RESEARCH PAPER

An Outbreak of Hand, Foot and Mouth Disease in Bhubaneswar, Odisha

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Objective: To describe the epidemiology and clinical features of cases in an outbreak of Hand, Foot and Mouth Disease (HFMD).

Design: Descriptive epidemiological study.

Setting: Hospitals and community in urban areas of Bhubaneswar city, Odisha.

Methods: Upon clinical suspicion of the first case as HFMD, local pediatricians and dermatologists were sensitized for case referral to Dermatology department of Institute of Medical Science and SUM hospital (IMS&SH) for evaluation and follow up. Community survey was undertaken by household visit by the team from Regional Medical Research Centre, Bhubaneswar in an outbreak area through hospital case tracing. Blood samples were tested for hematological counts and RT PCR assay done in a subset of samples for confirmation.

Results: Seventy eight cases of HFMD were detected between September 7 and November 6, 2009. Mean age (SD) was 5.13 (4.94) years (range 4 mo-31 yrs) and both sexes were equally affected. Fever and rash were the most common presenting symptoms with the rash distributed mostly over buttocks (83.3%), knees (77.5%), both surfaces of hands and oral mucosa (78.2%). Lesions healed in Mean (SD) 8.6 (1.5) days (range 7-15 d). Recovery was complete with minimal supportive treatment but, nail shedding was noted in three children within 4-5 weeks. CA16 was confirmed as the viral agent.

Conclusion: Children (5-14 yrs) were majorly affected and complete recovery without neurological complications were noted. The characteristic clinical features described will be useful for early clinical diagnosis where laboratory confirmation is not feasible.

Key words: *Coxsackie A 16, Enterovirus 71, Epidemic, Hand foot and mouth disease, India.*

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First diagnosed in a child suffering from fever with rash in Toronto in 1957 [1], Hand, foot, and mouth disease (HFMD) is caused by different types of Enteroviruses. CA16 and EV71 were reported as the major enterovirus types where as A4, A5, A8, A10, B3 and B7 act as the minor etiological agents causing HFMD [2].

Clinically, the condition is characterized by a combination of exanthems and enanthems. Reports from Asia-pacific region indicated occurrence of epidemics in 1997 (Sarawak) [3], 1998 (Taiwan) [4], 1999 (Perth) [5] and 2000 (Singapore, Korea, Malaysia and Taiwan) [6]. The first epidemic from India was reported from Kerala in 2003 [7]. The others were reported from Nagpur in 2005-06 [8] and West Bengal in 2007 [9]. HFMD was reported for the first time from state of Orissa (presently Odisha) in 2009 [10]**.** The clinical presentation and demography of the affected population in the above outbreak are described herein.

METHODS

The first suspected case was identified in the Dermatology outpatient department of IMS&SH, Bhubaneswar on 7 September, 2009. After clinical diagnosis of the case as HFMD, pediatricians and dermatologists serving in clinics and hospitals of Bhubaneswar were sensitized and requested to refer all the suspected cases to the Department for clinical evaluation. Sensitization was done through presentations about the case and importance of investigation in seminars and meetings organized by the local physician associations.

Besides case enrollment in the above hospitals, a community survey was undertaken by an epidemic investigation team from Regional Medical Research Centre, Bhubaneswar by visiting the households in an affected urban location. Cases were examined and extent of involvement was recorded. Detailed history was collected from the suspected patients that included contact history in the family or neighbours. Symptoms and signs were recorded in a structured format, after clinical examination. Stool, urine and blood samples (3-4 mL) were collected from subjects for investigation.

Routine blood examinations including complete blood count, Erythrocyte sedimentation rate, urine routine and microscopy and stool routine and microscopy were done in all cases. Histopathology was not done in any of the cases. Laboratory confirmation of the suspected viral etiology was carried out on a subset of serum samples (*n*=7). The samples were stored at -70^{0}C in the laboratory of Regional Medical Research Centre, Bhubaneswar and subsequently transported in cold chain and tested at National Institute of Virology, Pune by molecular diagnostics [10].

RESULTS

The first clinically suspected case was a 15-month-old female child from Rasulgarh area of Bhubaneswar. A total of 78 cases were recorded till November 6, 2009 and out of them 46 were followed up till recovery**.** The patients belonged to four urban locations, namely Rasulgarh (16 cases), Nayapalli (22 cases), Sahid Nagar (15 cases) and Dumduma (25 cases) under Bhubaneswar municipal corporation. One affected urban area (Nayapalli) was investigated by household visits, and survey was undertaken in 48 households covering 250 individuals, and recorded 9 cases of suspected HFMD. A typical index case in the area was not identified. However, household spread was evidenced by two cases from one family.

Age of the subjects ranged from 4 months to 31 years (Mean (SD) 5.13 (4.94) years **(*Table* I).** Fever (74.3%) with rash (100%) were the most common presenting symptom along with associated features like anorexia, irritability etc**.** The disease started as small (1-3mm) erythematous maculopapular rash that rapidly enlarged and progressed to papulovescicular lesions with a prominent erythematous halo. Most of the lesions turned to gray vesicles in 2-3 days time.

The lesions had a characteristic distribution with involvement of buttocks (***Fig*. I**), knees, hands and feet. Buttocks were the most severely and commonly affected sites in majority **(**83.3 %**)** of patients followed by the knees (77.5 %**)**. In very few cases, wrist, ankle area and trunk were involved. In the hands, vesicles were more pronounced over the dorsal aspect (***Fig*.2**) but papulovesicluar lesions were more on the palmar side. Lesions were localised to margins of fingers, hands, thenar and hypothenar eminences and dorsal surfaces than the volar aspect. Full blown vesicles were more common on the dorsal aspect.

TABLE I AGE AND SEX DISTRIBUTION OF HFMD CASES

	No. of cases (%)		
Age (yr)	*Male*	*Female*	*Total (%)*
<1	1 (33.3)	2 (66.6)	3 (3.8)
1-5	20 (48.7)	21 (51.2)	41 (52.5)
5-14	19 (59.3)	13 (40.6)	32 (41)
>14	2 (100)	0 (0)	2 (2.5)
Total	42 (53.8)	36 (46.1)	78 (100)

Secondary infection and impetigenization of the lesions were observed in 11 cases. The lesions were associated with itching in 24 cases which was more pronounced during the healing phase. In the 46 cases having complete follow-up, average healing time was 8.6 days (SD 1.6 days). Healing was uneventful except post inflammatory hypo and hyper-pigmentation. Three patients had shedding of nails 4-5 weeks after recovery from the acute symptoms.

Oral lesions were found in 61 (78.2%) cases. Sites involved were inner aspect of the lips, gums, buccal mucosa, tongue and the hard palate. Small aphthous like

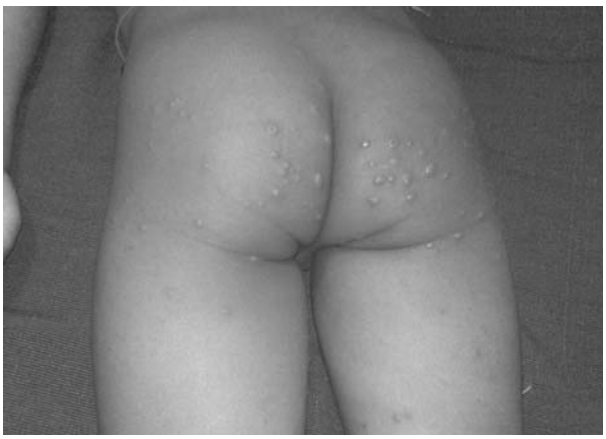

FIG 1. *Papulovesicular lesions on the buttocks.*

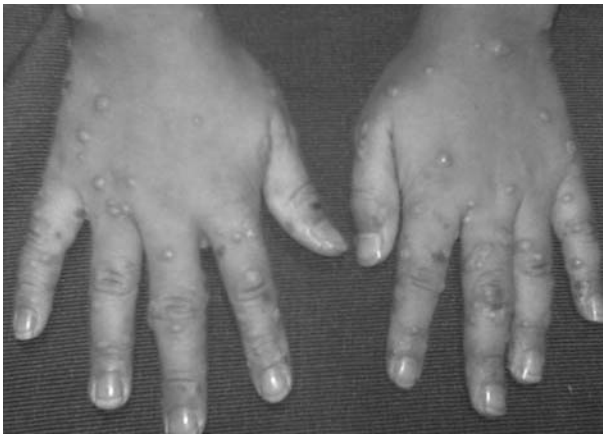

FIG 2. *Papulovesicular lesions on the dorsum of hand with involvement of margins of fingers.*

lesions measuring 1 to 3 mm were the usual mucosal presentation. Most common systemic symptoms (***Table* II**) were fever and anorexia. History of mild fever either preceding to or simultaneously with the eruption was present in 58 (74.3%) cases. Fever appeared on the same day in 70% cases and 1 day before onset of rash in 30% cases**.** Fever persisted for 1 to 2 days following onset. Sore throat was a symptom during the prodrome or on the first day in 38 (48.7%) patients. Malaise was also a dominant complain amongst 41 (52.5%) cases. Nine patients (11.5%) had a typical viral prodrome comprising of fever, sorethroat and malaise.

Anorexia was a presenting feature in 35 (44.1%) patients. The presence of oral ulcers might have contributed towards the manifestation of anorexia. Irritability was a predominant clinical presentation in 21(26.9%) patients. Mostly infants and young children presented with irritability.

Personal history of atopy was present in 22 (28.2%) patients and family history of atopy was recorded in 35(44.8%) patients, while 18 (12.8%) patients had both. Patients with personal history of atopy were more significantly associated with sorethroat compared to non-atopics (P=0.01). Average lesion healing time in patients with both personal and family history of atopy *vs non-atopics* was 10.13 (SD 1.25) *vs.* 7.27 (SD 0.65) days.

Blood counts were within normal range in most cases except, three cases showing eosinophilia and two cases with neutrophilia. Routine and microscopic examination of stool and urine samples did not reveal any abnormality. CA16 virus was identified as the causative agent for the outbreak [10].

Most patients were managed conservatively with topical antibiotics, oral antihistamines and antipyretics. Oral antibiotics were rarely required, *i.e.* only in two patients because of secondary impetigenization. All the subjects recovered with the above treatment.

TABLE II SYSTEMIC SYMPTOMS OBSERVED IN PATIENTS (N=78)

Systemic symptoms	*No (%)**
Fever	58 (74.3)
Sore throat	38 (48.7)
Malaise	41(52.5)
Pain abdomen	15 (18.7)
Diarrhoea	6 (8.5)
Constipation	4 (5.1)
Irritability	21 (26.9)
Anorexia	35 (44.8)

** Many patients had more than one symptom.*

DISCUSSION

EV71 and CA16 viruses belong to picornaviridae family of genus *Enterovirus*. They have single positive -strand genomic RNA with high mutation rate. Due to presence of multiple genotypes and sub genotypes of the two viruses, repeated epidemics of HFMD have occurred and others are expected in future. An outbreak is usually followed by a quiescent phase of few years. Like all other enteroviruses, children are the most significant target as well as reservoirs. Feco-oral route is the principal mode of transmission.

Diagnosis in most cases can be made from clinical presentation with certainty; if the clinician has a strong suspicion. Differentials include papular urticaria, chickenpox, mosquito bite etc. Rarity of cases and lack of suspicion as well as uneventful recovery are the most important causes of missing a case clinically. Though laboratory confirmation depends on direct isolation of virus in cell cultures, Indirect fluorescent assays (IFA), RT-PCR or serum neutralization techniques are also useful. Clinical presentation is quite characteristic to raise the suspicion of the condition and remains the sole diagnostic modality in resource constrained areas. Previous outbreaks in Kerala and West Bengal also showed predominant affliction of children [7,9] during the outbreak, there were two adults affected with the disease during the outbreak. The disease in these two adults was similar to the affected children. There was no statistically significant gender difference in disease. We found a significant association between the severity as well as healing time of the disease with either personal or family history of atopic diseases. Though the incidence of EV71 isolation from HFMD outbreaks is on the higher side in various reports [2-6], CA 16 was confirmed to be the viral agent in this outbreak. Follow up after healing of the lesions had revealed shedding of nail in three patients, which is a rare observation.

The report is important, as the large rural, especially tribal population, base with lack of general hygiene and water sanitation practices in Odisha can facilitate the spread of the disease [10]. The randomness of the epidemic and unequal time gap between epidemics also suggest possibilities of multiple such events in the coming years. The present report is expected to increase the awareness amongst the practitioners regarding the clinical presentation and benign and self-limiting nature of the presented HFMD cases. This will be helpful for early clinical diagnosis and case management, thereby supporting public health measures, during future episodes if any.

WHAT IS ALREADY KNOWN?

- Enteroviruses like CA16 and EV71 are known to cause HFMD outbreaks; but, many cases remain undiagnosed.

WHAT THIS STUDY ADDS?

- Clinical features of HFMD are described, mostly in children, which will help in early clinical diagnosis and case management.

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