

Incidence of light chain escape in myeloma patients at relapse

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Introduction: In recent case reports^{1,2} of “light chain escape” (LCE; rising monoclonal free light chain production at relapse without increased monoclonal intact immunoglobulin) it has been suggested that this might be more prevalent with modern chemotherapy and more visible with serum FLC analysis.

Aim: In this study, the frequency of LCE between patients with IgG and IgA myeloma and intensive versus non-intensive chemotherapy was compared.

Method: Stored sera from patients in the Myeloma VII trial (randomised between intensive and non-intensive chemotherapy) were utilised. There was sufficient frozen serum and complete data for 36/60 IgA myeloma patients and for 30/60 IgG patients (the first 60 selected chronologically). Representative sera from presentation, maximum response and relapse time points were utilised for sFLC measurement and results compared with recorded urine FLC (“Bence-Jones Protein” [BJP]: Urine light chain/Creatinine ratio) and intact immunoglobulin measurements. Results were classified as “true” LCE if there were rising sFLC concentrations with stable or falling intact immunoglobulin concentrations or “partial” LCE if there was some rise in intact immunoglobulin but the FLC rise was clearly greater.

Results:

1. Effect of paraprotein type on LCE incidence

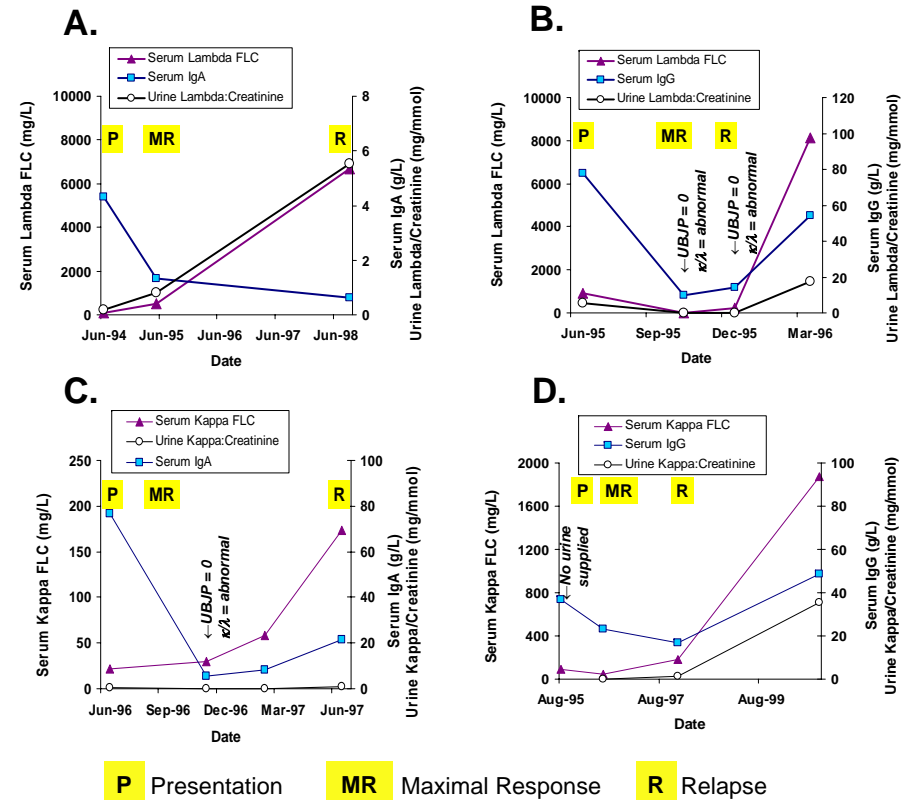
| | “True” LCE | “Partial” LCE |
|-------------|------------|---------------|
| IgA Myeloma | 3/36 (8%) | 4/36 (11%) |
| IgG Myeloma | 1/30 (3%) | 3/30 (10%) |

2. Effect of chemotherapy regimen on LCE incidence

| | “True” LCE | “Partial” LCE |
|---------------|------------|---------------|
| Non-intensive | 4/4 | 3/7 |
| Intensive | 0/4 | 4/7 |

Examples

A. “True” LCE: IgA λ patient treated on Non-intensive pathway. UBJP is negative whilst sFLC ratio remains abnormal at two time points.
B. “Partial” LCE: IgG λ patient treated on Intensive pathway. Relapse clearly associated with differential light chain expression. UBJP is negative whilst sFLC ratio remains abnormal at one time point.
C. “Partial” LCE: IgA κ patient treated on Non-intensive pathway. Relapse shown first by rising sFLC concentrations. No urine sample supplied for one time point.
D. “Partial” LCE: IgG κ patient treated on Intensive pathway.



3. Comparison of sFLC vs UBJP to detect LCE

For all 11 patients showing some form of LCE, this was corroborated by the urine results in 5/11. For 6/11 the amounts of FLC in the urine were insufficient for consistent analysis.

Conclusions:

- These preliminary findings do not indicate any greater frequency of LCE with intensive chemotherapy but suggest that it might be more apparent with serum FLC analysis.
- True LCE was seen in more IgA than IgG patients but the numbers were very small.

References:

1. Dawson *Haematologica* 2007; 92: 143 - 144
2. Kühnemund *Onkologie* 2005; 28 (suppl 3): 165