

Osteomyelitis variolosa: Forgotten complication of an eradicated disease

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ABSTRACT

Background: Orthopedic manifestations and sequelae of small pox disease are largely forgotten. Presenting features in the modern era are not only the classical deformities but also includes precocious arthritis, pathological fractures and joint instability.

Objectives: To conduct a thorough and systematic review of the literature for all articles reporting osteomyelitis variolosa and its sequelae post eradication and to present an additional case as an illustration.

Study design: Systematic review and case report.

Method: ology: PubMed, EMBASE and Google Scholar databases were searched for relevant articles using different combinations of the keywords till 20th June 2017. All articles reporting cases of osteomyelitis variolosa following small pox eradication were included. Pearlring of the bibliographies of selected articles was conducted to locate articles missed by the primary database search. Data from these reports were collected on pre-defined forms and the results were analysed.

Results: A total of 8 cases have been reported in the literature so far post-eradication of small pox and all cases are from India. These cases have predominant involvement of elbow followed by hands, feet and ankle. Characteristic clinical signs in the present era are secondary arthritis, pathological fractures, joint instability and some cases even have incidental presentation.

The diagnosis is further confirmed by plain radiographs which show pathognomonic features of this condition. Rate of missed/misdiagnosis is very high due to rarity of this condition. All cases in the published literature were managed conservatively except those presenting with pathological fracture.

Conclusions: The purpose of this study is to remind clinicians of an easily recognised sequelae of an eradicated disease and make them aware of its complications.

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1. Background

Smallpox was the first infectious disease to be eradicated¹ but its consequences including osteoarticular manifestations and sequelae can occasionally be encountered in countries like India where disease was rampant in the 20th century. Musculoskeletal complications following smallpox have been reported especially in young children in the pre-eradication era. Osteomyelitis variolosa is the accepted terminology for the skeletal involvement which appears during the recovery period from the smallpox eruption.

The sequelae of osteomyelitis variolosa may raise a diagnostic

challenge to the untrained eyes of the surgeon. Purpose of reporting this case is to recognize the characteristic features of osteomyelitis variolosa and its presentation in the present era, a condition very rarely encountered in clinical practice.

2. Methods

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) checklist was used for key aspects of this systematic review wherever applicable.² The PubMed, EMBASE and Google scholar databases were searched from 1980 (eradication of small pox) to 20th June 2017 using different combinations of keywords (Table 1). PEARLring of the references of full text articles included in the review was conducted to identify articles which were missed in the primary database search (see Table 2).

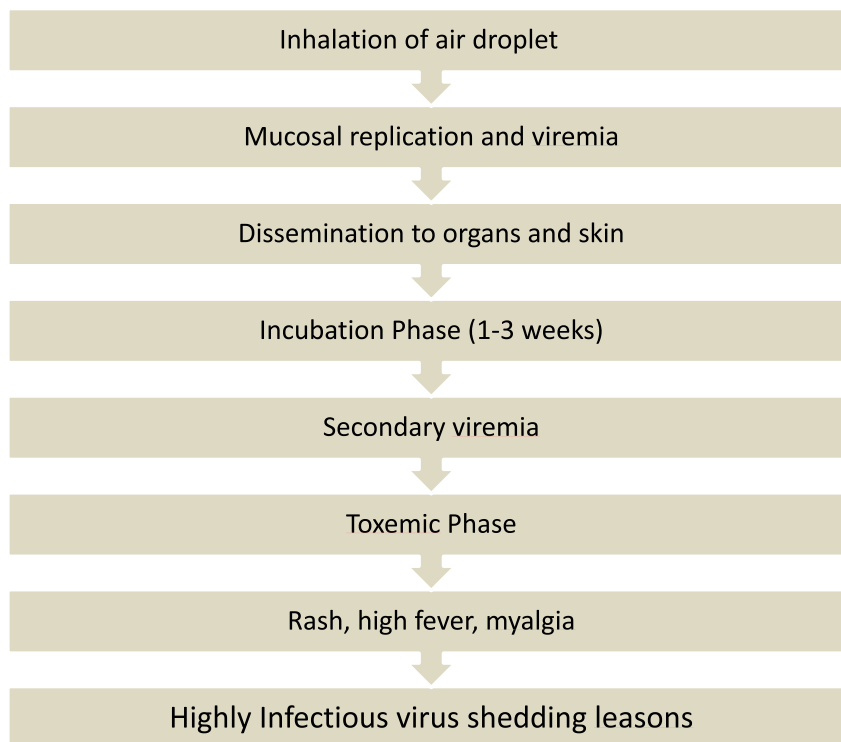
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Table 1
Search strategy used for this review.

Database searched	Results
1 PubMed (inception to 20th June 2017)	18
a ("Osteomyelitis"[MeSH Terms] OR "Osteomyelitis"[All Fields]) AND ("Variolosa"[All Fields])	studies
b ("Abnormalities, Musculoskeletal" [MeSH Terms] OR ("Musculoskeletal Manifestations" [All Fields] OR ("Osteoarticular Manifestations" [All Fields] OR "Bone lesions" [All Fields]) AND ("smallpox" [All Fields] OR "smallpox" [MeSH Terms])	1 Study
c a & b	
2 EMBASE (inception to 20th June 2017)	38
'osteomyelitis'/exp OR osteomyelitis AND ('variolosa'/exp OR variolosa)	studies
3 Google Scholar (inception to 20th June 2017)	24
	studies

Table 2
Pathophysiology of Small pox showing the various stages of infection. Infection involves the musculoskeletal system in the secondary viraemia stage.



2.1. Inclusion & exclusion criteria

We included all studies reporting osteomyelitis variolosa or musculoskeletal complications of small pox. Cases where the presentation was in the form of acute osteomyelitis variolosa and those predating 1980 were excluded. Cases of all age groups were included in the review. No language barrier was applied for the search.

2.2. Data collection & analysis

The search results were analysed by first observers independently by using the study title and abstract. In cases of ambiguity, inclusion was ascertained by analysing the entire article after obtaining the full-text and consulting the senior author (DN). Duplicates were excluded; reference manager software (Zotero[®] Standalone software, Fairfax, VA, USA) was used to ensure elimination of duplicity. Full-text was obtained for all studies included in the final analysis. All data from the studies selected for the

systematic review was collected on pre-defined, data collection forms. The following data were collected - journal name and year of publication, country of origin, demographic features of the patients, duration at presentation, clinico-radiologic features and details of management. This data was analysed qualitatively and the results were summarised in a tabular fashion (Table 3).

3. Results

3.1. Literature search

Out of the initial 48 records identified by our search, 7 studies were identified which fitted the inclusion & exclusion criteria of the review. According to study design all studies are isolated case reports. Altogether 8 cases of osteomyelitis variolosa have been reported till date following eradication. A flowchart of all the studies included and excluded in the review has been given in Fig. 1. The results of these studies has been summarised in Table 3 (see Fig. 2).

Table 3
Various Post-eradication studies on osteomyelitis variolosa.

Studies and number of cases	patients	Presentation	Bones affected
A Arora, A Agarwal, S Kumar (2008) ³	2	Pathological fracture, Secondary arthritis	Humerus, radius, ulna, ankle, feet
Douraiswami Balaji (2011) ⁴	1	Secondary arthritis	Distal femur, patella, humerus, metacarpals, ankle.
Nema et al. (2011) ⁵	1	Secondary arthritis	Distal Humerus, Metacarpals, metatarsals, phalynx, calcaneum
Andrews et al. 2011 ⁸	1	Asymptomatic	Humerus, radius, Ulna, metacarpals
Mugalur et al. (2015) ⁶	1	Secondary arthritis	Humerus, radius, Ulna, Metacarpals, ankle
Singh PK 2012 ⁹	1	Pathological fracture	Humerus, radius, Ulna, Metacarpals
Thomas J 2017 ⁷	1	Secondary arthritis	Humerus, radius, Ulna, Metacarpals, ankle
Present study	1	Asymptomatic incidental finding	Humerus, radius, Ulna,

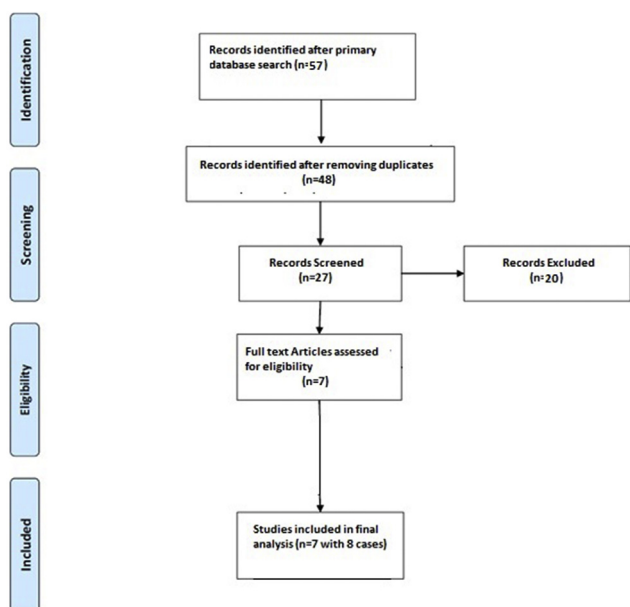


Fig. 1. PRISMA flowchart showing the study design and the details of inclusion/exclusion of articles.



Fig. 2. Clinical photographs showing facial stigmata of smallpox.

3.2. Demographic features

All 8 cases have been reported from India. These cases have been reported middle age to elderly individuals of age range 40–70 years (mean age-46.5 years). Seven cases were males and one was female.

3.3. Clinical presentation

Mean age at presentation was 46.5 years (Range: 40–70 years) for the 8 cases which have specified details. Vast majority of cases (100%) reported have affected the elbows. Involvement in six cases pertain to the hands and five with involvement of foot and ankle.^{3–7} Elbow involvement was bilateral in all cases.

The presenting features are precocious arthritis or pathological fracture. Some patients are asymptomatic and are observed when the present for unrelated complaints.^{3–9} All cases were diagnosed clinically with supplementary plain radiographs.

3.4. Management & complications

All cases were managed conservatively except those presenting with pathological fracture. Both cases with pathological fracture involved the distal shaft of the humerus. One was managed with square nailing while the other with plating with good results for both.^{3,9}

4. Discussion

Small Pox is an infectious disease caused by either of two virus variants, *Variola major* and *Variola minor* of the genus Orthopoxvirus, the family Poxviridae and subfamily chordopoxvirinae. The term osteomyelitis variolosa refers to the osteo-articular affection of *Variola major*, only seen in cases arising in childhood and tends to affect predominantly the elbow joints among other joints.^{10,11} The clinical and radiological features of osteomyelitis variolosa have been very well-described by Cockshott and MacGregor in their reports (10,11). The Manifestations in the post eradication era are somewhat different with complaints of deformities, arthritis and instability presenting especially in middle age to elderly population. The first reference to such osteoarticular complications of small pox was by Bidder in 1873.¹²

During smallpox epidemics, 0.25–0.5% of the patients or 2–5% of affected children had osteoarticular manifestation,¹³ most commonly in the elbows, wrists, ankles, hands, and feet.^{10,11} Osteo-articular complications of variola infection manifest between first and fourth week of illness with gradual swelling around the joints, finally involving adjacent long bones. 80% of these involved the elbow followed by hands, wrists, ankles and feet.^{10,11} Ribs, spine and pelvis are relatively spared. Characteristic radiographic features of disease during evolving phase are bone destruction in metaphysic more clearly defined on epiphyseal side with epiphyseal destruction, physeal separation and extensive periosteal reaction often extending along the whole length of shaft of the bone.^{2–4}

Viral invasion of bone is rare, with only the viruses of smallpox, vaccinia, and rubella known to invade bones and joints. Whether osteomyelitis variolosa is directly caused by the virus is controversial.¹⁴ Elementary bodies are present in fluid aspirated from the affected joints.¹⁵ As per available literature the infection involved the musculoskeletal system in the secondary viraemia stage. Though acute cases of osteomyelitis variolosa are not seen since the eradication of smallpox, the sequelae of the disease are still occasionally noticed in previously endemic areas.

The late changes are, as would be expected the presenting features in the modern era. These include ankylosis of the joints,

malformation of the bones (frequently with an intact joint space), flail joints and ultimately osteoarthritis. Even if the disease was diagnosed early the osteoarticular manifestations of small pox were deemed destructive, unpreventable and untreatable.¹² Sequelae of the disease have radiographic findings in the form of subluxated, flail, ankylosed, dislocated joints with precocious osteoarthritis. There is abnormal mobility at the ankles while movements at the elbows are restricted; the reason for this difference is not known.¹⁵ 80% cases have symmetrical involvement. Dwarfism has also been reported (see Figs. 3–5).

The bones can be irregular, sclerosed or thickened with Deformity and irregularity of short tubular bones.

Elbow, the most frequent joint involved shows central cavitation of distal Humerus with enlarged and deformed condyles, thickening and enlargement of Olecranon and Radial head with eventual



Fig. 3. Radiographs of the left elbow.

subluxation, dislocation or ankylosis of joint. There is absorption of central trochlea with elongation of both condyles around the elbows. Sclerosis around the elbow with enlargement of olecranon process of ulna and radial head has been reported.¹⁶

Analysis of post-eradication reports available on Osteomyelitis Variolosa show a predominant involvement of elbows followed by hands, feet and ankles.^{10,11} Of the 9 cases reported after eradication there is 100% involvement of elbow. The reason for predilection for the elbow is not known. It is hypothesised that high stresses in the joint predispose it to localization during viraemia.^{10,11}

The differential diagnosis for this condition includes sequelae of pyogenic septic arthritis,¹⁶ congenital dysplasia (Achondroplasia),¹⁵ Salmonella Osteitis,¹¹ pseudohypothyroidism,¹⁶ leprosy,¹⁷ Caffey's disease,¹⁸ and perthes disease.¹⁹

Sequelae of pyogenic septic arthritis does not involve all 3 bones of elbow joint and spares the epiphysis and is rarely bilateral.¹⁶ Caffey's disease often affects the mandible, clavicle, ribs, scapula, which is different from osteomyelitis variolosa.¹⁸ Most of these cases can be ruled out through a proper detailed history and clinico-radiological co-relation.

Deformities of the hands and feet following dactylitis¹² result in short stubby fingers and brachymetatarsalgia.^{5,6,8,9} There is deformity, instability and disorganization around the wrist and ankle joint caused by the disease process.^{3,4,6,7} Ankle involvement is further complicated by collapse of the talus.⁴

Arora et al.³ and Singh⁹ reported a distal humerus fracture around the elbow affected with osteomyelitis variolosa, which was managed operatively. Nema et al.⁵ also described a case report of a fracture around the involved ankle joint. The reason for this is the deformity, instability and disorganization around the joint predisposing it to abnormal stresses. Fracture union and functional outcome does not show any abnormality despite gross bony

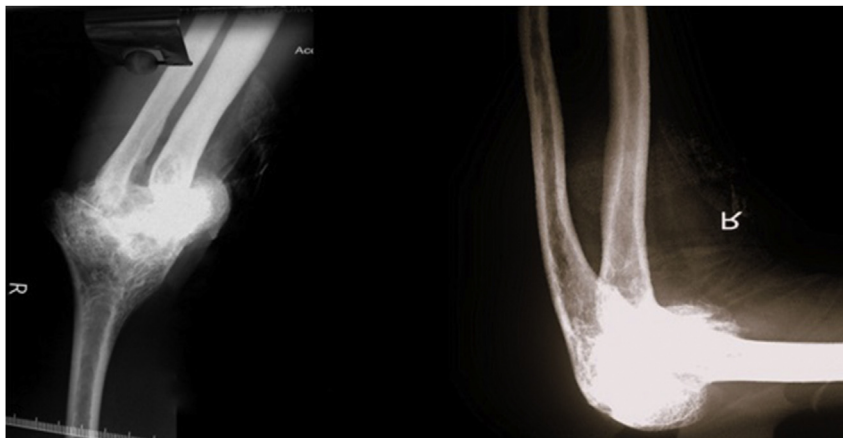


Fig. 4. Radiographs of the right elbow.



Fig. 5. Strikingly good function bilaterally despite the deformed and dislocated elbows on radiographs.

alteration.

Douraiswami Balaji⁴ described a case who presented with knee pain and had hypoplastic lateral condyle with involvement of bilateral elbows and ankles.

Previously referred to as an uncomfortable interference with function rather than an illness in the present scenario such complications like precocious arthritis, pathological fracture and joint instability which should be appropriately managed.

5. Case illustration

A 56 year-old male child presented with open grade IIIb fracture of the distal femur. The patient also had bilateral elbow deformity. On physical examination he had residual facial stigmata of variola. There was flexion deformity of both elbow joints but the patient had good range of motion within the functional range (20–140° bilaterally) for elbow. X-ray of both elbow joints showed sclerosis of bones around elbow joint, enlargement of olecranon process of ulna, and head of radius. The patient declined any treatment other than conservative management for his deformity. His compound fracture was managed by debridement, external fixator and later by definitive plating.

6. Conclusion

Deformities of osteomyelitis variolosa can be summed up as consisted of a bilateral, symmetrical osteomyelitis with arthritis predominantly affecting the upper limb.

Cases of osteomyelitis variolosa can still be encountered in previous endemic areas like India. The purpose of this report is not to describe a new condition but to remind clinicians of an easily recognised complication of an eradicated disease. Radiologically despite the serious manifestations like deformed and dislocated joints and bones, good functionality of patient may be in striking contrast. Also in various case reports patient has sought clinician's opinion for other conditions like a pathological fracture rather than the preexisting condition per se.^{3,5}

Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.jcot.2018.08.005>.

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