Pityriasis rosea - An update

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ABSTRACT

Recent controversies on the etiology, diagnosis and treatment have led to increased interest in pityriasis rosea (PR). We review these aspects of the disease. PR is universal. The incidence is around 0.68 per 100 dermatological patients, or 172.2 per 100,000 person-years. The prevalence in people aged between 10 and 29 years is 0.6%. The male to female ratio is around 1: 1.43. Evidence on seasonal variation is conflicting, but there is no evidence that the incidence is dependent on mean air temperature, mean total rainfall, or mean relative humidity. Spatial-temporal and temporal clustering of cases of PR has been reported. The association of PR with human herpesvirus-7 infection is still controversial. Owing to the extreme high sensitivities of sequence-based detection methods such as polymerase chain reaction, novel criteria should be applied to evaluate the evidence. There is no evidence that PR is associated with other viral or bacterial infections. The role of autoimmunity in PR warrants further investigations. Many patients with PR have one or more atypical features. Application of validated diagnostic criteria may be helpful for atypical cases. The efficacy of macrolides, including erythromycin, in PR is still under evaluation. There is no evidence that antiviral agents are effective. The efficacies of ultraviolet radiotherapy and systemic corticosteroids are not well established. In managing a patient with PR, we should concentrate more on how the eruption is affecting the quality of life, i.e. the illness, rather than the extent and severity of the eruption, i.e. the disease.

Key Words: Diagnostic criteria, Erythromycin, Human herpesvirus 7, Quality of life, Temporal clustering

INTRODUCTION

Despite active labor for nearly one and a half century by generations of researchers, the etiology of pityriasis rosea (PR) fails to be demystified. Recent controversies on the role of human herpesvirus-7 (HHV-7) in the etiology, the discovery of significant temporal clustering, the establishment of diagnostic criteria, and controversies on the role of macrolides in treatment have led to increased interest in this eruption.

HISTORICAL ASPECTS

PR was probably first described by the Edinburgh dermatologist Robert Willan under another terminology in 1798.[1] The macular variety of PR was first named as such by the French dermatologist Camille Melchoir Gibert in 1860.[2] The more usual annular variety was first described by another French dermatologist Pierre-Antoine-Ernest Bazin in 1862.[3] Jean Baptiste Emile Vidal, another French

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dermatologist, described *pityriasis circiné et marginé* in 1882.[3] It has fewer and larger lesions, often localized at the axillae or groins, and runs a longer course.[4] The herald patch was first described by a French dermatologist Louis-Anne-Jean Brocq in 1887.[1]

Nomenclature

In ICD-10, pityriasis rosea is coded L42X00. Pityriasis rosea due to a drug is considered a distinct condition. Pityriasis circinata et marginata of Vidal is considered a synonym of PR.

EPIDEMIOLOGY

PR is universal. Early epidemiology reports were from France and the United Kingdom[2] and more recent ones from the United Kingdom,[5-8] Uganda,[9] Nigeria,[10] United States,[11] Brasil,[12] Sudan,[13] Lagos,[14] Singapore,[15],[16] Turkey,[17] Kuwait,[18] Burkina Faso,[19] and Hong Kong.[20]

These studies reported a range of incidence from 0.39[12] to 4.80[14] per 100 dermatological patients. Analyzing all patients in nine recent studies,[9],[10],[12-14],[16-18] we found an overall incidence of 0.68 per 100 dermatological patients. The community-based incidence of PR was reported to be 172.2 per 100,000 person-years.[11] The prevalence was reported to be 0.6% for young people aged between 10 and 29 years.[19]

Most patients are between the age of 10 and 35 years.[22] Analyzing 15 recent epidemiology studies,[5],[6],[8-20] we found that out of a total of 3850 patients, 1584 were males and 2266 were females. The overall male to female ratio is thus 1:1.43.

Conflicting results were reported for seasonal variation in PR. A higher incidence in the colder months was reported by investigators in England,[8] United States,[11] and Sudan.[13] A higher incidence in the early part of the rainy season was reported in Lagos.[14] A bimodal distribution was reported in Brasil[12] and in Singapore.[15] Other studies reported no seasonal variation. [9],[10],[16],[17],[20] The incidence of PR has been reported to be independent of the monthly mean air temperature, mean total rainfall and mean relative humidity in Hong Kong.[20]

Clusters of cases have been frequently reported.[7] Spatial-temporal[8] and temporal[8-20] clustering has been reported, offering epidemiological support for an infectious etiology.

ETIOLOGY

PR has long been suspected to have an infectious, mainly viral, etiology because of a distinct clinical course akin to those of viral exanthems. That most sufferers will not have a relapse in their lifetime is suggestive of immunity against the virus upon the first attack. And, as discussed in the preceding paragraph, clustering of cases[8],[20] also indirectly supports an infective etiology. There have also been reports associating PR with a history of respiratory tract infections,[23] unfavorable social and economic backgrounds,[19] and contact with patients with PR.[24] PR is not associated with atopy or an atopic tendency.[23]

Recent controversy is centered on the association of PR with HHV-7 infection. Investigators have reported positive[25-31] and negative[32],[33] results. A systematic review of the evidence has been published.[34] Association is best considered controversial. Owing to the extreme high sensitivities of sequence-based laboratory detection methods, a logical step would be to apply standard criteria to evaluate the strength of association. There is convincing evidence that PR is not associated with cytomegalovirus,[26],[35] Epstein-Barr virus,[35] parvovirus B19,[35] picornavirus,[36] influenza virus,[37] parainfluenza virus,[37] *Chlamydia pneumoniae*,[38] *C. trachomatis*,[38] *Legionella longbeachae*,[38] *L. micdadei*,[38] *L. pneumophila*,[38] and *Mycoplasma pneumoniae*[37],[38] infections.

A study reported that 28% of patients with PR have T lymphocytotoxic antibodies.[39] Thes autoantibodies can be detected in 82% of patients with systemic lupus erythematosus. Patients with PR are significantly more likely to have anti-nuclear antibodies detectable.[40] The role of autoimmunity in PR warrants further investigations.

Clinical presentation and diagnosis

The incidence of the herald patch varies to a great extent, from 40-76% in various studies.[5],[11],[15],[19] Its absence does not exclude the diagnosis. The range of the interval between the primary and secondary eruptions is also wide, from 2 to 84 days. It is predominantly around 7 to 14 days. Recognition of the peripheral collarette-scaling pattern was reported to be enhanced by epiluminescence dermatoscopy.[41] Characteristic orientation of the secondary eruption is best described as "along lines of skin cleavages". "Christmas-tree", "inverted Christmas-tree", "fur tree", and "parallel to the ribs" are imprecise and probably obsolete descriptions of the orientation.[42]

African patients have a more extensive rash,[9],[10] with more frequent involvement of the face and scalp.[9] The rash is not erythematous.[13] Post-inflammatory hypopigmentation is a cosmetic concern for dark-skinned patients.

The incidence of patients with atypical clinical features is difficult to quantify, but is likely to be high.[43] Rash morphology may be atypical, as vesicular, purpuric or hemorrhagic, and urticarial variants. PR with enormous plaques is known as pityriasis rosea gigantea of Darier. The other extreme is very small lesions in papular PR. The face, axillae, and groins are predominantly involved in PR inversus. The shoulders and hips are predominantly affected in limb-girdle PR. Involvement of the face, scalp, hands, and feet is not rare in PR. Involvement of mucous membranes such as the oral cavity has been reported. The severity may also be atypical. Patients with severe pruritus, pain, and a burning sensation can be said to have PR irritata.

A set of diagnostic criteria has been devised and validated for PR [Table 1],[44] but its reliability and applicability in other ethnic groups remain to be ascertained.

Table 1: Diagnostic criteria of pityriasis rosea[44]

Essential clinical features:

1. Discrete circular or oval lesions
2. Scaling on most lesions
3. Peripheral collarette scaling with central clearance on at least two lesions

Optional clinical features (at least one has to be present):

1. Truncal and proximal limb distribution, with less than 10% of lesions distal to mid-upper-arm and mid-thigh
2. Orientation of most lesions along direction of the ribs
3. A herald patch (not necessarily the largest) appearing at least two days before the generalized eruption

Exclusional clinical features:

1. Multiple small vesicles at the center of two or more lesions
2. Most lesions on palmar or plantar skin surfaces
3. Clinical or serological evidence of secondary syphilis

{Table 1 is reproduced from Chuh[44] with permission}

TREATMENT

Antibiotics such as erythromycin and other macrolides are being used to treat PR, probably on the basis of a pseudo-randomized study using erythromycin.[45] We believe that the use of macrolides is best considered experimental, and should not be adopted into routine clinical practice until results of further studies are published. Even if macrolides are finally proven to be effective in modifying the course of PR, this does not substantiate that PR is caused by a bacterial rather than a viral infection. Macrolides have anti-inflammatory and immunomodulating effects that might affect the course of PR or other cutaneous eruptions independent of their antibacterial properties.

Acyclovir has been recently advocated in an indexed article for the treatment of PR.[46] However, it is too premature to adopt the use of anti-viral agents into routine clinical practice. The association of PR with any virus, including HHV-7, is not yet firmly established. Even if PR is caused by primary infection or reactivation of HHV-7, acyclovir is a poor choice for antiviral therapy[47] since it has little to no action against HHV-7 in vitro. HHV-7 lacks the thymidine kinase gene while the action of acyclovir is thymidine kinase-dependent.

The use of ultraviolet radiotherapy is controversial, as studies have reported conflicting results. We understand that some dermatologists are using systemic corticosteroids for patients with particularly recalcitrant PR.[16] A Cochrane review is in progress on the interventions in PR.[48] It might shed more light on the issue.

To many patients, PR means nothing more than a weird dermatological diagnosis. Many do not experience any

pruritus despite an extensive eruption. For adults with PR, the effects on the quality of life are independent of the rash severity.[49] For children with PR, the quality of life is only affected to a very limited extent.[50] However, most clinical trials adopt physician-rated outcome measures such as extensiveness of rash, rather than patient-rated outcome measures such as pruritus or quality of life measurements. These trials might document the efficacy of the intervention on the *disease* as experienced by the doctor, but not the *illness* as experienced by the patient. We shall leave the reader to decide which of these two is the more pertinent issue.

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