Correspondence

Hodgkin’s disease and common variable immunodeficiency

We read with interest the paper by Chris- topoulos et al. Several points raised by the authors require comment. In the literature, other cases of Hodgkin’s disease complicating primary hypogammaglobulinemia have been reported and sometimes in relatives of patients with common variable immunodeficiency (CVID). Another case has been reported recently in a Spanish woman with CVID by Españaol et al. Among the 500 cases of cancer in primary immunodeficiency from the Immunodeficiency Cancer Registry, the international database located at the University of Minnesota, 43 cases of Hodgkin’s disease have been collected (from 1973 to 1991). Eight cases were reported in association with CVID. We recently reported two cases of Hodgkin’s disease complicating IgA and IgG subclass deficiency. There is, possibly, an increased frequency of cancer in this group of patients, as is the case with CVID. IgA deficiency and CVID may represent polar ends of a clinical spectrum, reflecting a common underlying genetic defect.

We disagree with the assertion that CVID is an important risk factor in Hodgkin’s lymphoma, mostly of the T cell type. Of the 55 cases of non-Hodgkin’s lymphoma associated with CVID from the Immunodeficiency Cancer Registry, the majority were considered to be of B cell origin on the basis of histological classification or immunophenotyping, in the cases of patients with primary hypogammaglobulinemia: a rare association. BMJ 1964;1:1156–8.


Dr. Zenone’s comments on Hodgkin’s disease in CVID are summarised on two points: the number of reported cases of Hodgkin’s disease in patients with CVID and the immunophenotype of non-Hodgkin’s lymphoma (NHL) complicating CVID.

According to the criteria of the Immunodefi-ciency Clinic at the Clinical Research Centre, Northwick Park Hospital, UK, the diagnosis of CVID requires the presence of B cells or onset of symptoms after the age of 5 and persistently low levels of more than one class of immunoglobulin. On this basis, there were no patients included in the list of cases published by Zenone et al. (detailed analysis of which is beyond the scope of this letter), either do not meet the diagnostic criteria for CVID or refer to hypogammaglobulinaemia discovered simultaneously or shortly prior to the diagnosis of Hodgkin’s disease; in the latter, the immunodeficiency could in fact have been caused by the lymphoproliferative disorder. In the Newfoundland family reported in reference 7 there were no patients with CVID who developed Hodgkin’s disease. The report by Filipovich and Shapiro (reference 9) giving the updated number of Hodgkin’s disease entries in the Minnesota Immunodeficiency Cancer Registry was not accessible by Medline when our article was written and, in any case, it does not contain any detailed case reports; the same applies to the Spanish sur-voy reported in reference 8. We acknowledge that Fesus et al. could probably be credited with the first documented case of Hodgkin’s disease in CVID in the English literature, even though the time interval between verified hypogammaglobulinaemia and onset of Hodgkin’s disease in their patient was not clear. Their patient was referred for effective treatment (with the potential of masking the clinical picture) which preceded the diagnosis of the lymphoproliferative disorder. It is nevertheless interesting to note the similarities between their patients and ours: they both presented with extensive extralymphatic disease and showed a similar spectrum of severe, chemotherapy related complications, including possible reactivation of herperviruses. Our patient was fortunate to receive effective treatment and is today well, on monthly immunoglobulin infusions, two years after completion of chemotherapy. Detailed re-porting of more of these cases would help to establish patterns of Hodgkin’s disease complicating CVID, resulting in earlier diagnosis and more effective treatment. In this context, we welcome the publication by Zenone et al. of two cases of Hodgkin’s disease occurring in a similar immunodeficiency setting.

Regarding the immunophenotype of NHL complicating CVID, nowhere in our report is stated that the majority of these lymphomas are of T cell lineage. In the recent survey by Hermszewski et al. in the United Kingdom, NHLs were found in 240 British patients with CVID seen over a period of 20 years, the largest single centre series reported so far. These authors state that “to date, all the lymphomas have been undifferentiated or of T cell origin.” Given the fact that less than 20% of NHL in the general population are of T cell lineage, our statement that in CVID there is “an apparently high frequency of undifferen-tiated and T cell tumours” is justified.


Frequency of coincident iron deficiency and β-thalassaemia trait

We agree with interest the letter by Hinchliffe et al. describing coincident iron deficiency and β-thalassaemia trait. β-thalassaemia is the commonest haemoglobinopathy in India. We investigated 463 patients heterozygous for β-thalassaemia trait, 88 (19%) of whom were children. Of the children, 126 (27.2%) had iron deficiency, 33 (26.2%) of whom were of 195 iron deficient subjects without β-thalassaemia trait, 116 (59.5%) were children. Of these, 75.9% were under five years of age. Seventy two per cent of patients with β-thalassaemia trait but without iron deficiency were anaemic compared with 90.4% of those with β-thalassaemia trait and coinci-dent iron deficiency. This difference was highly significant (p < 0.001). The mean (SD) haemoglobin concentration was significantly lower in the (10.7 ± 1.5 g/dl) than in the former patients (11.6 ± 1.6 g/dl), as were the mean cell haemoglobin and the mean corpuscular volume (p < 0.0001).

Mean (SD) HbA2 was 5.11 (0.8%) in patients with β-thalassaemia trait and iron deficiency and 5.19 (0.73%) in those without (NS). Mean (SD) HbA2/cell was 1.002 (0.207) pg in the former and 1.069 (0.248) pg in the latter. This difference was signifi-cant (p < 0.05).

We agree with Hinchliffe et al. that iron deficiency occurs with a high frequency in children under five years of age and that any advantage in iron supply conferred by β-thalassaemia trait does not protect against iron deficiency in either adults or children. In our study, HbA2 concentrations were in-creased in all patients, irrespective of their iron status, and did not preclude the detection of the heterozygote state.

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