Letter to Editor

HAEMATOLOGICAL PROFILE OF PATIENTS INFECTED WITH MONKEY POX VIRUS

To the Editor,

Dear Sir,

Mpox or monkey pox is a zoonotic disease caused by monkeypox virus. It belongs to the genus Orthopoxvirus in the Poxviridae family. It occurs in the tropical rain forests of central Africa and west Africa. It may be exported to other regions. The disease is transmitted via close intimate contact or through fluids in dermal lesions [1]. The sexual mode of transmission was predominantly responsible for the recent outbreak.

Mpox has an incubation period of 5-21 days [2]. Patients infected with mpox may present with rash, fever, headache, lymphadenopathy, muscle ache, sore throat and fatigue. Blood sample, urine sample, swab of persistent lesion or lesion fluid and upper respiratory tract swabs are collected from a patient presenting with symptoms suggestive of mpox.Monkey pox virus PCR is highly specific for diagnosis [3].

The first outbreak of Monkey Pox, was confirmed in May 2022. The first case was detected in London, United Kingdom in a patient with travel history from Nigeria[1]. Few cases of mpoxwere reported in Delhi, India.Lok Nayak Hospital, Delhi was made the designated hospital to admit patients infected with the monkeypox virus.The blood samples of first twelve cases reported in Delhi admitted to Lok Nayak Hospital between 28 July- 28 September 2022 were analysed. Only those patients who tested positive for monkeypox virus by RT-PCR were included in the study. Of these twelve, eleven patients were from Africa.

Patients admitted at Lok Nayak Hospital, Delhipresented with intermittent mild to moderate grade fever, myalgia, lesions on upper and lower limbs, trunk, groin and genitals. Lymphadenopathy was noted in four cases.

The patients were admitted in an isolation ward. Samples were sent to National Institute of Virology, Pune for diagnosis of Monkey Pox virus by RT- PCR. The haematology samples were received in our laboratory. The first sample for hemogram was sent on the first day of admission. For a few patients' subsequent blood sampling was done every few days to assess the treatment response and clinical condition of patient. The haematology parameters of the patients were obtained using automated haematology analyser Mindray BC-6200. Peripheral blood smears were prepared taking all necessary precautions.

White blood cell (WBC parameters) included in the study were total leucocyte count (TLC), percentage of polymorphs, lymphocytes, monocytes and eosinophils. Of the twelve patients infected with mpox, three patientsshowed anincrease in percentage of lymphocytes (Table 1). The lymphocyte count was not raised in the other nine patients. No other abnormal counts were detected in other patients. Few transformed lymphocytes (TL) were noted in all patients (Figure 1A). Activated monocytes (AM) with cytoplasmic vacuolation were noted in four

cases (Figure 1B). Large granular lymphocytes (LGL) were noted in two cases (Figure 1C).Two patients showing lymphocytosis were found to need a longer period of hospital stay as the patients were clinically sicker than others. The absolute lymphocyte counts gradually reduced and the patients were discharged after they tested negative by RT-PCR.

Continuous variables were expressed as mean and categorical variables were expressed as proportion. Data was analysed using SPSS version 25. P values ≤ 0.05 were used to declare statistical significance. No significant association was noted between presence of transformed lymphocytes, activated monocytes, large granular lymphocytes and the various white blood cell parameters. However, in cases with large granular lymphocytes, a strong negative correlation was noted between total leucocyte count (TLC) and percentage of lymphocytes (P=0.01). An increase in lymphocyte percentage was noted with decrease in TLC.

Table 1: White blood cell parameters in monkey pox infected patients

PATIENT NO.	TLC	POLYMORPHS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILS (%)	TL	AM	LGL
1.	11700	57.7	37.1	1.2	3.8	+	-	-
2.	3340	42.6	50.5	5.5	1.5	+	+	-
3. i	12300	57.9	35.8	4.5	1	+	-	-
ii	8070	28.7	64.7	2.1	3.9	+	-	-
iii	6610	39	52	3	6	+	-	-
4.i	10,300	58	26	11	5	+	-	-
ii	8900	89	6	2	3	+	-	-
5.	7500	48	33	10	6	+	-	-
6.	7700	56	39	4	1	+	-	-
7.	11,100	42.6	46.5	7.9	3	+	+	-
8.	9500	57.6	36.5	3.9	2	+	+	-
9.	8660	43	52	2	3	+	-	-
10.	4640	56	41	2	1	+	-	+
11.	7550	53	40	4	3	+	+	+
12.	10700	55.5	33.1	10	1.4	+	-	-

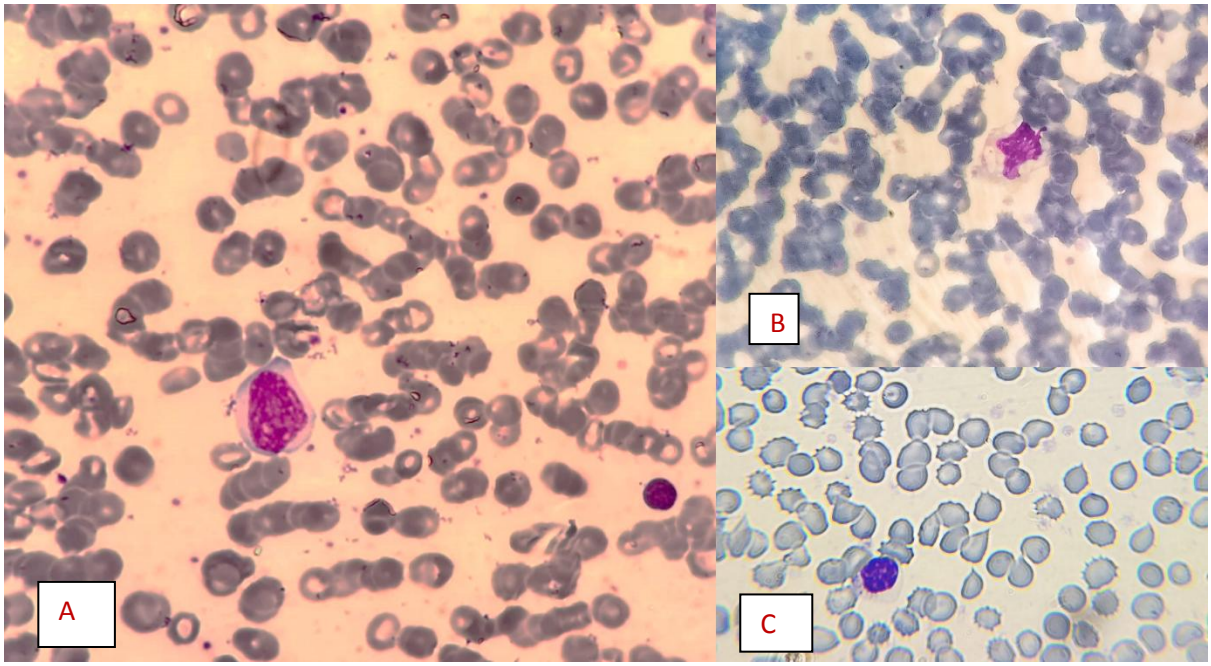

Figure1: Peripheral smear findings- A. Transformed Lymphocyte B. Activated Monocyte C. Large Granular Lymphocyte

The patients admitted at Lok Nayak Hospital, Delhi were found to be infected with the west African lineage which is less severe than the central African lineage. All the patients were clinically stable with mild symptoms and good recovery.

Transformed lymphocytes maybe seen in both viral and bacterial infections. Large granular lymphocytes are lymphoid cells of T-cell or natural killer cell phenotype. Their expansion may be seen in infectious and neoplastic conditions. They help in immunosurveillance. Vacuolations of monocytes are associated with infections and toxic conditions [4].

Atypical lymphocytes seen in monkeypox infection occur due to immune activation causing mature lymphocytes to change morphologically. These atypical cells are larger in size with abundant dark blue to pale greycytoplasm and finer immature nuclear chromatin [5].

Clinical studies have shown that monkeypox viral replication typically occurs in the lymphoid tissue of the neck and throat region. Pox virus tropism in lymphoid tissue has been associated with infection of B cells, activated T cells, monocytes and dendritic cells. After infection of lymphoid tissue, the mpox virus disseminates through the lymphohematogenous route [6].

Though mpox is a self-limiting disease, few cases have progressed to severe disease around the world. The case fatality rate of Mpox infection has been reported to be around 3-6% by the WHO [7]. Analysis of clinical symptoms along with haematological parameters is important in assessing severity of infection for proper management of confirmed cases.

The role of innate immune cells- monocytes, neutrophils, lymphoid cells and dendritic cells in mpox infection is currently not known. Further characterisation and profiling of these

immune cells during infection may help in understanding their role against mpox virus. Further studies may help in identifying biomarkers for disease prognosis [2].

REFERENCES:

1. Monkeypox outbreak 2022- Global. World Health Organization. https://www.who.int/emergencies/situations/monkeypox-oubreak-2022. Published August 31, 2022. Accessed October 5, 2022.
2. Lum F, Torres-Ruesta A, Tay M, Lin R, Lye D, Renia L. et al. Monkeypox: disease epidemiology, host immunity and clinical interventions. Nature reviews immunology. 2022; 22: 597-613.
3. Adler H, Gould S, Hine P, Snell L, Wong W, Houlihan C. et al. Clinical features and management of human monkeypox: a retrospective observational study in the UK. Lancet Infect Dis. 2022; 22: 1153–62.
4. Bain B. Blood Cell Morphology in Health and Disease. In: Bain B, Bates I, Laffan M. Dacie and Lewis Practical Haematology. 12th ed. London: Elsevier; 2017.
5. Debuysschere C, Beukinga I, Hernado C, Blairon L, Tre-Hardy M, Cupaiolo R. Atypical lymphocytes associated with monkeypox virus infection, Br J Haematol. 2022; 199: 306.
6. Song H, Josleyn N, Janosko K, Skinner J, Reeves R, Cohen M. et al. Monkeypox virus infection of rhesus macaques induces massive expansion of natural killer cells but suppresses natural killer cell functions. PLoS One. 2013;8: e77804.
7. Singh T, Baskaran P, Raghav P, Naveen KH. Monkeypox: Current Situation in India: An Old Virus, A New Menace? Indian J Community Med. 2022; 47 :628-30.