

Study of cutaneous manifestation of chikungunya and its serological correlation

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Abstract

Aim: To assess the hyperpigmentation after fever and joint pain as a cutaneous marker of chikungunya fever and to assess with serological correlation.

Methods: A total of 15 patients comprised of 9 males, 6 females and neonate have aged between 14 days to 60 years presented with the pigmentation after the fever subsided were enrolled in the study. The diagnosis of chikungunya was made by detecting virus specific IgM ELISA in the serum.

Results: Serological immunoglobulin M enzyme – linked immunosorbent assay (IgM ELISA) test of chikungunya virus was positive in all the patients. Generalized dark coloured pigmentation was the most common finding after the fever subsided. On examination, out of 15 cases, in most of the cases, hyperpigmentation was observed all over the body with the facial involvement. Few cases showed pigmentation over nose, centre of upper lip, on palm, sole, eyelid, dorsum, centofacial, reticulate pattern on the face and blotchy pigmentation.

Conclusion: The presence of pigmentation after fever and joint pain helps to make a retrospective diagnosis of chikungunya fever and this may be considered as a cutaneous marker of chikungunya fever in recent past.

Keywords: Chikungunya, Hyperpigmentation, IgM ELISA, Reticulate pattern.

1. Introduction

Chikungunya is a vector borne arboviral disease, caused by chikungunya virus (CHIKV) of genus alpha virus and family Togaviridae transmitted by mosquitoes of the genus Aedes (mainly *A. aegypti* and *A. albopictus*) [1]. It was first reported in Tanzania during 1952-53. Etymologically, chikungunya owes its origin to Kungunyala, a word from the Makoude language of Tanzania meaning “that which bends up”, which aptly conjures up the image of a patient who adopts a stooped posture because of severe arthritis [1].

The first reported outbreak of the disease in India was in Calcutta city in 1963 and the last in Barsi in Maharashtra in 1973. After an interval of 32 years, India has witnessed a massive epidemic in 2005, which is still ongoing in different parts of the country [2].

Chikungunya fever is an acute febrile illness presenting with symptoms like intense asthenia, arthralgia, myalgia and headache [3,4]. Apart from fever, joint pain and other constitutional symptoms, various mucocutaneous changes also occur. Of these, maculopapular rash is common in several viral illnesses, therefore, not useful in suspecting chikungunya fever. On the other hand, hyperpigmentation is a unique feature noted in chikungunya fever. Knowledge of this pigmentary change is essential, both amongst the physicians and dermatologists, since it can act as an indicator for an undetected outbreak of chikungunya fever; especially in a health set up where it is not possible to screen every case of viral fever for chikungunya fever. Hyperpigmentation associated with chikungunya fever is macular and most commonly affects nose and cheeks [5,6]. It may develop soon after the rash has resolved, and has an acute onset [6].

Usually pigmentary changes develop after two weeks or more after the rash; by the time fever has subsided; hence it may be termed as post chikungunya pigmentation (PCP). PCP may occur in the form of discrete macules, freckle-like, diffuse, flagellate, Addisonian type of palmar pigmentation, periorbital melanosis and pigmentation of pre-existing acne lesions [5,6]. Involvement of centropalmar face (nose and cheeks) mimics melasma and in a busy outpatient department (OPD), is likely to be missed especially if proper history is not taken [5]. Patients with PCP give a history of high grade fever 2-4 weeks before onset, acute onset of hypermelanosis and many times, persistent asthenia and joint pain even after defervescence of fever. All these points should alert the dermatologist to think of CF. Interestingly, these patients do not have any preceding erythema or eruption over the affected areas during the acute febrile phase [7]. Hence the present research was carried out to assess the hyperpigmentation after fever and joint pain considered as a cutaneous marker of chikungunya fever and to have a serological correlation.

2. Materials and Methods

Total 15 patients of aged between 14 days - 60 years presented with chief complaint of fever, joint pain and dark colored pigmentation on various part of body from 2-10 days after the fever subsided were included in the study.

A detailed history with a special emphasis on the nature of fever, joint pain and appearance of the skin lesion was taken. Clinical examination was performed and the findings were recorded. The sera collected from patients and analyzed for specific chikungunya antibody by IgM antibody capture enzyme linked immunosorbent assay (ELISA). Other laboratory investigations like hemoglobin, leucocyte count and platelet count were done in all patients. Routine investigations were done in all cases and daily follow-up was performed and serial order of appearance of clinical features was noted till complete recovery.

3. Results and Discussion

Out of the 15 patients, 9 (60%) were males and 6 (40%) were females. The youngest patient was a 14 days old neonate and the oldest was a 55 year old man. Maximum patients (13; 86.66%) were in the 18–50year age group, with the mean age being 26.54 years. Chikungunya fever may be seen in all age groups and both sexes. In current study, males outnumbered females similar to other studies [5,8] while both sexes were equally affected in another study [9]. Generalized dark colored pigmentation was the most common finding after the fever subsided. Patients presented with either a single lesion or a combination of lesions. Table 1 show the description of all the cases. Patients had shown positive chikungunya IgM antibody in all cases.

Table 1: Description of cases

Age	Sex	Site affected	Type of Rash	Chikungunya IgM antibody
14 Days	F	All over body	Hyperpigmentation	Positive
45 Years	F	Only on face	Hyperpigmentation	Positive
18 Years	M	Centre of upper lip	Hyperpigmentation	Positive
55 Years	M	Face with reticulate pattern	Hyperpigmentation	Positive
21 Years	F	Centropalmar	Hyperpigmentation	Positive
32 Years	M	Face with reticulate pattern	Hyperpigmentation	Positive
28 Years	M	Centre of upper lip	Hyperpigmentation	Positive
30 Years	M	Face with reticulate pattern	Hyperpigmentation	Positive
31 Years	F	Nose	Hyperpigmentation	Positive
19 Years	M	Centropalmar	Hyperpigmentation	Positive
20 Years	F	Nose	Hyperpigmentation	Positive
18 Years	M	Palm	Hyperpigmentation	Positive
33 Years	M	Sole	Hyperpigmentation	Positive
22 Years	M	Eyelid	Hyperpigmentation	Positive
25 Years	F	Dorsum of Finger	Hyperpigmentation	Positive

Chikungunya fever, re-emerging as a public health problem, is caused by Arbovirus after bite of infected Aedes mosquitoes. Disease is usually self limiting but joint pains and cutaneous features may persist. There are differences in the clinical presentation of infants and adults with chikungunya. Infants have an abrupt onset of fever lasting 1 day, followed by the development of maculopapular rash [10]. The common sites of pigmentation in chikungunya fever include the nose, trunk, face, shoulders (shawl-like distribution), and palms. [8].

3.1 Post- Chikungunya Pigmentation in a Neonate

In present study, youngest patient was a 14 days neonate, contributed to vertical transmission based on positive IgM in neonate. In literature, a case series of eight neonatal chikungunya cases of vertical transmission, presented at 5th day of life has been reported by Mangalgi *et al* [11]. Chikungunya is an emerging viral disease that can be transmitted maternally during pregnancy and in the peripartum period. Mother's history was common in adults but few cases have been reported by perinatal transmission

or vertical transmission. Chikungunya can be added to the list of viral infections that can lead to fetal demise or, when present during labor and delivery, can cause neonatal disease with cutaneous signs. Vasani *et al* [10] reported a case of 12 day old neonate presented with ill-defined dark pigmentation over the centofacial area with flagellate pigmentation on the trunk and patchy pigmentation on the extremities. The mother had a history of fever starting a week before delivery and continuing for 3 days in the postpartum period. Together these led to consideration of a possible diagnosis of congenital chikungunya, which was confirmed according to the immunoglobulin M antibodies to chikungunya in the mother and child. They reported that the rare occurrence of cutaneous pigmentation was the only clue to the retrospective diagnosis of neonatal chikungunya.

Similarly, in present study, a 14 days neonate was born of non-consanguineous marriage admitted in NICU for fever with convulsion, generalized tonicity and diminished food intake since 6-7 days. Have a history of full term birth by normal vaginal delivery weighing 2.1kgs with no history of respiratory distress and skin at birth while with dark colored pigmentation on all over body with subsiding fever noticed 2 days back. Mother gave history of multiple joint pains and high grade fever few days before delivery and she taken some antipyretics and analgesics. The baseline blood investigations and urine analysis reports were normal. Cutaneous examination of neonate revealed generalized blotchy and reticulate hyperpigmentation all over the body including face, trunk, perineum and proximal extremities, (Figure 1). Provisional diagnosis of post chikungunya

hypermelanoses, universal acquired hypermelanoses and familial progressive hyperpigmentation were thought of. Baseline investigations of baby- Hb: 15.2mg/dl, TLC: 12,300, Platelets: 51000, Blood group: B +ve, T. bilirubin: 2.48, D. bilirubin: 0.68, Chest x-ray: WNL were normal except a serum IgM level of chikungunya was positive. Mother was also investigated and tested negative for serum IgM level for chikungunya. The neonate was diagnosed with post chikungunya Hypermelanoses. No specific treatment was given for skin lesions except treated with emollients. Hence the partial clearance of pigmentation seen after 2 weeks and complete resolutions of cutaneous lesions were seen within 4-6 weeks (Figure 2).

Figure 1: Generalized blotchy and reticulate hyperpigmentation all over the body



Figure 2: Partial and complete resolutions of cutaneous lesions in neonate



A large series of chikungunya cases demonstrating vertical or maternal–fetal transmission were reported during the chikungunya outbreak in 2005–2006 on Reunion Island off the coast of Africa [12]. Viremia in the peripartum period carries the maximum risk of vertical transmission of chikungunya but a higher risk of abortion has been reported with maternal infection during 1st trimester than acquired during last trimester [13]. Congenital infection can lead to cardiac, hematological, rheumatological and neurological involvement, which can be fatal. On the basis of review of literature [14], hyperpigmentation is considered mainly due to post-inflammatory response. It is proposed that the Chikungunya virus may be triggering the intraepidermal melanin dispersion or retention and presence of melanophages seen on histology may be the cause of persistent pigmentation. The Chikungunya virus IgM antibodies are detectable on an average of 3–5 days after infection using ELISA and remain positive for few weeks to 3 months [10].

That's why in our case, maternal IgM chikungunya antibody test came out to be negative. IgG antibody testing is not available in India. So, if there is clinical suspicion of chikungunya hyperpigmentation but IgM antibody testing is negative, we can advise Reverse transcriptase Polymerase chain reaction or Serology, as it can diagnose acute stage of disease. But the main drawback is that these tests are very expensive and not affordable for all patients. Though uncommon, the sudden appearance of such extensive pigmentation in a neonate should prompt the suspicion of perinatal transmission of chikungunya, especially in an endemic country like ours.

3.2 Post- Chikungunya Pigmentation in Adults

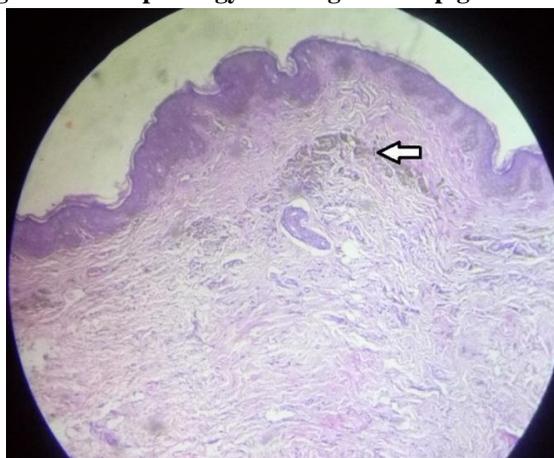
Most of the adult patients had complaints of fever, joint pain, headache and backache 7 days to 15 days before appearance of pigmentation. Different types of pigmentation have been reported in chikungunya. It was most common presentation reported in study by Inamdar *et al* [8] and second most common presentation in study by Riaz *et al* [5]. Similarly in present study chief complaint of adult was pigmentation over nose, face, centre of upper lip, centropacial, over palm, sole, eyelid and dorsum of finger. A 45 year's old female presented with history of dark colored pigmentation only on face and lesion within 4–5 days after the fever subsided, (Figure 3a). A 18 years old male child presented with history of dark colored pigmentation on centre of upper lip (Figure 3 b) and one had pigmentation on nose with history of fever and joint pain, (Figure 3c). Similar type of nose pigmentation was reported in previous studies [7,15]. Three patients were admitted in MICU presented with history of fever, joint pain with dark colored pigmentation on face with reticulate pattern since 8–10 days, among them one male patient having age of 55 years (Figure 3 d) and was treated with emollients. The complete resolutions of cutaneous lesions were seen within 4–6 weeks after the treatment (Figure 4). Two patients had centropacial pigmentation, (Figure 3e). Hyperpigmentary changes were seen later in the disease after the subsidence of fever (1–2 weeks). These patients also complained of photosensitivity. Pigmentation was diffuse. Pigmentation over palm, (Figure 3f), sole, (Figure 3g), eyelid and dorsum of finger (Figure 3h) each was noted in one case. All the patients were evaluated and turned out to be chikungunya based on serology.

Figure 3: Various types of pigmentation, (a) Facial pigmentation, (b) Pigmentation on centre of upper lip, (c) Pigmentation on nose, (d) Pigmentation on face with reticulate pattern, (e) Centropacial pigmentation, (f) Pigmentation over palm, (g) Reticulate hyperpigmentation over toes, (h) Reticulate hyperpigmentation over knuckle



Figure 4: Complete resolutions of cutaneous lesions in 55 years old patient

The hyperpigmentation may be of different types including centrofacial and freckle-like, diffuse pigmentation of face, pinna, and extremities, flagellate pigmentation, and pigmentation of existing acne lesions. Predominant affection of the exposed skin raises the possibility of the role of ultraviolet exposure in the distribution pattern of the pigmentary anomaly. Similar findings were noted in present study. Histopathology of the pigmented lesion may show increased basal pigmentation, pigmentary incontinence and melanophages. The pathogenesis for pigmentation is not clear, and it could be post inflammatory pigmentation or an increased intra epidermal melanin dispersions/ retention triggered by the virus [14], (Figure 5).

Figure 5: Histopathology showing dermal pigmentation

Treatment of cutaneous manifestation required only symptomatic measures. Pigmentation of the face was treated with sunscreens and low potent corticosteroids creams for duration of 2 weeks only. Kojic acid cream was also added in a few patients with persistent pigmentation. Desquamation was treated with topical emollients [14].

4. Conclusion

Chikungunya fever can present with varied morphological patterns of cutaneous manifestations. Hyperpigmentation is a less common finding but is so

distinctive that its appearance should immediately trigger concern for chikungunya infection. Hence this may be considered as a marker of chikungunya fever in recent past. The exact cause of hypermelanosis after chikungunya fever remains a mystery, although it is primarily considered a postinflammatory response. It has been proposed that the chikungunya virus may trigger intraepidermal melanin dispersion or retention.

References

- [1]. Kalantri SP, Joshi R, Riley LW. Chikungunya epidemic: an Indian perspective. *Natl Med J India*. 2006; 19(6):315-22.
- [2]. Mohan A. Chikungunya fever: Clinical manifestations and management. *Indian J Med Res*. 2006; 124:471-4.
- [3]. Weaver SC, Lecuit M. Chikungunya virus and the global spread of a mosquito-borne disease. *N Engl J Med*. 2015; 372:1231-9.
- [4]. Lo Presti A, Lai A, Cella E, Zehender G, Ciccozzi M. Chikungunya virus, epidemiology, clinics and phylogenesis: A review. *Asian Pac J Trop Med*. 2014; 7:925-32.
- [5]. Riyaz N, Riyaz A; Rahima, Abdul Latheef EN, Anitha PM, Aravindan KP, *et al*. Cutaneous manifestations of chikungunya during a recent epidemic in Calicut, north Kerala, south India. *Indian J Dermatol Venereol Leprol*. 2010; 76:671-6.
- [6]. Bandyopadhyay D, Ghosh SK. Mucocutaneous manifestations of Chikungunya fever. *Indian J Dermatol*. 2010; 55:64-7.
- [7]. Prashant S, Kumar AS, Basheeruddin DD, Chowdhary TN, Madhu B. Cutaneous manifestations in patients suspected of chikungunya disease. *Indian J Dermatol*. 2009; 54:128-31.
- [8]. Inamdar AC, Palit A, Sampagavi NV, Raghunath S, Deshmukh NS. Cutaneous manifestations of Chikungunya fever: Observations made during a recent outbreak in South India. *Int J Dermatol* 2008; 47:154-9.

- [9]. Bandyopadhyay D, Ghosh SK. Mucocutaneous features of Chikungunya fever: A study from an outbreak in West Bengal India. *Int J Dermatol* 2008; 47:1148-52.
- [10]. Vasani R *et al.* Congenital Chikungunya—A Cause of Neonatal Hyperpigmentation. *Pediatric Dermatology* 2016; 33(2): 209–212.
- [11]. Mangalgi SM, Shenoy SS, Maralusiddappa PG, Aprameya IV. Neonatal Chikungunya aâ , A Case Series. *J Pediatr Sci.* 2011; 3(2): 74.
- [12]. Gerardin P, Barau G, Michault A *et al.* Multidisciplinary prospective study of mother-to-child chikungunya virus infections on the island of La Reunion. *PLoS Med* 2008; 5:e60.
- [13]. Simon F, Tolou H, Jeandel P. The unexpected chikungunya outbreak. *Rev Med Interne* 2006; 27: 437–441.
- [14]. Chavan RB, Sakunke AS, Belgaumkar VA, Bansal NM, Tharewal SS. Varied cutaneous manifestation of chikungunya fever: a case series. *Int J Res Dermatol* 2017; 3:289- 92.
- [15]. Seetharam KA, Sridevi K, Vidyasagar P. Cutaneous Manifestations of Chikungunya Fever. *Indian Pediatr* 2012; 49:51-3.