18.3.5. Monitoring patients treated with monoclonal antibody-based therapies

Monoclonal antibody (mAb)-based therapies represent a major advance in the treatment of multiple myeloma (MM). However, they can present a challenge to diagnostic laboratories when the therapeutic antibody migrates as a discrete band on serum protein electrophoresis (SPE) and serum immunofixation electrophoresis (sIFE) \( ^{[1]} \). For example, daratumumab (an IgG\(\kappa\) anti-CD38 mAb) migrates as a discrete band in the \(\gamma\)-region \( ^{[2]}[3][4] \). Tang et al. \( ^{[5]} \) observed that therapeutic mAbs produce a false positive electrophoretic result in the majority of treated patients, which may persist for several months after therapy has ended. The authors noted that in approximately 20% of cases, the mAb was indistinguishable from the tumour-derived monoclonal protein, and therefore may prevent assessment of complete response. The limitations of SPE are further discussed in Section 17.4.

Murata et al. \( ^{[2]} \) demonstrated that daratumumab also produces an increase in IgG\(\kappa\) concentrations measured by the Hevylite assay. In such cases, Freelite sFLC assays may offer an alternative means of monitoring patients, as they do not recognise intact monoclonal antibodies \( ^{[5]} \). Rosenberg et al. \( ^{[4]} \) investigated if daratumumab produced significant interference on Freelite sFLC assays by spiking serum samples from MM patients containing monoclonal intact immunoglobulins (IgG\(\kappa\) n=20; non-IgG\(\kappa\) n=10) with the drug. There was no significant effect of daratumumab on the measured \(K, \lambda\) or \(K/\lambda\) sFLC ratio when the maximal clinically relevant concentration of the drug (1 g/L) was added. In addition, super-therapeutic concentrations of the drug (2 g/L) gave very low \(K\) sFLC values (0.4 – 1.4 mg/L). The authors concluded that it is unlikely that daratumumab interacts with the FLC assay, and represents a practical alternative to SPE and sIFE to monitor response to therapy. Similar results were reported by Jenner et al. \( ^{[6]} \). The use of sFLC assays to monitor intact immunoglobulin patients may become increasingly important as the use of mAb therapy become more widespread and there is increasing awareness of the ability of mAbs to potentially interfere with serum electrophoretic assays.

References
