http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v7i10.05

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

B19 Parvovirus Triggered Reactive Arthritis in Older Women– Case Reports from Eastern India

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Abstract
B19 Parvoviruses are ubiquitous pathogens capable of causing arthritis and erythemas in adult immunocompetent individuals. B19 virus mediated viral inflammation and immune-complex deposition generates mainly short term manifestations in these affected individuals. In this case report we present the cases of two adult females diagnosed with B19 parvovirus associated reactive arthritis and exanthemas. One of them showed recurrent manifestations for over a year, while for the other one it resolved in a few weeks. Exanthems were associated with infections and joint effusions in both the cases and in one of the cases erythema nodosum was associated with arthritis. This case report provides for the first time from eastern India some important leads on the variable manifestation of parvovirus associated arthritis in adult women which will surely benefit the medical practitioners while dealing with these patients.
Keywords: *B19 Parvovirus, Reactive arthritis, Exanthems, Erythema nodosum.*

Introduction

The B19 parvovirus (B19V) belongs to the Parvoviridae family of ssDNA viruses. Most of the B19V infections are either asymptomatic in nature or do present with very mild symptoms[(1)]. In contrast to this, the B19 parvovirus can also cause many severe and acute diseases like erythema infectiosum, hemolytic disorders, hydropsfetalis, aplastic crisis etc[(1)]. B19V can also give rise to chronic ailments like general and aplastic anaemia in immunocompromized patients and arthritis/arthropathy or arthralgias in adult individuals. B19V induces erythema infectiosum in many individuals[(2)]. After about two weeks since the inception of the infection a peculiar facial cutaneous rash appears[(5)]. The perioral pallor and the characteristic maculopapular erythema on the cheeks confluence to produce a unique "slapped cheek" appearance. After a few days cutaneous eruptions or rashes in reticular or lacy pattern occur on the limbs and trunk, which consists of peculiar pink maculae[(3)]. These rashes typically disappear after about three weeks only to reappear again due to higher temperature conditions or direct exposure to sunlight[(4)]. Another typical cutaneous manifestation called Erythema nodosum though not frequent but occurs in B19V patients with arthritis and diverse

inflammatory conditions[4]. Erythema nodosum is characterized by reddish painful inflammatory eruptions on upper fatty layer of skin, typically forming tender lumps below the knees in the frontal side of both the legs. These nodules or lumps gradually shrink after few weeks leaving a characteristic bruised appearance[5].

Reactive arthritis is a specific rheumatologic disease with a short clinical span but characterized with non-purulent arthritis and extremely painful swelling of the joints[6]. Mostly caused by bacteria, recent evidences has shown that a growing number of viruses including parvovirus, HIV and Hepatitis virusare also involved in many cases as the probable inducer. Viral arthritis involving HIV has also been reported previously [6]. Though parvovirus B19 does trigger chronic arthritis/arthralgias in adult females but parvovirus triggered reactive arthritis is much less heard of and has only been reported in a few instances[7]. Here we report two very interesting cases involving Parvovirus induced reactive arthritis in two adult females, one with the associated condition of erythema nodosum, presenting perhaps for the first time from eastern India. Thus this case report is indeed important as it gives an important lead on this topicto the practitioners who are dealing with such cases.

Case Report 1

A 43-year-old immunocompetent woman was admitted with severe pain in the joints of both of her hands. Blood tests for Rheumatoid Factor (RF) and Anti-cyclic citrullinated peptide (anti-CCP) gave normal results. Ultrasonography and radiologic investigations revealed substantial effusion in her joints. She was diagnosed with reactive arthritis that affected the elbows and the joints of her hands. B19V-specificIgM along with HCMV-specific IgM was found in her blood. Brucella agglutination test, ANA test, and anti-dsDNA tests were negative.B19 virus was detected in her blood by isolation of viral DNA using PCR. HCMV PCR provided negative results. B19 DNA viral load was measured using real time PCR. Liver function tests and urinalysis showed no abnormality. Detailed report of biochemical and other analyses has been provided in table 1. Hypoalbuminemia and hypergammaglobulinemia were observed in the patient. Acemetacin 90 mg twice daily was prescribed by the rheumatologist for one month. After two months of NSAID treatment substantial reduction in joint pain and swelling was observed. She stopped taking medications after that. At month 4, after start of initial treatment an exanthem developed with the classic slapped cheek appearance. The facial exanthema lasted 2–3 days without involvement of the trunk and limbs. The same thing occurred again at month 8. In both cases she was bought to the hospital.B19V DNA was detectable by PCR during both instances but B19V specific IgM was found to be negative. IgG and IgM were tested for rubella, measles, Epstein Barr virus, varicella-zoster virus, human herpesvirus5, human herpesvirus 7, toxoplasmosis, and *Borellia*, to ascertain thecause of infectious exanthems, all of which gave negative results. The patient denied exposure to potential environmental causes of rashes. After 2-3 days when the exanthems vanished she was released. At month 10, arthralgias without rash generated, but, at month 12 again, the erythema was accompanied by arthralgias with painful and swollen joints of the hands. B19V DNA was detectable in her blood during both of these incidents. Anaemia and fever were never observed throughout the course of treatment and follow up. B19 DNA was found to be cleared from the blood 15 months after the first blood sample was obtained. After the clearance of the virus, no reappearance of the rash or symptoms of reactive arthritis was recorded during another 1 year follow-up period.

Case Report 2

A 55-year-old perfectly immunocompetent woman was admitted with ask in lesion at the lateral side of her right ankle and distal anteriorside of both left and right thigh and with a

3 weeks history of bilateral knee and right ankle joint pain. The patient's complaints first appeared with fever, dry cough and sore throat about 1 month ago. She was diagnosed with acute pharyngitis and used amoxycillin 500mg twice daily for one week. During the course of antibiotic therapy, she noticed a skin lesion atthe lateral side of her right ankle, which was followed by lesions at the distal anterior side of both left and right thigh. A day following this, joint pain on her bilateral ankle and knee began. She had no history of recent urinary tract infection, acute gastroenteritis, renal complications, uveitis, or sexually transmitted diseases. On admission, her body temperature, pulse rate and blood pressure were normal. There was swelling, tenderness, and redness on her right ankle along with erythematous skin lesions on the lateral side and distal anterior side of both thighs. She was diagnosed with erythema nodosum. Ultrasonography of the joints revealed effusionin the bilateral wrists, knees, and tibio-talar joints. Direct radiographic examination using X-ray, of the ankle, knee, sacroiliac (SI) joint, and chest were found to be normal. All relevant parameters of laboratory investigations have been provided in the associated table 1. Liver and renal function tests and urinalysis showed no abnormality. ASO, RFand anti-CCP tests were normal. While the anti CMV IgM test, Brucella agglutination test, ANA test, and anti-dsDNA tests were negative, the parvovirus B19 IgM test was positive. IgG and IgM were tested for rubella, measles, Epstein Barr virus, varicella-zoster virus, human herpesvirus5, human herpesvirus 7, toxoplasmosis, and *Borellia*, to ascertain the cause of infectious exanthems, all of which gave negative results. B19 virus was detected in her blood by isolation of viral DNA using qualitative PCR, DNA viral load was measured using real time PCR. The patient was diagnosed as having Reactive Arthritis due to parvovirus B19 and prescribed acemetacin 90 mg twice daily and asked her to visitus for a follow-up examination. After four weeks of follow-up she reported a significant reduction in joint pain and swelling. There was no new skin lesion thereafter and the redness of the lesions disappeared after about 2 more weeks. Meanwhile, joint effusions detected by ultrasonography were found to be significantly reduced. Follow-up for 1 year showed no recurrence of arthritis or exanthema symptoms. B16V DNA was cleared from blood after 2 months from the date of presentation.

Table 1-Demographic and serum biochemical profile of the two patients

Parameters	Patient1	Patient 2
Age	57	43
Sex	Female	Female
Weight (Kgs)	72	76
Height (cms)	161.54	170.6
BP	130/80	135/85
BMI	27.3	26.1
WBC($X10^6$/L) Neutrophils Lymphocytes Eosinophylls Monocytes Basophills	4500 71.3% 18.5% 8.2% 1.4% 0.6%	7700 69.5% 20.6% 7% 2.1% 0.8%
Platelets($x10^6$/L)	22.6	28.5
Hb(gm/dl)	8.3	10.3
ESR	78	81
Cholesterol (mg/dl)	155	164
Triglycerides (mg/dl)	110	103
LDL (mg/dl)	89	84.5
ALP (IU/L)	110	85
SGPT IU/L)	21	18
SGOT (IU/L)	22	17
Ammonia (□mol/L)	13.5	24.7
Creatinine (mg/dl)	1.1	0.9
Sodium (mEq/L)	128	149
Potassium (mEq/L)	3.4	5
Fasting Glucose(mmole/L)	7.9	7
LDH(IU/L)	183	212
Urea (mg/dl)	13.5	20
INR	1.1	0.9
Hematocrit (%)	48	51
Gammaglobulin (gm/dl)	2.5	3.8
Albumin (gm/dl)	1.2	3
CRP(mg/dl)	5.4	3.2
B19V IgM	7.89	8.95
B19V IgG	9.11	8.2
B19V DNA viral Load	$3x10^5$	$5x10^8$

Discussion

Very few cases of B19 parvovirus caused reactive arthralgias and erythemas in adult women have been reported till date. All these reported cases are presented with short term manifestations resulting

due to viral inflammation and immune-complex deposition[8]. Recurrent and long term manifestations of arthritis or exanthems involving B19V, continuing for months or years have been reported in only one or two instances[9]. As of the current available knowledge regarding B19V infections, it has been noted that the symptoms does not last more than few weeks since the initial onset[9]. The aim of the present report is to suggest the possibility that B19-V can vehemently cause reactive arthritis with exanthems and these can be recurrent, even for many months after initial infection. The detection of B19V DNA in the blood alone can accurately diagnose the viral involvement in these recurrent cases because, at the time of the appearance of recurrent rashes, B19-specific IgM may have already been cleared [10]. In the present study, both patients who experienced reactive arthritis and rashes were adult aged women. However, we cannot rule out the possibility that the same feature could also occur in younger patients.

In one of the cases, the patient showed both erythema nodosum and joint symptoms attributed to reactive arthritis which is a very rare finding in itself. Because of the asymptomatic cases, parvovirus B19-associated ReA may remain under-diagnosed. When the physicians suspect ReA, or joint effusions with exanthems parvovirus B19 tests should be conducted together with conventional laboratory investigations.

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