

# Large nocturnal eyes causing gastrointestinal bleeding in asymptomatic multiple myeloma

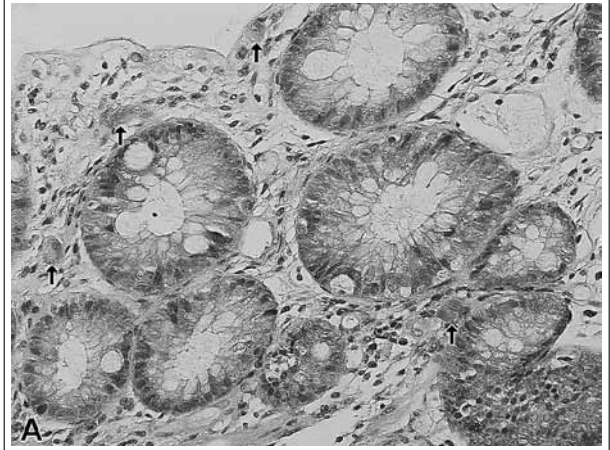
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## CASE REPORT

A 67-year-old male was transferred to our Intensive Care Unit because of recurrent severe gastrointestinal bleeding after treatment for *Enterococcus faecalis* urosepsis with amoxicillin, corticosteroids, fluid resuscitation and norepinephrine. About six months earlier, multiple myeloma (MM) IgG-lambda type had been diagnosed with 15% bone marrow infiltration. Since no evidence of related end-organ damage was present, fulfilling the criteria for asymptomatic myeloma, an expectative management was chosen.<sup>1</sup> At admission, laboratory examination showed elevated C-reactive protein (177 mg/l) with leucocytosis ( $16 \times 10^9/l$ ) and lymphopenia ( $0.5 \times 10^9/l$ ). Blood and stool cultures remained negative. Angiography revealed contrast extravasations in the upper gastrointestinal tract, but unsuccessful coil embolisation necessitated short bowel resection. Histologically, the resected specimen showed generalised ulcerations. T-cell counts were decreased ( $CD4\ 0.23/CD8\ 0.22 \times 10^9/l$ ) with ANA/ANCA, HIV and Epstein-Barr virus testing negative. Colonoscopy also showed a diffuse ulcerative mucosa with biopsies demonstrating reactive colonic mucosa with some inflammation (*figure 1*). A few microthrombi were found in submucosal vessels.

**Figure 1.** Reactive colonic mucosa with viral inclusions, mainly in endothelial cells (arrows)



## WHAT IS YOUR DIAGNOSIS?

See page 327 for the answer to this photo quiz.

LARGE NOCTURNAL EYES CAUSING GASTROINTESTINAL BLEEDING IN ASYMPTOMATIC  
MULTIPLE MYELOMA

DIAGNOSIS

Our patient had positive cytomegalovirus (CMV) IgG and negative IgM serum antibodies with high levels of CMV viraemia ( $2.2 \times 10^5$  c/ml) indicative of acute reactivated CMV infection. Immunohistochemical staining for CMV on colonic biopsies was positive (figure 2). CMV is an extremely common pathogen worldwide, with 50 to 80% of adults infected by the age of 40 years. Although most healthy people infected by CMV have no symptoms, CMV infection can be life-threatening in immunocompromised patients, affecting different organ systems including the gastrointestinal tract. The CMV enterocolitis of our patient was probably induced by multiple myeloma associated T-cell dysfunction and perhaps worsened by the corticosteroids used to treat his initial *E. faecalis* sepsis. Despite initiation of ganciclovir, our patient died as anastomotic leakage resulted in abdominal sepsis with multiple organ failure.

Multiple myeloma (MM), also known as Kahler's disease, is the second most prevalent haematological malignancy representing 2% of all cancer deaths. At diagnosis, before treatment, a significant number of MM patients exhibit impaired cellular and humoral immune responses.<sup>2</sup> In one study, about 10% of patients died early after MM diagnosis as a result of bacterial infections, in particular with *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Escherichia coli*.<sup>3</sup> However, fatal CMV infection in untreated MM is rare, with to our knowledge only a few cases published.<sup>4</sup> Gastrointestinal CMV infection induces

mucosal ulcerations resulting in abdominal pain, fever and bloody diarrhoea. CMV also promotes the formation of micro-thrombi, leading to secondary ischaemic damage. Diagnosis may be obtained by colonoscopy with biopsies. Upon direct visualisation by colonoscopy, inflammation with focal mucosal haemorrhage, oedematous folds, and polypoid lesions can be seen. Histological specimens typically show viral inclusions, referred to as owl's eyes (arrows figure 1).

In conclusion, asymptomatic and thus often untreated myeloma patients may display cellular and humoral immunodeficiencies which constitute an important predisposing factor for fatal opportunistic bacterial and viral infections.

REFERENCES

1. Kyle RA, Rajkumar SV. Criteria for diagnosis, staging, risk stratification and response assessment of multiple myeloma. *Leukemia*. 2009;23(1):3-9.
2. Pratt G, Goodyear O, Moss P. Immunodeficiency and immunotherapy in multiple myeloma. *Br J Haematol*. 2007;138(5):563-79.
3. Augustson BM, Begum G, Dunn JA, et al. Early mortality after diagnosis of multiple myeloma: analysis of patients entered onto the United Kingdom Medical Research Council trials between 1980 and 2002. *J Clin Oncol*. 2005;23(36):9219-26.
4. Manna A, Cordani S, Canessa P, Pronzato P. CMV infection and pneumonia in hematological malignancies. *J Infect Chemother*. 2003;9(3):265-7.

Figure 2. The immunohistochemical stain for CMV is positive in the nucleus of virus containing cells (black dots)

