Journal of Pakistan Association of Dermatologists. 2014;**24 (1)**:79-82.

Case Report

Association of pandemic H1N1 influenza and pityriasis rosea - A case report

Vijay Zawar*, Antonio Chuh**

*Department of Dermatology, Godavari Foundation Medical College and Research Center, DUPMCJ, India
**Faculty of Medicine, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong

Abstract Pityriasis rosea (PR) is an inflammatory papulosquamous disease of unknown etiology. Different viral infections have been implicated as causative agents for PR. We herein report an adult male patient who clinically manifested as pityriasis rosea (PR) during an episode of infection caused by pandemic H1N1 influenza virus, in whom the clinical progression and regression of both the diseases were in tandem.

Keywords
Pityriasis rosea of Gibert, polymerase chain reaction, seasonal influenza, viral exanthem, viral rash.

Introduction

The H1N1 influenza pandemic in 2009 involved more than 399,000 laboratory-confirmed cases from 192 countries.[1] After the pandemic, H1N1 viruses are still circulating in many parts of the world, and it is likely that the novel H1N1 – now known as A(H1N1)pdm09 – is becoming seasonal influenza.[2-4]

Pityriasis rosea (PR) is suspected to be caused by various viruses. However, a single definite viral cause has not been identified. We report here a case of PR suspected to be associated with H1N1 Influenza virus infection.

Case Report

A 31-year-old man was being managed by a physician for acute onset of flu-like illness and fever. His brother was diagnosed as having pandemic influenza A 2009 one week ago, and was hospitalised for severe acute respiratory distress. The patient developed a mildly pruritic generalised skin eruption five days after onset of fever, and was referred to us.

Before the onset of his skin eruption, the patient received oral paracetamol and diphenhydramine for two days. He had taken the same medications previously, with no history of adverse reactions or drug allergy. His drug history before onset of the rash was unremarkable otherwise. His past health was good. He did not have clinical influenza over the past three years. He had not been vaccinated against pandemic H1N1 influenza or seasonal influenza.

Our examination revealed a large scaly oval plaque of about 3 cm X 1.5 cm at his right scapular area. Further history taking revealed that such occurred on day three of the fever. Numerous oval-shaped scaly plaques were noted on trunk and proximal aspects of four extremities. The lesions were oriented along the lines of skin cleavage. Collarette scales were evident on some of the lesions (**Figure 1**).

Address for correspondence
Prof. Vijay Zawar
Shreeram Sankul Opp. Hotel Panchavati
Vakilwadi, Nashik - 422002
Maharashtra State, India
Email: vijayzawar@yahoo.com

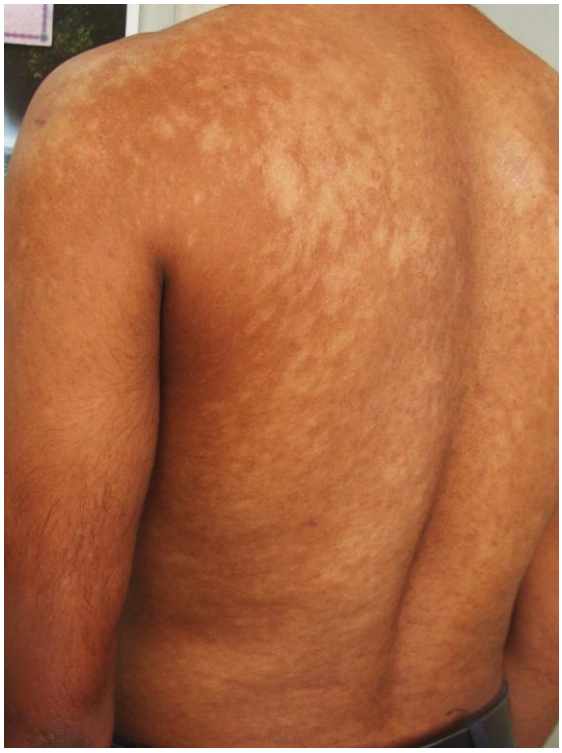

Figure 1 Large scaly oval plaque on right scapular area with multiple smaller eruptions oriented along lines of skin cleavage on the posterior trunk. Some post-inflammatory hypopigmentation is already evident.

His external genitalia, mucous membranes, palms, soles, axillae and groins were uninvolved. His throat was inflammed. Chest was slightly congested. There was no generalised lymphadenopathy.

His blood counts revealed marginal lymphocytosis (lymphocytes 7.4 X 10^9/L, neutrophils 47%, lymphocytes 49%, monocytes 3%, eosinophils 0%, and basophils 1%). Blood glucose, liver function tests, renal function tests, and electrolytes were normal. ASOT was not elevated. VDRL and HIV antibodies were negative. Urinalysis revealed no abnormality. Chest X-ray was normal. Serum sample collected more than 14 days after onset of illness was positive against pandemic influenza H1N1 2009 at a titre of 1:80 (reference range: less than 1:40) by haemagglutination inhibition assay. Skin scrapings for potassium hydroxide smear revealed no evidence of dermatophytosis.

Our clinical diagnosis was PR. The patient was closely observed on an out-patient basis by us and by his physician. Oseltamivir was not prescribed. We prescribed topical white petrolatum and oral cetirizine 10 mg once daily for five days. We noted almost complete regression of his scaly lesions two weeks later. Some post-inflammatory hypopigmentation was noted. He was systemically well then.

Discussion

Our patient represents the third reported case of suspected association of PR and pandemic H1N1 infection. For this patient, the diagnosis of H1N1 infection was established based on the epidemiological link and serology. We did not perform PCR on his nasopharyngeal secretions and skin biopsy. We did not arrange for PCR for other viruses (such as herpesviruses) on his plasma, peripheral blood mononuclear cells, and skin biopsy specimen. Serological examinations for viruses other than H1N1 were also not performed. Therefore, the possibility of having co-infection(s) as the true culprit of PR could not be excluded.

A possible association of PR with viruses causing upper respiratory tract infections is not a novel idea. A report in 1981 indicated that out of 11 patients with PR, six (55%) gave a history of antecedent upper respiratory illness. However, when examined for antibodies against influenza A, influenza B, parainfluenza I, parainfluenza II and parainfluenza III viruses from paired acute and convalescent sera, no significant rise in antibody titre was noted.[5]

If viruses causing respiratory tract infections are associated with PR, a seasonal variation or variations associated with flu epidemics would be expected. However, previous reports do not document such variations.[6-16] We have previously reported a meta-analysis on 1379 patients with PR in vastly different

geographical locations. No seasonal variation or correlation with flu epidemics was found.[17] However, seasonal influenza differs from pandemic influenza as the latter may be associated with a more prolonged virus replication and thus a more intense stimulation to the immune system. Thus, PR may only be a consequence of pandemic influenza but not seasonal influenza.

As for pandemic (H1A1) 2009 influenza specifically, a four-year-old-girl with PR and H1N1 influenza occurring in June 2009 was reported in Saudi Arabia.[18] The clinical features were conclusive with PR, and lesional skin biopsy features were compatible with PR. The H1N1 was confirmed by PCR on the nasopharyngeal wash. However, PCR was not performed on the skin biopsy specimen owing to lack of such facilities. As a result, the authors admitted that the evidence was inconclusive whether the H1N1 infection is the sole cause of PR, or whether H1N1 infection is just a trigger for endogenous reactivation of other viruses which then caused PR.[18]

Subsequently, in 2010, a six-year-old girl in Korea was reported to have a herald patch, followed by the concomitant occurrence of flu symptoms and generalised PR rash four days later.[19] PCR was positive for H1N1 on her nasopharyngeal secretion, but not on her skin biopsy specimen. The authors believed that the time sequence is supportive of reactivation of H1N1 directly causing PR, as the appearance of the herald patch was within the incubation period of H1N1, and there was no evidence of other viral infections. They attributed the failure of detecting H1N1 DNA by PCR on the skin biopsy specimen to the delay of specimen collection (17 days after onset of herald patch).[19] Nevertheless, one should note that viruses can cause skin rash either by direct invasion or immune-mediated mechanisms, and viruses are only present in lesions in the former.

However, other investigators argued that virology studies (such as those for human herpesvirus 6 and 7) have not been performed.[20] Moreover, the concept that H1N1 can remain latent and then subsequently reactivated was unsubstantiated, such being applicable to the herpesviruses only.[20] These arguments seem to be in line with previous findings of ours[21,22] and possibly other investigators.

It is never easy to attribute causal relationships between a viral infection and a skin eruption based on DNA/mRNA sequence-based investigation findings. This is particular so if PCR is positive in only one of the specimens. In a systematic review,[23] we have applied the guidelines according to Fredericks and Relman[24] to assess such associations. We believe that such and other guidelines should be consulted and the entire virological picture be assessed collectively before attributing causal relationships of viral infections and skin rashes.

In conclusion, based on the two previous case reports and the one presented here, we hypothesise that pandemic influenza may trigger PR in certain predisposed individuals either directly or via reactivation of another latent virus. Further studies are worthwhile to improve our understanding and management of this intriguing disease.

Acknowledgements

The authors thankfully acknowledge expert inputs in preparing this manuscript from Prof Paul KS Chan MD FRCPath, Department of Microbiology, The Chinese University of Hong Kong.

References

1. Craig AT, Kasai T, Li A *et al*. Getting back to basics during a public health emergency: a framework to prepare and respond to infectious disease public health emergencies. *Public Health*. 2010;**124**:10-3.
2. Centres of Disease Control and Prevention. 2009 H1N1 Flu: International situation update. Available at: www.cdc.gov/h1n1flu/updates/international/. Accessed on 20 September 2012.
3. World Health Organization. Evolution of a pandemic A (H1N1) 2009. Available at: http://whqlibdoc.who.int/publications/2010/9789241599924_eng.pdf. Accessed on 20 September 2012.
4. Lee A, Chuh AA. Facing the threat of influenza pandemic - roles of and implications to general practitioners. *BMC Public Health*. 2010;**10**:661.
5. Hudson LD, Adelman S, Lewis CW. Pityriasis rosea. Viral complement fixation studies. *J Am Acad Dermatol*. 1981;**4**:544-6.
6. Vollum DI. Pityriasis rosea in the African. *Trans St Johns Hosp Dermatol Soc*. 1973;**59**:2269-71.
7. Jacyk WK. Pityriasis rosea in Nigerians. *Int J Dermatol*. 1980;**19**:397-9.
8. Messenger AG, Knox EG, Summerly R *et al*. Case clustering in pityriasis rosea: support for role of an infective agent. *Br Med J (Clin Res Ed)*. 1982;**284**:371-3.
9. Chuang TY, Ilstrup DM, Perry HO, Kurland LT. Pityriasis rosea in Rochester, Minnesota, 1969 to 1978. *J Am Acad Dermatol*. 1982;**7**:80-9.
10. de Souza Sittart JA, Tayah M, Soares Z. Incidence pityriasis rosea of Gibert in the Dermatology Service of the Hospital do Servidor Publico in the state of Sao Paulo. *Med Cutan Ibero Lat Am*. 1984;**12**:336-8.
11. Ahmed MA. Pityriasis rosea in the Sudan. *Int J Dermatol*. 1986;**25**:184-5.
12. Olumide Y. Pityriasis rosea in Lagos. *Int J Dermatol*. 1987;**26**:234-6.
13. Cheong WK, Wong KS. An epidemiological study of pityriasis rosea in Middle Road Hospital. *Singapore Med J*. 1989;**30**:60-2.
14. Harman M, Aytekin S, Akdeniz S, Inaloz HS. An epidemiological study of pityriasis rosea in the Eastern Anatolia. *Eur J Epidemiol*. 1998;**14**:495-7.
15. Tay YK, Goh CL. One-year review of pityriasis rosea at the National Skin Centre, Singapore. *Ann Acad Med Singapore*. 1999;**28**:829-31.
16. Chuh A, Lee A, Molinari N. Case clustering in pityriasis rosea – a multi-center epidemiologic study in primary care settings in Hong Kong. *Arch Dermatol*. 2003;**139**:489-93.
17. Chuh A, Molinari N, Sciallis G *et al*. Temporal case clustering in pityriasis rosea – a regression analysis on 1379 patients in Minnesota, Kuwait and Diyarbakýr, Turkey. *Arch Dermatol*. 2005;**141**:767-71.
18. Mubki TF, Bin Dayel SA, Kadry R. A case of pityriasis rosea current with the novel influenza A (H1N1) infection. *Pediatr Dermatol*. 2010;**27**:1-2.
19. Kwon NH, Kim JE, Cho BK, Park HJ. A novel influenza a (H1N1) virus as a possible cause of pityriasis rosea? *J Eur Acad Dermatol Venereol*. 2011;**25**:368-9.
20. Rebora AE, Drago F. A novel influenza a (H1N1) virus as a possible cause of pityriasis rosea? A comment. *J Eur Acad Dermatol Venereol*. 2011;**25**:991-2.
21. Chuh AAT, Chiu SSS, Peiris JSM. Human herpesvirus 6 and 7 DNA in peripheral blood leukocytes and plasma in patients with pityriasis rosea by polymerase chain reaction – a prospective case control study. *Acta Derm Venereol*. 2001;**81**:289-90.
22. Chuh AA, Peiris JS. Lack of evidence of active human herpesvirus 7 (HHV-7) infection in three cases of pityriasis rosea in children. *Pediatr Dermatol*. 2001;**18**:381-3.
23. Chuh A, Chan H, Zawar V. Is human herpesvirus 7 infection the causative agent of pityriasis rosea? – a critical review. *Int J Dermatol*. 2004;**43**:870-5.
24. Fredericks DN, Relman DA. Sequence-based identification of microbial pathogens: a reconsideration of Koch's postulates. *Clin Microbiol Rev*. 1996;**9**:18-33.