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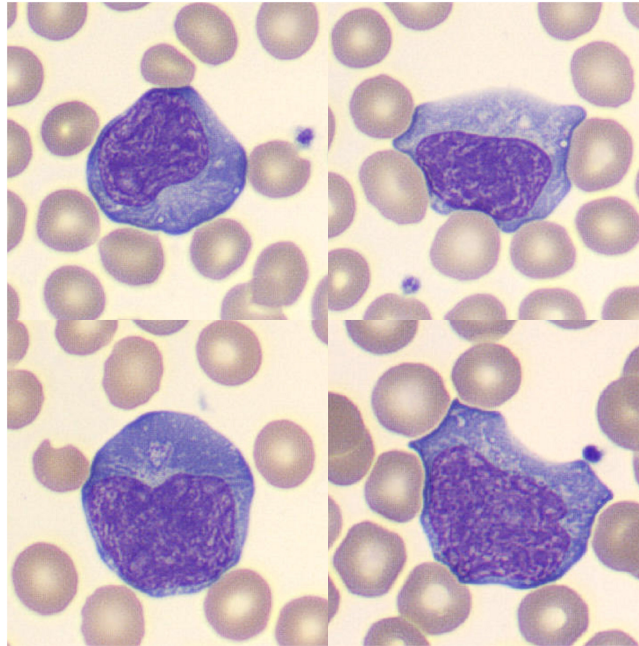
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Atypical lymphocytes associated with monkeypox virus infection








The monkeypox outbreak that started in May 2022 in non-endemic countries represents a new and challenging public health concern. Currently, the diagnosis is suggested by a rash and vesicles throughout the body, mainly located on anal and genital parts. The diagnosis is confirmed by PCR performed on a sample of fluid swabbed from lesions and the throat.

In our institution, we noticed atypical lymphocytes in blood films in some of our patients (6/14) with active monkeypox infection confirmed by multiplex PCR (herpes simplex virus type 1/2, varicella-zoster virus, monkeypox). No co-infections were identified. Among the 14 cases (who were all men – median age 31 years, range 20–45), 11 were investigated haematologically. Six cases out of 11 were flagged by the Sysmex XN-3100 analyser and blood film examination was then performed. All flagged samples had atypical lymphocytes in the blood film (median 14% of all lymphocytes, range 7–36). Of note, except for one patient who had an absolute lymphocyte count of $4.59 \times 10^9/l$, lymphocytosis was not observed (median $2.71 \times 10^9/l$, range 1.28–3.12).

Atypical lymphocytes are characterised by a morphological modification of mature lymphocytes due to immune stimulation. The cell size is increased with abundant basophilic, dark blue to pale grey, cytoplasm and a finer and more immature chromatin than in mature lymphocytes. They are typically found in infectious mononucleosis (Epstein–Barr virus infection), viral hepatitis, toxoplasmosis and malaria

but also in other infectious diseases which, depending on the stage of the disease, may be associated with an eruptive presentation (chicken pox, herpes simplex virus, human immunodeficiency virus, syphilis...).

Our recent findings lead us to consider that the visualisation of atypical lymphocytes in a blood film could suggest a monkeypox virus infection in patients with an eruptive disease. However, atypical lymphocytes are not pathognomonic of a specific infectious disease and the differential diagnosis should lead to serological and/or molecular investigations.

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