in a minority of patients. Itching is often mild to moderate. The eruptions disappear spontaneously within 6 to 8 weeks with temporary post inflammatory hypo- or hyperpigmentation. Thus, treatment is supportive, although mid-potency topical corticosteroids can reduce pruritus; high-dose acyclovir may speed up recovery. Recurrence or relapse is very rare.

INTRODUCTION

Pityriasis rosea or "pink scaly eruption" is a common acute, self-limited papulo-squamous skin condition. This benign non-contagious disorder was first described by Gilbert in 1860.[1] It typically begins as a single oval scaly plaque known as the herald patch.[2] This initial eruption is followed several days to weeks later by numerous widespread similar, but smaller rashes. Pityriasis rosea can present in a variety of manners. PR affects children and young adults.[2,3]

EPIDEMIOLOGY

About 75% of Pityriasis rosea cases are observed in the age bracket of 10-35 years in the temperate countries.[3] However the age range is quite wide (3 months to 83 years).[3] The disease is present worldwide and has been estimated to account for 2% of dermatologic outpatient visits.[3,4] The incidence of PR in Nigeria ranged from 2.4 [5] to 3.7[6] per 100 dermatological patients. Most studies have shown a slight female preponderance of approximately 1.5:1[7,8] No racial predominance has been reported. The prevalence may be higher in middle and lower social class.[4]

Previous studies have reported contradicting results for seasonal variation of PR. Studies in the UK,[9] USA[10]and Sudan[11] reported higher incidence of PR in the colder months. One study in southern Nigeria[12] reported higher incidence in the early part of the rainy season. The study in Brasil[13] and another study in Singapore[14] reported a bimodal distribution. No seasonal variation was reported by studies in Turkey[15] and another study in Singapore.[16]

AETIOLOGY

Pityriasis rosea is essentially a disease of unknown aetiology but is probably viral in origin though no specific virus has been isolated or shown to be directly linked. Recent work has focused on the role of human herpes virus HHV-6(the causative agent of roseola) and HHV-7.[17,18] Many different investigations have been done e.g. polymerase chain reaction, nested PCR and in situ hybridization which implicated these agents.[19,20] However some other studies were unable to replicate some of these findings.[21] Another recent study found evidence of systemic active infection of both HHV-6 & 7 in lesional skin, non-lesional skin, saliva and peripheral blood lymphocytes and sera of patients with pityriasis rosea.[22] These two herpes viruses may be acquired early in childhood[31] and remain latent in peripheral blood lymphocytes, mainly the CD4 cells, and the saliva. What triggers HHV-7 reactivation is unknown but once triggered it causes HHV-6 reactivation. It is believed that pityriasis rosea is not caused by direct viral infection of the skin but possibly by cutaneous infiltration of latently infected lymphocytes.[23]

At the time of presentation there is increased incidence of local mononuclear cells in the deeper perivascular and superficial dermis.[23] Immuno-histologic data show perivascular aggregates of predominantly active CD4 cells in superficial dermis. There is increase in Langerhan's cells and a higher ratio of T – helper to T-suppressor cells correlates with stage and severity of disease. It has been reported that there is both increase in circulating IgM and decrease in C_3 and total T cell counts with normal levels of IgG and IgA.[24]

These findings are consistent with defence mechanisms mediated by immunoglobulins. This supports the theory that viruses interfere with the ability of lymphocytes to respond which may further explain the development of pityriasis rosea.[24,25] Anti-

IgM to keratinocytes has been found and may cause widespread eruption. The chemokine CX3C which is expressed in normal human skin by dendritic cells has been found to be elevated in serum of patients with PR.[26] This chemokine activates multiple intracellular signals via its receptor in NK (natural killer) cells, monocytes CD_4 and CD_8 T cells directly contributing to leucocyte joining and capturing.

Though no aetiology has been proven, it has been shown that the disease is not related to many common infectious agents such as influenza A & B, para-influenza, CMV, EBV, parvovirus, chlamydia, streptococcus and legionella.[27]

It has also been hypothesized that many an autoimmune process may be responsible for PR. A positive ANA is observed more commonly in PR patients even without clinical evidence of autoimmune disease.[28] The association of PR with autoimmune markers may be explained by genetics. One hypothesis is that PR patients share the same HLA-DR haplotypes as patients with a high incidence of autoantibodies and autoimmune diseases. These patients will genetically be predisposed to develop PR when triggered by viral infection. A particularly strong association has been found between HLA DQB_1 allele and PR in Brazilian black population.[29]

Many drugs have been implicated in causing PR-like eruptions in susceptible individuals. These include captopril,[30] metronidazole,[31] hydroxychloroquine,[32] omeprazole,[33] barbiturates,[34] gold,[35] imatinib,[36] adalimumab,[37] eternecept,[38] terbinafine,[39] lisinopril, bismuth and clonidine.[40] Similar eruptions have also been reported with administration of certain vaccinations e.g. BCG, pneumococcal and HBV vaccines[41-43]

Stress has also been advanced as a cause of PR.[44,45] Though considered unlikely, it may be due to the depressant effect of stress on the immune system that may predispose such individuals to PR. The disease has also been reported following bone marrow transplantation.[46]

CLINICAL CHARACTERISTICS

The most common initial sign of the disease is a pink macule or papule usually on the trunk or neck which gradually expands over a few days to become a single salmon-pink oval patch or plaque. This heralds the widespread eruption and is called the herald patch or primary plaque.

The occurrence of a herald patch was seen in 40-76%[47,48] of patients with the most commonly reported site being the trunk in 48.7-57.2 %[48,49] Variations are common; in pigmented patients the lesions may be dark in colour and may not appear erythematous.[50] The lesions may appear in atypical sites e.g. face, scalp, genitalia and dorsum of the feet. There may be multiple herald patches in up to 5.5% of cases and the herald patch may even occur at the same time as the generalized secondary lesions. Prodromal symptoms e.g. headache, gastrointestinal discomfort, malaise, fever and arthralgia may precede a few cases of clinically typical pityriasis rosea.[51]

From the onset of the herald patch, it takes several days to weeks before secondary rashes usually appear but this can vary from hours to 3 months.[3] The secondary eruptions are bilateral and symmetrically arranged with their long axes parallel to lines of cleavage resulting in the characteristic 'Christmas tree' or 'fir tree' distribution. These commonly used terms usually describe pityriasis rosea involving the upper chest and upper back. Langer's cleavage lines have 3 major patterns on the trunk which describes the characteristic rash of pityriasis rosea.[52] These include V–shaped distribution on upper chest and upper back, A circumferential pattern around the shoulders and hips and A transverse pattern on lower anterior trunk and lower back.[52]

The mechanism by which the rashes follow Langer's lines is unknown. The macules resemble the herald patch and consist of fine scales surrounded by a peeling darker scaling border 'the collaret scale'. The typical distribution is on the thorax, back, abdomen and proximal extremities. In adults the face, hands and feet are usually spared.[53] Lesions may however be found anywhere including the palms. The disease may be confined to tanned skin or paradoxically spare sun-exposed areas.

Mode of rash distribution may be atypical in up to 20% of cases. Pityriasis rosea may present with atypical morphology which include vesicular, purpuric, haemorrhagic and urticarial forms. The vesicular form is commoner in children and young adults and may mimic varicella infection.[54] The papular variant is more common among toddlers, pregnant women and those of black African lineage.[11] In dark skinned patients the macules may appear darker than the surrounding skin without the classic rose colouration.[50] The lesions present as numerous 1-2mm papulo-squamous eruptions. These widespread lesions tend to leave post-inflammatory hypo- and hyper-pigmentation upon resolution especially in pigmented people.[50] The urticarial form of pityriasis rosea is an infrequent variant and may resemble acute urticaria.

The size of the lesions may be atypical. In this rare presentation, PR presents with enormous plaques so termed pityriasis rosea gigantea of Darier. Distribution of PR may also be atypical, these include pityriasis rosea inversa that presents with lesions on the extremities, flexural areas and face. The eruptions are restricted to the shoulders or hips in the limb girdle distribution. In localized PR, eruptions are limited to a

small area such as the breast or axillae.

In a few cases of PR, atypical sites for the rash have also been reported. These sites include the scalp, face, hand and feet. Oral involvement is generally uncommon though incidence of up to 16% has been reported in some studies.[53] It is however relatively commoner in black individuals and those with widespread disease.[4] Oral lesions encountered include punctate haemorrhage, ulcerations, bullae, erythematous macules and plaques.[57,58,59] The disease may be more widespread in blacks[4] in whom it may be associated with generalized lymphadenopathy.[50] Pitting of the nail plate is an infrequent finding in pityriasis rosea.

Figure 1 Showing classic plaque type of pityriasis rosea with the oval shaped plaques following the Langer's skin lines

The rash evolves over a period of approximately 2 weeks at which time it reaches its peak intensity. Thereafter, lesions at different stages of healing will be observed. This disseminated phase then slowly resolves over the following 2-4 weeks. In some cases it may last 3-5 months and such protracted courses are commoner in drug-induced cases of pityriasis rosea.[12]

Recurrent or relapsed cases have been reported. Recurrent episodes have been estimated to occur in 1.8 - 3.5% of cases.[60]

PR may lead to undesirable outcomes when affecting pregnant women. It has been associated with neonatal hypotonia, hypoactivity, and premature delivery. An increased risk of miscarriage may occur, especially in mothers who developed pityriasis rosea within the first 15 weeks of their pregnancy.[61,62]

HISTOPATHOLOGY

A skin biopsy typically shows a pattern of superficial perivascular dermatitis. Epidermal findings include slight hyperplasia, focal spongiosis and focal parakeratosis in mounds.[63] In

Figure 2: Showing papular type PR and the lone herald patch on left upper chest

Figure 3: Showing large oval plaques of PR gigantea of Darier

the dermis there is superficial perivascular infiltrate of lymphocytes, histiocytes and occasionally oesinophils.[63] There is papillary dermal edema and variable number of extravasated red blood cells. Papillary dermal RBCs are particularly prominent in purpuric pityriasis rosea[64] dyskeratotic cells with oesinophilic homogenous appearance of upper dermis, multinuclear epidermal giant cells and focal acantholytic dyskeratosis have been described.[64]

DIAGNOSIS

The diagnosis of PR is essentially clinical. History should focus on the details of the eruptions, presence of prodromal symptoms e.g. features of upper respiratory tract infection, medications used etc. Examination reveals the typical papulosquamous eruptions. Proposed diagnostic criteria[65] includes three required essential features: discrete circular or oval macules, scaling on most of the lesions and peripheral collarette scaling with central clearance of at least two. However atypical forms of PR may present without the above characteristics in which case skin biopsy may be required for diagnosis.[66]

DIFFERENTIAL DIAGNOSIS

Secondary syphilis: should be suspected in sexually active patients with atypical lesions and affectation of palms and soles.[67,] The lesions are non-itchy. Patient presents with generalized lymphadenopathy and may have evidence of a primary chancre. Serological tests and organism identification e.g. via dark ground microscopy may be required for diagnosis.[68]

Other differentials include guttate psoriasis, nummular eczema, parapsoriasis, pityriasis versicolor, taenia corporis and seborrhoic dermatitis. Pityriasis

Figure 4: Showing PR with facial affectation with oval shaped scaly plaques

versicolor and taenia corporis can be ruled out by fungal studies and examination under Wood's light. Since certain drugs cause PR-like eruptions, they must be considered in the differentials of PR. However, such cases are more likely to present atypically e.g. they may lack a herald patch and may be associated with oral lesions and postinflammatory hyperpigmentation.[12]

PR-like lesion may occur in HIV seroconversion illness but is usually distinguished by involvement of the soles and palms and preceded by flu-like illness, lymphadenopathy and lymphopenia.[69] A positive HIV serology clinches the diagnosis but may be negative at this stage. Thus in suspected cases a repeat serology a few weeks later or more advanced tests e.g. PCR or P24 antigen may be useful.[69]

TREATMENT

Pityriasis rosea is a self-limiting disease, and therefore treatment may be unnecessary. Where symptoms are severe, relief of pruritus may be achieved with topical steroids, topical menthol-phenol lotions, oatmeal baths or oral antihistamines. Systemic steroids are not recommended because, though they suppress pruritus, they do not shorten the overall disease but may rather prolong or exacerbate it.[70] Ultraviolet B (UV-B) light therapy, starting at 80% of the minimum erythrogenic dose, may rapidly relieve pruritus in resistant cases.[71] If itching is not controlled, the dose of UV-B light should be increased by 20% until symptoms decrease. However, a recent study failed to find improvement in the pruritus but did note decreased lesion severity with UV-B light therapy.[70,71] One must take into consideration the possibility of post-inflammatory pigmentation with light therapy.[71]

Other treatments that have been successfully tried include dapsone especially in vesicular pityriasis rosea and intramuscular triamcinolone.[3]

Recent studies have shown that erythromycin helps in accelerating rash resolution,[72,73] though this was refuted by other studies.[74] Azithromycin has also been tried and generated similar results as erythromycin.[75] Other antibiotics have also been tried but with modest results. Ampicillin has been found to worsen the distribution of the rashes as it does in infectious mononucleosis.[12]

The antiviral agent acyclovir at very high doses (800mg qid) may shorten disease duration especially if instituted early though more studies are needed to confirm this.[76,77] However, in vitro studies have shown little activity of this drug against HHV-7, one of the agents currently being evaluated for an aetiological role in PR.[77]

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