To the Editor:

Chronic granulocytic leukemia (CGL) that develops during the course of chronic lymphocytic leukemia (CLL) has been reported by Whang-Peng et al. in two patients.1 The clinical and hematologic criteria for CGL were confirmed by finding the Ph1 chromosome in bone marrow cells.

We have, however, observed the patient with CLL who did not develop clinical and hematologic features of CGL, although we identified a Ph1 chromosome, i.e., 22 Gq−, in her bone marrow cells. The patient was a 70-yr-old woman with CLL of 10-yr duration. The patient was treated with chlorambucil 0.1 mg/kg body weight (b.w.) and did well. The deterioration occurred after smallpox vaccination in 1972 when the patient was referred to our hematologic service. The hematologic findings were indicative of advanced CLL. The bone marrow of the patient was hypercellular, almost completely replaced by matured lymphocytes and with a scatter proportion of the myeloid series.

Routine cytogenetic examination of the bone marrow using a direct technique revealed two clones: 22 cells had a normal 46,XX chromosome complement, while nine cells had 47,XX, +C, Gq−, Ph1-like +. Proteolytic enzyme technique for chromosome mapping2 showed that the Ph1-like abnormality originated from 22 pairs of chromosomes (Fig. 1). For 2 yr. the patient was treated with chlorambucil 0.1 mg/kg b.w. and corticosteroids 0.5 mg/kg b.w. and blood transfusion. In 1974 the patient was readmitted to the hospital because of rapid deterioration of the disease. The clinical and hematologic features were at that time corroborative with the final stage of CLL. A cytogenetic examination showed again the existence of 47,XX,+C,

![Fig. 1. Karyotype of a bone marrow cell with 47 chromosomes. Chromosomes of G-group are presented both classically and marked by bands.](image)

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22q−,Ph1+ clone in the bone marrow without additional clonal evolution. Chromosomal analysis from peripheral blood culture showed a normal complement. All granulocytes in peripheral blood smears were alkaline phosphatase positive. The patient was not responsive to therapy and expired. Autopsy was not performed.

The significance of the presence of the clone with the Ph1 chromosome in the bone marrow of our patient is unknown. One may postulate the existence of the silent CGL which would have been evolved adventitiously in overt CGL, as was reported by Whang-Peng et al.1

To the Editor:

The case of Drs. Rolović and Ćirić of a patient with CLL and Ph1 chromosome (30% of metaphases) in the marrow is reminiscent of the patient described by Propp et al. (1972). They described a roentgenologist with acute lymphocytic leukemia who had a high percentage of Ph1 chromosome in his marrow cells (49%-64%). This patient also expired before any stigmata of CML had developed. They suggested that a lymphocytic stem cell affected by the chromosomal change eventuated in a clone of leukemic cells. Another possibility they raised was that repeated exposure to irradiation caused chromosome damage and the occurrence of the Ph1 anomaly in lymphocytic leukemia. In our two patients, no cytogenetic studies were performed before the development of clinical or morphologic CML. Both patients were noted to have the Ph1 chromosome after 2 yr of CLL.

The Ph1 chromosome is thought to be a unique chromosomal abnormality found only in patients with CML, although a few cases of the Ph1 chromosome have been reported in other hematopoietic disorders.

Although many environmental and iatrogenic mechanisms may be involved in the development of the Ph1 in CLL, we believe that it represents another example of the high incidence of second malignancies observed in CLL. The case described in the accompanying letter apparently had CLL in the bone marrow and lymph nodes and no evidence of CML (other than chromosomal). It is unfortunate that a postmortem examination was not performed on this patient, since in one of our patients the spleen contained granulocytic hyperplasia (CML) and little evidence of lymphocytic leukemia, while the liver biopsy demonstrated no evidence of CML but infiltrates consistent with CLL.

It is not known how long it takes to develop clinical CML after the discovery of the Ph1 chromosome. We believe that cytogenetic studies should be performed on any patient with neoplastic disease in an attempt to detect the presence of other malignancies either related to the primary neoplasm or to chemo- or radiotherapy of the disease.

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myeloma nephropathy, oliguria, and heavy
proteinuria. In one case, a 39-yr-old woman
with a double, IgA-IgG paraproteinemia, the
last urine specimen before total shut-down
contained peculiar, very large, foamy protein-
containing cells, (Figs. 1, 2), which are prob-
ably to be identified with atypical myeloma
cells, although the possibility exists, that they
may also be renal tubular cells with engulfed
protein.

Immunofluorescent tubular casts have been
already found in renal tissue,2,3 but not in urine
sediments. Pringle et al.\(^1\) have found them in one case, and they stained them both anti-light chain antibodies. In one of our cases the large tubular casts reacted only with the paraprotein antibody ("monoclonal casts," Figs. 3, 4).


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Fig. 4. (Right). Same type of cast from same patient stained with anti-IgG tetramethylrhodamine isothiocyanate (TRITC). Cast did not react with another antisera. Fresh preparation examined under incident illumination with a peak in the 540 \(\mu\)m region and appropriate filter combinations.