Disseminated mucormycosis of an immunocompromised multiple myeloma patient: impact of biopsy of extramedullary tumours in refractory multiple myeloma

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Dear Editor,

We present the case of a 43-year-old female patient with an anaplastic IgG kappa multiple myeloma (MM) confirmed by morphological and molecular genetic analyses showing a tumorous bone marrow infiltration by highly atypical plasma cells (Fig. 1a) with strong expression of the plasma cell marker CD138 (Fig. 1b) and the kappa light chain (Fig. 1c, d reveals negative staining for lambda light chain) as well as a monoclonal rearrangement of the immunoglobulin heavy chain (IgH; Fig. 1e). In her 4-year treatment history, she underwent conventional chemotherapies as well as two autologous and one allogeneic peripheral blood stem cell transplantation from a matched related donor. Ten months after the latter, she presented with tumorous lesions in the left acetabulum, soft tissue, liver and dura mater coincidental with serum IgG kappa increase (IgG 2,400 mg/dL, free kappa light chains 1,550 mg/L), suggesting extramedullary manifestations of MM. After a third, salvage high-dose chemotherapy with autologous stem cell support, the patient received haplo-identical blood stem cell transplantation [1] in partial remission. However, due to an enlargement of the extramedullary infiltrates with increasing IgG values and an antibiotic/antimycotic therapy comprising fluconazole 400 mg/day, posaconazole 400 mg/day, voriconazole

400 mg/day, anidulafungin 100 mg/day and caspofungin 50 mg/day without substantial serological/microbiological hints at an infectious etiology, a renewed progression of MM was suspected. In a dramatically worsened terminal course with multiorgan failure and progressive cerebral clouding, the patient died under the suspicion of a progressive extramedullary relapsed anaplastic MM.

In autopsy, we found multiple nodular infiltrates in the liver (Fig. 2a, arrows) with parenchymatous scars and subacute infarctions (Fig. 2b) as well as a subtotal infarction of the right kidney and acute haemorrhagic infarctions of the lung and the cerebellum (Fig. 2d, arrow) showing fresh haemorrhages and necrosis in the cerebellar cortex (Fig. 2e). However, no residuals of the MM were detectable in the organ infiltrates neither by immunohistochemistry nor by molecular genetic analyses (Figs. 2c and f, showing polyclonal amplificates for the IgH rearrangement). By contrast, we could demonstrate an extensive vascular permeation with apparent occlusion of small to medium arteries by hyphae (Fig. 3) in all organs involved with subsequent haemorrhagic infarctions and the morphological diagnosis of mucormycosis (Fig. 3, inset) was confirmed by specific polymerase chain reaction amplification detecting *Rhizopus* species.

Extramedullary manifestations of MM occur in approximately 20% of patients and diffuse hepatic infiltration was even described in up to 50% of advanced cases [3]. However, since the differential diagnosis of extramedullary tumours in the refractory phase of MM includes other malignancies (e.g. transition to lymphoproliferative disorders [2]) as well as infectious diseases, a proper diagnostic clarification of any recurrent extramedullary tumour in MM by histological/molecular genetic analyses should be performed to improve the management and prognosis of such lesions.

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Fig. 1 Tumourous bone marrow infiltration by highly atypical plasma cells (**a**) with strong expression of the plasma cell marker CD138 (**b**) and the kappa light chain (**c**) as well as negative staining for lambda light chain (**d**) and a monoclonal rearrangement of the immunoglobulin heavy chain (**e**)

Fig. 2 Multiple nodular infiltrates in the liver (**a**, *arrows*) with parenchymatous scars and subacute infarctions (**b**) as well as a subtotal infarction of the right kidney and acute haemorrhagic infarctions of the lung and the cerebellum (**d**, *arrow*) showing fresh haemorrhages and necrosis in the cerebellar cortex (**e**). **c** and **f** Polyclonal amplificates for the IgH rearrangement

Fig. 3 Extensive vascular permeation with apparent occlusion of small to medium arteries by hyphae in all organs involved with subsequent haemorrhagic infarctions and the morphological diagnosis of mucormycosis (*inset*)

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