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Variant Translocation in a Non Endemic Case of Burkitt's Lymphoma: t (8;22) in an Epstein–Barr Virus Negative Tumour and in a Derived Cell Line

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Abstract—*After clinical and histopathological diagnosis of Burkitt's lymphoma (BL) in a male Caucasian child with jaw and abdominal tumours, both Epstein–Barr virus (EBV) and cytogenetic studies were performed. The absence of EB viral markers within the tumour cells and the normal EBV serological profile of the patient indicated that this non-endemic BL case was not associated with the virus. Cytogenetic examination of the tumour cells showed a t(8;22) translocation, suggesting that this case represents an example of the variant translocations newly observed in cases of BL. It indicates that chromosome 8 rearrangement with a break-point at 8q23 is a characteristic feature of this particular lymphoma.*

INTRODUCTION

A RECIPROCAL (8;14) translocation (q23;q32) has been found in the majority of Burkitt's lymphoma (BL) cases in both endemic and non-endemic areas [1, 2]. This non-random chromosome abnormality is present in such lymphoma cases, independent of their association with the Epstein–Barr virus (EBV) and appears to be a good marker of Burkitt cells; it has also been found in Burkitt-type leukemias [3]. However, recent data on variant translocations in non-endemic BL indicate that the chromosome 8 rearrangement with a break-point at 8q23 may be a more characteristic feature of BL [4–6]. The observation of a (8;22) translocation reported here supports that hypothesis. This variant translocation was observed in a Caucasian child whose BL was not associated with EBV, although clinically tumours of the jaw and abdomen were present, as reported in most African cases.

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CLINICAL REPORT

The case was in a Caucasian boy, born on 15 February 1972 of healthy parents. The family history revealed two cases of cancer: the paternal grandfather had died from multiple myeloma and a paternal aunt from breast cancer. The boy, who lived in France, remained well until May 1979 when eyelid oedema, bone pains and a tumour in the right maxillary sinus developed gradually. When the boy was referred to our hospital on 15 June 1979, facial asymmetry was apparent, due to swelling of the right upper maxilla (Fig. 1). Enlarged lymph nodes in the cervical region and two abdominal masses were discovered. Clinical investigations of liver, spleen, testis and other organs were normal.

The histopathological analysis of a biopsy showed a 'starry sky' picture and abnormal proliferation consisting of large, regularly shaped, round basophilic and monomorphic cells with numerous mitotic figures characteristic

of BL. Staging led to a final diagnosis of BL stage III, according to Murphy's classification [7].

Chemotherapy was started immediately (C.O.P.A.D. regimen Vincristine 1.5 mg/m^2 day 1; Adriamycin 75 mg/m^2 day 2; Cyclophosphamide 300 mg/m^2 days 3 and 4; Prednisone 60 mg/m^2 days 1–6). On the 17th day of treatment, complete remission was achieved. One month later (July 1979), the presence of headache, vomiting and bilateral Babinski sign indicated a central nervous system relapse. The maxillary tumour and enlarged lymph nodes quickly reappeared; the right testis was also involved by the disease, but the bone marrow remained normal. After radiotherapy of the central nervous system and the maxillary area, and before starting a new chemotherapeutic regimen, bone marrow was collected, frozen and stored (17 August 1979). A second complete remission was obtained in September 1979 (using the same chemotherapeutic regimen with Bleomycin added on day 1, 20 mg/m^2). Unfortunately, a further relapse occurred in October 1979 with 100% invasion of bone marrow and the cerebrospinal fluid, and recurrence of the abdominal masses. Three days later, the abdomen was found to be totally invaded, and a left pleurisy was discovered by chest X-ray. The boy died on 5 November 1979.

METHODS

Virological and immunological studies

EBV serology, performed at the time of first admission, was positive but showed titres as those found in normal populations: antiviral capsid antigen, 40; anti-early antigen, $\leqq 5$; anti-EBV specific nuclear antigen, 20. An immunofluorescence test done on the tumour cells in order to detect the EBV nuclear antigen was negative. These results indicate that the tumour was not associated with EBV, as confirmed later by the negative results of EBV nucleic hybridization tests done on a biopsy (kindly performed by Dr. Bornkamm, Freiburg, Federal Republic of Germany).

Immediately after the patient's death, bone marrow aspiration was performed. Immunological studies showed B-cell proliferation with surface μ chains. A bone marrow sample was also cultured by diluting the cells in RPMI medium 1640 supplemented with 20% foetal calf serum; three weeks later, growing lymphoid cells appeared, and the culture was then divided. After three more weeks, a continuous cell line was considered to have been established, and samples of the cells were frozen. They were found to have characteristics similar to those of the original malignant lymphoma cells, i.e. they presented surface immunoglobulins (μ chains) and did not express EBV antigen.

Cytogenetic investigations

Three sample types were made available for cytogenetic investigations: bone marrow cells obtained immediately after death, the continuous cell line, and bone marrow cells collected and frozen during remission (17 August 1979). The latter were used to obtain the constitutional karyotype, since no chromosome preparation from peripheral blood was available.

Cytogenetic investigations were performed in laboratories of the Centre Léon-Bérard and the Hôpital Saint-Louis. Cultures were set up without phyto-haemagglutinin. RHG and GTG banding techniques were used.

RESULTS

The chromosome counts are summarized in Table 1. In thawed bone marrow cells obtained during remission, the karyotype was a normal 46 XY (24 cells available). In fresh bone marrow cells obtained during relapse, three karyotypes were observed (62 mitoses available on direct analysis:

(1) Normal 46 XY;
(2) 46 XY t(8;22) (q23;q12);
(3) 46 XY t(1;6) (1qter→1q23::6q26 →6pter) t(8;22) (q23;q12) (Fig. 2 and 3a).

In the established cell line, more than 100 mitoses were observed, 80 of which were photographed and analysed. Only one karyotype was observed: 46 XY t(1qter→1q23 ::6q26→6pter t(8;22) (q23;q12) and 1q+: t(1;?) (q44;?). The cells in this line are then definitely trisomic for 1q23→1qter. This 1q+: t(1;?) (q44;?) was detected only in the cell line and not in the malignant bone marrow cells (Table 1).

DISCUSSION

The histological diagnosis of this tumour, made by one of us (P.A.B.), was a small, non-cleaved Burkitt-type of the Rappaport classification. This diagnosis was confirmed by Dr. Gerard-Marchant (Pathology Dept., I.G.R., Villejuif, France) using the Kiel classification, as a lymphoblastic Burkitt-type tumour. Virological studies

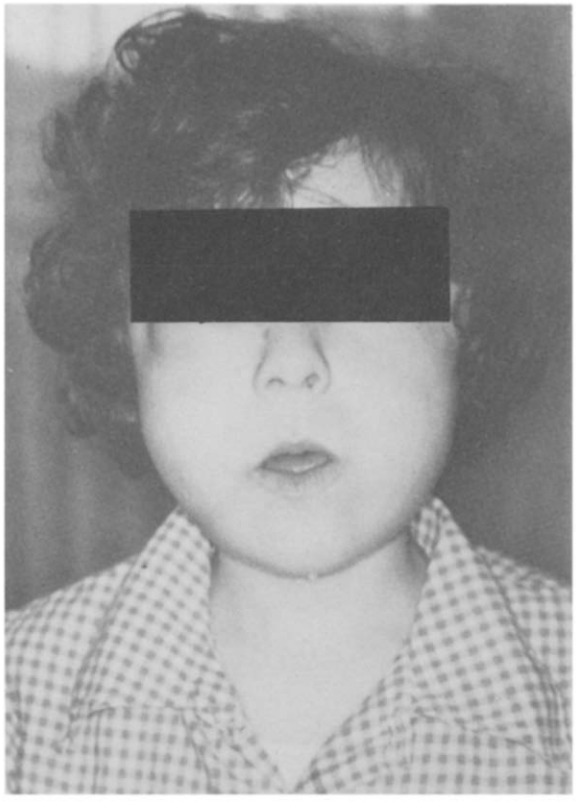

Fig. 1. *Photograph of the patient, taken at admission to hospital, showing facial asymmetry due to tumour in the right upper maxilla.*

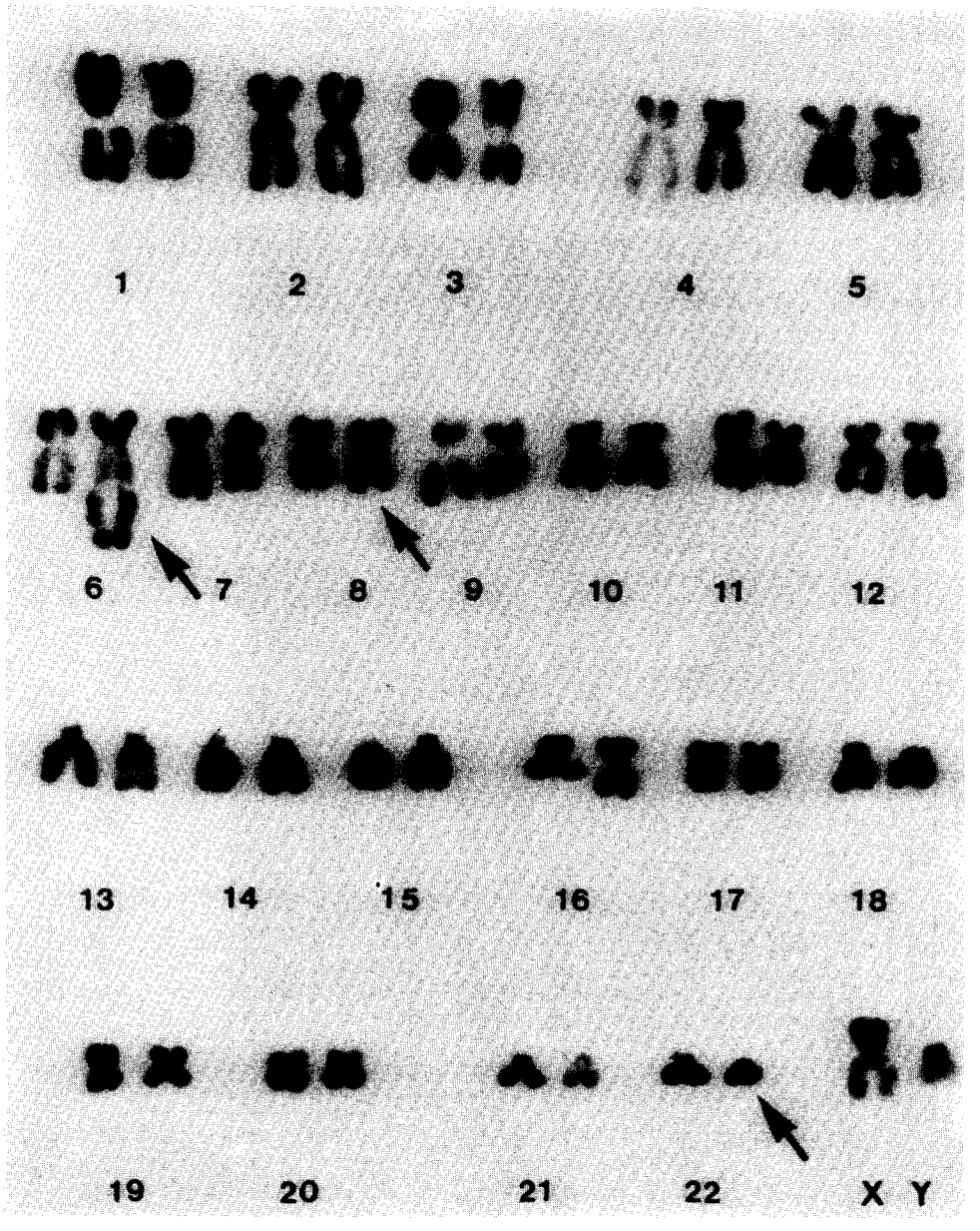

Fig. 2. *Karotype of bone-marrow cells obtained during relapse* (*RHG bands*): 46 XY t(8;22) (q23;q12) t(1;6) (1qter→1q23: :6q26→6pter).

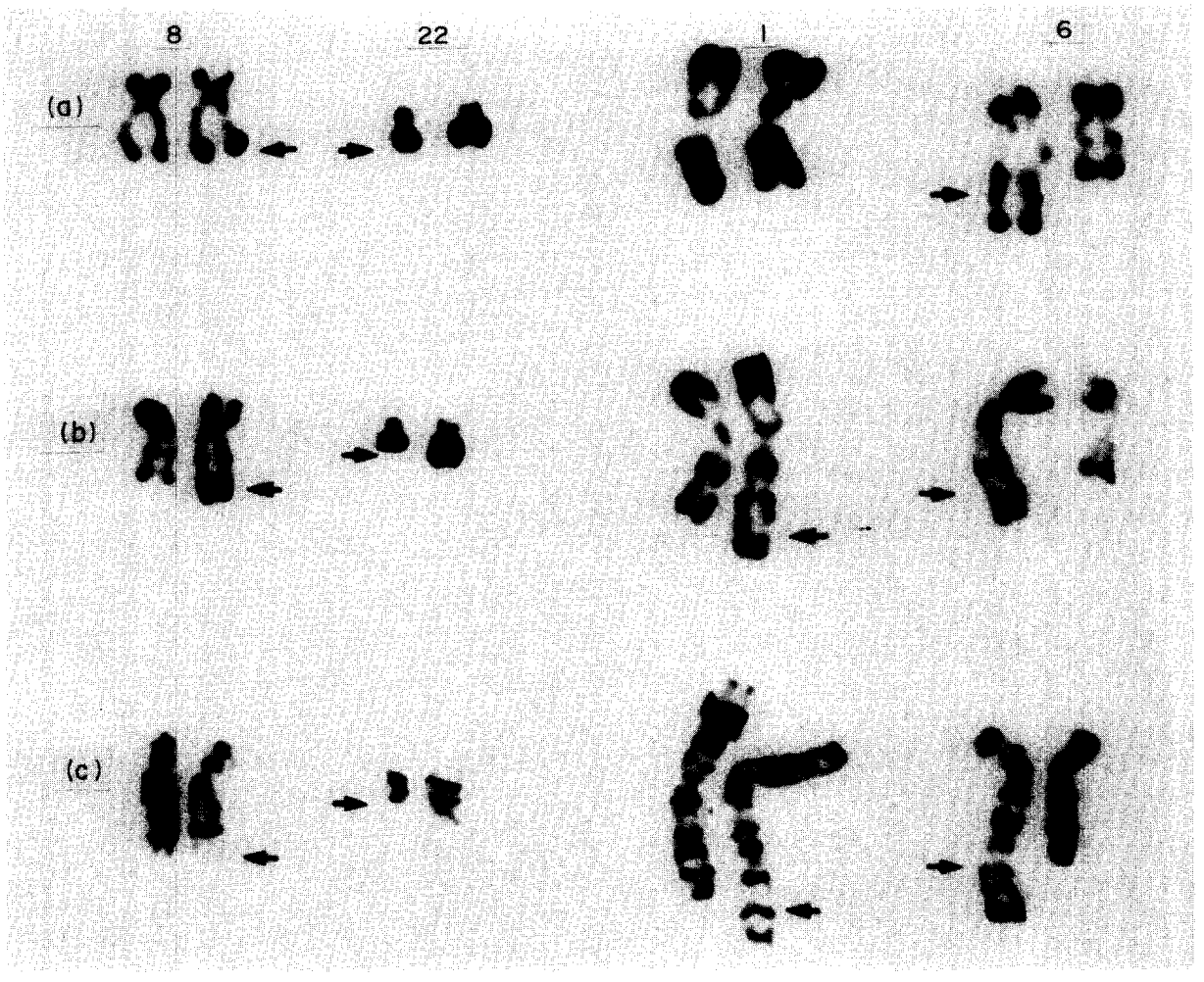

Fig. 3. *Partial karotypes, showing chromosomes* 8, 22, 1 *and* 6: (a) *RHG bands (bone marrow cell)*—t(8;22), *normal chromosome* 1 *and* 6q+; (b) *RHG bands (cell line)*—t(8;22) *chromosome* 1 *rearrangement and* 6q+; (c) *GTC bands (cell line)*—t(8;22) *chromosome* 1 *rearrangement and* 6q+.