

## Short report

# Leukaemic mantle cell lymphoma with t(11;14) and trisomy 12 showing clinical features of stage A0 B cell chronic lymphocytic leukaemia

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### Abstract

The precise diagnosis of lymphoma usually requires the histological examination of lymph nodes or involved tissues. Mantle cell lymphoma is a form of intermediate grade non-Hodgkin's lymphoma in which typical morphological immunophenotypic and cytogenetic features have been recognised. A case of leukaemic mantle cell lymphoma with the characteristic reciprocal translocation t(11;14) together with trisomy 12, a chromosomal abnormality usually associated with B cell chronic lymphocytic leukaemia (CLL), is presented. This combination of cytogenetic abnormalities has not been reported previously. The lack of lymphadenopathy and hepatosplenomegaly in this patient is more in keeping with stage A0 CLL. This case demonstrates the close clinical and biological relationship between mantle cell lymphoma and CLL.

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Keywords: Mantle cell lymphoma, t(11;14), trisomy 12.

Mantle cell lymphoma is a form of intermediate grade non-Hodgkin's lymphoma that is normally defined histologically and is characterised by a predominantly diffuse or vaguely nodular proliferation of atypical small lymphoid cells effacing the nodular architecture.<sup>1</sup> The relatively frequent occurrence of leukaemic phase in mantle cell lymphoma has resulted in the recognition of typical morphological and immunophenotypic features.<sup>2,3</sup> The chromosomal translocation t(11;14)(q13;q32) is characteristic of mantle cell lymphoma and occurs in up to 75% of cases,<sup>3</sup> but this translocation has also been described in B prolymphocytic leukaemia (18% of cases),<sup>4</sup> plasma cell leukaemia (15% of cases)<sup>5</sup> and rarely in chronic lymphocytic leukaemia (CLL) (2% of cases).<sup>6</sup> Trisomy 12 is the commonest chromosomal abnormality in B-CLL and has been correlated with atypical morphology.<sup>7</sup> Here, we describe a case which we feel demonstrates the close clinical and biological relationship between mantle cell lymphoma and B-CLL.

### Case report

An 82 year old woman presented with fatigue and was found on routine full blood count to have a lymphocytosis; haemoglobin 11.5 g/dl, white blood count  $33.2 \times 10^9/l$ , lymphocytes  $26.9 \times 10^9/l$ , and platelet count  $219 \times 10^9/l$ . Clinical examination was unremarkable and there was no lymphadenopathy or hepatosplenomegaly. In a Romanowski stained blood film the lymphocytes had a pleomorphic appearance with small and intermediate sized cells predominating (fig 1); some of the cells had obvious clefted nuclei.

Immunophenotyping was performed on Ficoll-trisil separated mononuclear cells by flow cytometry and this showed CD5 49%, CD19 80%, CD23 7%, CD10 <1%, FMC7 86%, and there was strong surface immunoglobulin expression with  $\kappa$  restriction. Karyotyping was performed following culture of peripheral blood lymphocytes for four to five days in the presence of TPA at a final concentration of 50 ng/ml, followed by G banding by standard methods. This showed both trisomy 12 and t(11;14)(q13;q32) in 15 of 15 cells examined (fig 2). Fluorescence in situ hybridisation using a cen-

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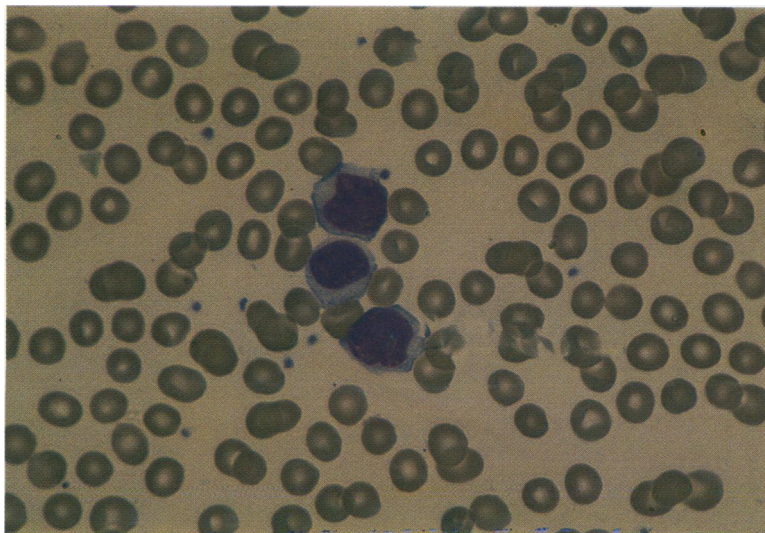


Figure 1 Peripheral blood film showing medium sized lymphoid cells with irregular and clefted nuclei.

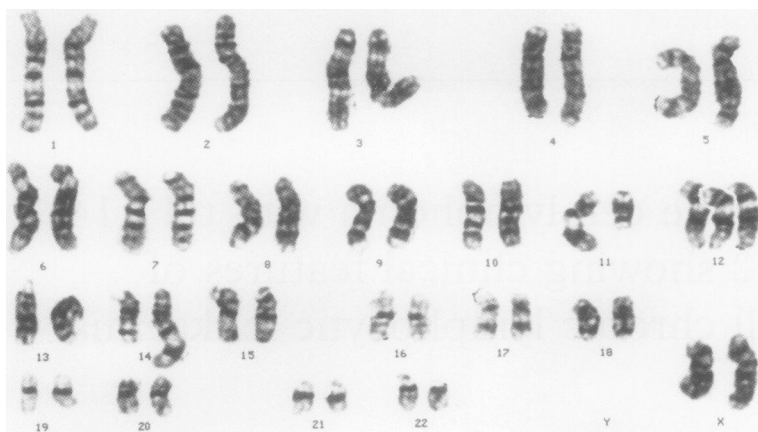


Figure 2 Karyotype showing  $t(11;14)$  translocation and trisomy 12.

tromeric probe for chromosome 12 was performed as previously described,<sup>8</sup> and three signals were present in 220 of 300 (73%) cells examined.

### Discussion

In our case the membrane markers and morphology best fit a diagnosis of mantle cell lymphoma which is supported by the presence of  $t(11;14)$ . The progression to leukaemic phase in mantle cell lymphoma is usually associated with significant lymphadenopathy, often splenomegaly and is representative of worsening prognosis.<sup>9</sup> This case is unusual in presenting in leukaemic phase in the absence of both lymphadenopathy and hepatosplenomegaly, a clinical presentation that would favour a diagnosis of stage A0 CLL. The presence of trisomy 12 would also seem to be more in keeping with CLL. One study demonstrated trisomy 12 in three of 12 cases of intermediate grade lymphoma (diagnosed histologically).<sup>10</sup> However, the presence of both  $t(11;14)$  and trisomy 12 in the same patient with mantle cell lymphoma has not been described before. This combination of cytogenetic abnormalities and the clinical features in this case could be interpreted as an overlap syndrome between mantle cell lymphoma and B-CLL. It is probable that these two diseases are closely related because it is generally accepted that the malignant cells in both conditions are

derived from CD5 positive B cells situated in the mantle zone of lymphoid follicles.

The prognosis of patients with mantle cell lymphoma presenting without lymphadenopathy and hepatosplenomegaly is not known.

Whether this case represents an overlap syndrome between CLL and mantle cell lymphoma or is an atypical example of mantle cell lymphoma is not clear, nor is the likely prognosis. Similar cases might be overlooked and diagnosed as CLL (mixed cell type) if immunophenotyping and cytogenetics are not performed.

It may be argued that the diagnosis of mantle cell lymphoma in the absence of lymph node histology is presumptive but we feel that the combination of morphological, immunophenotypic and cytogenetic features in this case are sufficient to make this diagnosis. Whilst haematologists probably accept the existence of mantle cell lymphoma as a subgroup of intermediate grade non-Hodgkin's lymphoma, many histopathologists remain unconvinced. Perhaps the future development of in situ cytogenetic techniques may make the detection of  $t(11;14)$  on histological sections possible and this may eventually lead to the inclusion of mantle cell lymphoma in histological classifications of non-Hodgkin's lymphoma.

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