Development of Polycythaemia rubra vera following Treatment for Centroblastic Lymphoma

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A 74-year-old woman developed polycythaemia rubra vera (PRV) with deletion of the long arm of chromosome 20 (20q-) 11 years after successful treatment of high grade non-Hodgkin’s lymphoma (NHL). The 20q- abnormality is a common finding in PRV but has also been described in lymphomas. To our knowledge this is the first reported case of PRV following treatment of NHL.

A 62-year-old woman presented with weight loss and left inguinal lymphadenopathy in 1982. A lymph node biopsy showed diffuse centroblastic NHL. Other investigations included a full blood count (Hb 11.3 × 10⁹/1, PCV 0.37, WBC 6.2 × 10⁹/1, platelets 454 × 10⁹/1), a normal bone marrow aspirate and trephine and a normal abdominal ultrasound. She received 7 courses of combination chemotherapy (cyclophosphamide, Adriamycin, vincristine, prednisolone and methotrexate) and has since remained in remission.

By 1994 her Hb had risen to 17.1 g/dl with PCV 0.53. Further investigation showed a raised leucocyte alkaline phosphatase score, a raised red cell mass, a raised serum B₂⁺ and normal arterial oxygen saturation. Bone marrow aspiration and biopsy showed a hypercellular marrow with increased megakaryocytes and increased erythropoiesis. Cytogenetic analysis showed 46XX, del(20)(q11) [12], 46XX [8].

Although PRV has not been reported after treatment of NHL, the development of both lymphoproliferative and other myeloproliferative disorders in patients with PRV is well recognised. The transformation of PRV to acute lymphoblastic leukaemia (ALL) is described in five separate reports which were reviewed by Neilson et al. [1]. Chronic lymphocytic leukaemia has developed in patients with pre-existing PRV and has presented simultaneously [2, 3]. The development of NHL in a case of PRV is the subject of a single report [2]. Myelodysplastic syndromes (MDS), acute myeloid leukaemia (AML) and lymphomas have all been described following therapy of lymphomas [4]. Chromosomal abnormalities are usual in secondary MDS and AML, occurring in up to 93% of cases, and 20q- is a recognised, though rare, finding in both MDS and AML. A recent report has shown that the 20q- abnormality can occur simultaneously in both myeloid and lymphoid cells in MDS [5]. In untreated PRV an abnormal karyotype is found in approximately 14% of cases, the commonest defect being 20q-.
The 20q- abnormality has also been described in NHL [6]. In one case of lymphoblastic transformation of PRV cytogenetic analysis of the bone marrow demonstrated the presence of two clones, one of which had an interstitial deletion of the long arm of chromosome 20q- as the only abnormality [7]. PRV following treatment for a haematological malignancy has only been described on one previous occasion: 6 years after treatment for ALL in a 10-year-old [8]. No cytogenetic data was given in this case.

Several cell proliferation-associated genes have been mapped to the deleted part of 20q- and work is on-going to establish the likely effects of these deletions. Candidate tumour suppressor genes include SRC and HCK (both non-receptor tyrosine kinases), TOP1 (topoisomerase I) and PCL1 (phospholipase Cγ) [9].

The nature of the relationship between high grade NHL and PRV in our patient is not clear and a coincidence cannot be excluded. However, as 20q- may occur in both lymphoid and myeloid disorders, and in both cell types in the same patient, it is possible that both malignancies in this case may have evolved from the same pluripotent clone. We await advances in in situ hybridisation techniques that will enable histological sections of the lymphoma to be examined for 20q- abnormality. Another possible explanation would be that PRV developed as a consequence of therapy for the NHL. This seems unlikely as, given the increasing numbers of patients surviving long term after chemotherapy for malignant disease, there has only been one such case reported previously [8]. We would encourage others to report any similar cases.

References


