Chronic neutrophilic leukaemia: 14 new cases of an uncommon myeloproliferative disease

J Böhm, H E Schaefer

Background: Chronic neutrophilic leukaemia (CNL) is a rare BCR/ABL negative myeloproliferative disorder characterised by persistent neutrophilia and splenomegaly. Most patients with CNL have a poor prognosis, with a mean survival time of 21 months. The diagnosis of CNL was established on morphological findings and on clinical and laboratory data. All the patients showed chronic neutrophilia, and most of them had splenomegaly. Clinically, in all the cases an underlying leukaemoid reaction had been ruled out, and a myeloproliferative disorder (mostly: “CML?”) was suspected. Morphologically, the bone marrow was strongly hypercellular because of the expansion of neutrophilic granulopoiesis, which was only slightly left shifted and produced mature neutrophils. Both erythropoiesis and megakaryocytes were normocellular and without cytological abnormalities. The iron load of the phagocytic reticulum cells and the reticulin fibre network was normal. In the blood there was moderate leucocytosis (mean white blood cell count, 45.5 × 10⁹/litre), including up to 95% mature neutrophils and band forms, but often also up to 20% myelocytes. In most of the cases the neutrophil alkaline phosphatase (NAP) score was greatly increased, and mild anaemia and thrombocytopenia were present. In no case was plasma cell dyscrasia found. On investigation of fresh blood samples of the patients taken at the time of diagnosis, no BCR/ABL translocation was detected using standard methods, including fluorescence in situ hybridisation. In the course of the disease, 10 of the patients died, with a mean survival time of 14.7 months. Cerebral haemorrhage (in six cases) was the most important cause of death. Two patients died of generalised haemorrhage seen in patients with CNL may be the result of plasma cell dyscrasia. The term “true” CNL recently introduced by Reilly1 highlights the need for more experience with further CNL cases to improve the diagnostic criteria. Therefore, we present our findings in a large group of 14 new cases of CNL, and discuss clinicopathological aspects of the disease.

REPORT OF THE CASES

In our institute, approximately 10 000 bone marrow biopsies are investigated every year, in many cases together with bone marrow and blood smears. Therefore, from the beginning of computed records in 1989, our archives have included probes of approximately 120 000 haematological patients. Among these records, we found 14 cases of CNL (comparative figure for chronic myeloid leukaemia (CML), 4597 cases). This “Freiburg collective” of patients with CNL consisted of eight women and six men, 10 of whom died (table 1). The mean age of the patients at diagnosis was 64.7 years (range, 37 to 81). The diagnosis of CNL was established on morphological findings and on clinical and laboratory data. All the patients with rare exceptions,4 CNL is a disease of older adults (fig 1). At the time of diagnosis, 88% of the patients with CNL in the literature were older than 50 years. The sex distribution in CNL is nearly equal. There is doubt about whether all of the CNL cases in the literature represent true CNL. Some authors1,2,3 have suggested

Abbreviations: CML, chronic myeloid leukaemia; CNL, chronic neutrophilic leukaemia; NAP, neutrophil alkaline phosphatase
that those cases of CNL that occurred in association with plasma cell dyscrasias like myeloma were in fact neutrophilic reactions. Moreover, it was suggested that cases of CNL showing dysplastic features would be better classified as a myelodysplastic entity. Thus, reviewing the data of all CNL cases in the literature, Reilly defined a group of 33 cases of true CNL, including one unpublished case of his own. This group of 33 selected patients with CNL also showed a high mean age (62.5 years) and short survival times (mean survival, 30 months), but had a 2 : 1 male to female ratio. The term true CNL used by Reilly reveals the need for an even more precise definition of CNL as an entity. Thus, the diagnostic criteria of CNL should be applied in a strict manner, especially for the conditions mentioned above.

“...To date, because of the rarity of the disease, no therapeutic standard has been determined in chronic neutrophilic leukaemia”
agents, such as hydroxyurea, may temporarily control leucocytosis and splenomegaly, and the use of interferon α may induce long standing clinical remission. So far, allogeneic bone marrow transplantation represents the only treatment modality with curative potential.

We conclude that it is important to recognise CNL as a rare, but distinct, disease entity different from CML, and in particular to distinguish CNL from leukaemoid reactions, because patients with CNL generally have a poor prognosis. To gain a better understanding of the nature of true CNL the reporting of new cases must be encouraged.

Take home messages

- Chronic neutrophilic leukaemia (CNL) is a rare myeloproliferative disease, mainly found in elderly patients
- This disease has a mostly fatal outcome—three quarters of our patients died within two years of diagnosis, mainly as a result of severe cerebral haemorrhage
- Two younger patients were successfully treated with allogeneic bone marrow transplantation or interferon, which resulted in haematological remission for years
- Thus, it is important to recognise CNL and to develop appropriate therapeutic strategies for affected patients

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