Pulmonary mucosa-associated lymphoid tissue lymphoma with strong nuclear B-cell CLL/lymphoma 10 (BCL10) expression and novel translocation t(1;2)(p22;p12)/immunoglobulin κ chain-BCL10

Mucosa-associated lymphoid tissue (MALT) lymphoma is associated with recurrent chromosomal translocations t(11;18)(q21;q21), t(14;18)(q32;q21), t(1;14)(p22;q32) and t(3;14)(p14.1;q32).^{1,2} While t(11;18)(q21;q21) fuses the N-terminus of the *API2* (11q21) gene to the C-terminus of the *MALT1* (18q21) gene and generates a functional API2-MALT1 product, t(1;14)(p22;q32), t(14;18)(q32;q21) and t(3;14)(p14.1;q32) bring the *BCL10* (1p22), *MALT1* (18q21) and *FOXP1* (3p14) genes, respectively, under the control of the immunoglobulin heavy chain (*IGH*, 14q32) enhancer, leading to their overexpression.¹ Interestingly, the oncogenic activity of the first three chromosomal translocations is linked by the physiological role of BCL10 and MALT1 in antigen receptor-mediated nuclear factor kappa B (NF κ B) activation.¹

Primary pulmonary MALT lymphomas show heterogeneous cytogenetic abnormalities, including aneuploidy and translocations. Among the translocations described in MALT lymphoma of this site, t(11;18)(q21;q21) is the most common, occurring in up to 50% of cases, and t(14;18)(q32;q21) and t(1;14)(p22;q32) are relatively rare.³⁻⁵ The overall incidence of t(1;14)(p22;q32) is approximately 3% in MALT lymphomas of different sites, and can be up to 10% in pulmonary cases.⁴⁻⁶ Recently, Achuthan *et al*⁷ reported t(1;2)(p22;p12) involving the *BCL10* and the immunoglobulin kappa (*IGK*) light chain genes as a novel translocation in a gastric MALT lymphoma. Here we report the first case of pulmonary MALT lymphoma with this translocation, indicating that the t(1;2)(p22;p12) is a recurrent cytogenetic event in MALT lymphoma.

Case report

A 60-year-old Taiwanese lady presented with two abdominal wall masses for 1 month, and intermittent, productive cough for years. She was afebrile, without weight loss or night sweating. She was uraemic, with haemodialysis for 9 years, and had malignant fibrous histiocytoma (MFH) in the abdominal wall,

with five excisions over the past 4 years. She had received transurethral resection of a high-grade, transitional cell carcinoma of the bladder 4 months ago. Physical examination revealed protruding masses at the left abdominal wall and left flank (8 cm each), without lymphadenopathy. Her haemoglobin was 11.2 g/dl; leucocyte and platelet counts and lactate dehydrogenase (LDH) level were normal. Her serum was positive for hepatitis B surface antigen (HBsAg) and anti-hepatitis C virus (HCV) and negative for anti-human immunodeficiency virus (HIV). Chest x ray revealed a few nodules in the right upper lung and was confirmed by CT scan without lymphadenopathy or splenomegaly. CT-guided biopsy of the largest tumour (3.6 cm) revealed MALT lymphoma. Marrow biopsy was not performed. She did not receive chemotherapy or radiotherapy. Excision of the abdominal tumours 1 month later revealed recurrent MFH with mesocolonic metastasis. After 5 months, multiple pulmonary masses up to 10 cm were noted in the right lung, and CT-guided biopsy revealed metastatic MFH, which had probably over-run the MALT lymphoma.

Microscopically, the first pulmonary needle biopsy showed total effacement of pulmonary parenchyma by a diffuse infiltrate of atypical

Figure 1 (A) H & E stain of the pulmonary needle core showing small centrocyte-like lymphocytes with marked plasma cell differentiation and intranuclear Dutcher body formation (inset). (B) Immunohistochemical staining showing strong nuclear expression of B-cell CLL/lymphoma 10 protein. Interphase fluorescence in situ hybridisation with dual-colour break-apart probes for *BCL10* (C) and immunoglobulin kappa chain (*IGK*) (D) genes, and dual-colour dual-fusion *IGK* (red)-*BCL10* (green) translocation probes (E) showed several cells (arrows) displaying either a split of the red and green signals (C and D) or co-localisation of red and green signals (E), indicating t(1;2)(p22;p12)/*IGK*-*BCL10* translocation.

small lymphocytes with three colonised follicles. These atypical lymphocytes exhibited twisted nuclei, with focal plasmacytic differentiation and some intranuclear Dutcher bodies (fig 1A). These atypical lymphocytes expressed CD20, CD27, CD43, IgM, BCL2 and strong nuclear BCL10 (fig 1B)⁶ but not CD3, CD5, CD10, CD23, IgD or BCL6, and were monotypic for λ light chain. The diagnosis of pulmonary MALT lymphoma was made.

Reverse transcription-PCR for *API2-MALT* fusion transcripts using paraffin-wax sections, as described previously, was negative.⁹ Fluorescence in situ hybridisation (FISH) studies using paraffin-wax sections with *IGH*, *BCL6* and *MALT1* dual-colour break-apart rearrangement probes (Vysis/Abbott Laboratories, Maidenhead, Berkshire, UK) were negative; however, three copies of the *MALT1* and *BCL6* genes were identified in 73% and 45% of cells, respectively, suggesting the presence of trisomies 18 and 3. The latter was confirmed by FISH with chromosome enumeration probes for chromosomes 18 and 3 (Vysis/Abbott). Further FISH experiments with *BCL10* and *IGK* locus dual-colour break-apart rearrangement probes were both positive in 78% and 75% cells, respectively (fig 1C,D).⁵⁻¹⁰ *t(1;2)(p22;p12)/IGK-BCL10* was confirmed by using *IGK-BCL10* dual-colour dual-fusion translocation probes (fig 1E).⁵⁻¹⁰ As *t(1;14)(p22;q32)*-associated MALT lymphoma was reported to involve recurrent trisomy 12,¹¹ FISH with a probe for centromere 12 (Vysis/Abbott) was also performed, and showed trisomy 12 in this case.

Discussion

The *BCL10* gene-involved translocation occurs in approximately 3% of MALT lymphomas.³ The translocation is described primarily in those from the stomach and lung and commonly involves the *IGH* locus at 14q32, resulting in overexpression of BCL10.^{5-6,8} Consequently, strong BCL10 expression in the nuclei of lymphoma cells has been invariably demonstrated in all the translocation-positive cases immunostained for BCL10.^{3-6,8} This is in contrast with nearly all *t(11;18)(q21;q21)*-positive MALT lymphomas and up to 20% of cases without *t(11;18)(q21;q21)*, where BCL10 shows a moderate level of nuclear expression, and with other MALT lymphomas and normal germinal centre B cells where BCL10 is expressed weakly in the cytoplasm. Therefore, a strong nuclear BCL10 staining pattern in MALT lymphoma has been suggested as a marker of *t(1;14)(p22;q32)*.^{5-8,12} Furthermore, BCL10 has been found to be expressed at high level in the nuclei of splenic marginal-zone B cells in transgenic mice in which *BCL10* gene expression was driven by *IGH* enhancers.¹³ The mechanism of transportation of BCL10 from the cytoplasm to the nucleus and how it contributes to lymphoma development is still unclear. However, the deregulated expression of BCL10 resulting from translocation is undoubtedly important in MALT lymphoma-genesis. Studies have shown that BCL10 is a molecule essential for NF κ B activation by antigen receptor stimulation in both the development and function of lymphocytes, and that NF κ B activation may contribute to the antiapoptotic effect.¹⁴⁻¹⁵

Translocations involving the *IGK* or *IGL* loci represent 5–10% of all *IG* translocations in lymphoid malignancies.¹⁶ Achuthan *et al*⁷ reported a novel *t(1;2)(p22;p12)/BCL10-IGK* in

a gastric MALT lymphoma without information on BCL10 expression. Our case is the first pulmonary MALT lymphoma with this translocation, and shows strong nuclear BCL10 expression. Our finding confirms that BCL10 is upregulated in *t(1;2)(p22;p12)* as well as in *t(1;14)(p22;q32)*, and strong nuclear BCL10 staining is highly suggestive of the presence of *BCL10*-involved translocation. Like *t(1;14)(p22;q32)*, which is mutually exclusive from *t(11;18)(q21;q21)* and *t(14;18)(q32;q21)*, but may display additional genomic abnormalities, our present *t(1;2)(p22;p12)*-positive case did not carry *IGH*, *API2*, *MALT1* or *BCL6* translocations, but showed trisomies 3, 12 and 18, which are typical secondary aberrations in *t(1;14)*-positive MALT lymphomas.¹¹ Recognition of this translocation is important, as it might constitute a specific clinicopathological subtype among MALT lymphomas, which usually presents at a more advanced stage and, if arising in the stomach, does not respond to *Helicobacter pylori* eradication.¹²

In conclusion, our case is the first pulmonary MALT lymphoma carrying *t(1;2)(p22;p12)/IGK-BCL10*, indicating that the *t(1;2)(p22;p12)* is a recurrent cytogenetic event in MALT lymphoma.

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SHORT REPORTS

Myelolipoma of the lung: a case report and brief review

Myelolipomas are rare tumours composed of mature adipose tissue and normal haematopoietic cells. They commonly occur in the adrenal glands, and involvement of the lung is extremely rare.^{1–6} We report a case of pulmonary myelolipoma presenting as an asymptomatic nodule unchanging in size for 10 years after being detected.

Case report

A man in his 70s, a smoker, had a nodule in the left lower lobe (LLL) of the lung detected on a chest radiograph 10 years earlier. The nodule, 2 cm in maximal diameter, had not changed in size. The patient had never had haematological disorders including anaemia. He presented with intractable lumbago since 6 months, and MRI detected multiple bone tumours. CT of the chest indicated a large mass in the right lower lobe (RL) and a small solitary nodule with rim-like calcification in the LLL of the lung (fig 1A). Sputum cytology showed carcinoma cells. He was clinically diagnosed as having lung cancer with multiple bone metastases. Chemotherapy and radiation