Light chain MGUS was proposed by Dispenzieri et al.\(^1\) as a separate clinical entity and the pre-malignant precursor of LCMM. The authors defined light chain MGUS as an abnormal \(\kappa/\lambda\) sFLC ratio with an increased concentration of the involved sFLC, no expression of monoclonal intact immunoglobulin, and an absence of end-organ damage that can be attributed to the plasma cell proliferative disorder. An example is shown in Figure 13.10: No abnormality was detected by SPE or urine protein electrophoresis (UPE), but an abnormal \(\kappa/\lambda\) sFLC ratio indicated the presence of monoclonal FLCs. This finding was confirmed by the detection of \(\lambda\) uBJP by urine IFE (uIFE).

In the study by Dispenzieri et al.\(^1\) the prevalence and risk of progression of light chain MGUS amongst 18,357 residents of Olmstead County, Minnesota aged 50 years or older was assessed. 610 (3.3%) individuals had an abnormal \(\kappa/\lambda\) sFLC ratio, of whom 213 had an intact immunoglobulin MGUS. This included 57/213 additional patients whose monoclonal intact immunoglobulin had not previously been detected by screening with SPE, and so the prevalence of conventional MGUS in this population was revised from 3.2% to 3.4% (95% CI 3.2 - 3.7). Of the 397 individuals with an abnormal sFLC ratio but no abnormality detected by SPE, a total of 146 met the definition of light chain MGUS, equivalent to a prevalence of 0.8% (95% CI 0.7 - 0.9). This represented 19% of the total MGUS population; a proportion that matches the relative incidence of LCMM compared to all MM. The light chain type was identified as \(\kappa\) or \(\lambda\) in 108 and 38 individuals, respectively. Overall, involved sFLC concentrations tended to be low; only around 10% of patients had concentrations greater than 200 mg/L. It was noted that 23% of light chain MGUS patients either had or subsequently acquired, renal disease; an observation of relevance to the later proposal for monoclonal gammopathy of renal significance to be considered as a separate entity (Section 26.4.1). A similar incidence of light chain MGUS (0.7%) was confirmed by the German population-based Heinz Nixdorf Recall study of 4702 individuals aged 45 - 75 years\(^2\).

Pelzer et al.\(^3\) studied disease progression in 75 light chain MGUS patients enrolled in the Heinz Nixdorf Recall study at 5 and/or 10 year time points. Although no patients progressed to overt lymphoproliferative disease (including LCMM), light chain MGUS patients had a 1.5-fold higher risk of having a coexisting solid tumour (\(p=0.04\)). Additionally, 3 individuals with progressively increasing sFLC concentrations developed conventional MGUS. There were no differences in overall survival between patients with and without light chain MGUS, but individuals with monoclonal \(\lambda\) FLCs had shorter overall survival compared to those with monoclonal \(\kappa\) FLCs and normal controls (\(p=0.01\)). During follow-up, light chain MGUS was a persistent finding in 45% (14/31) patients, but in the remaining 55% (17/31) of patients the monoclonal protein became undetectable. The authors concluded\(^3\) that light chain MGUS is a relatively benign disorder with a high rate of monoclonal protein disappearance.
Serum analysis for FLCs showed an abnormal κ/λ ratio. TP: urine protein excretion. (Courtesy of J.A. Katzmann.)

References

