Chloramphenicol-Induced Aplastic Anemia Terminating with Acute Nonlymphocytic Leukemia

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Therapy-related acute nonlymphocytic leukemias (ANLL) are characterized by a high number of preleukemic cytopenias [1, 8]. In contrast chloramphenicol (CAP)-induced bone marrow aplasia rarely constitutes a preleukemic state evolving into acute leukemia. Since Brauer and Dameshek [2] described the appearance of ANLL following aplastic anemia after CAP therapy in 1967, a small number of similar cases have been published [3-7, 10], indicating a low incidence of this complication. We report an additional case, in which a relation of CAP to secondary leukemia must be taken into consideration.

In 1968, a 28-year-old man received CAP (cumulative dose 31 g) for pneumonia. In the last part of this period, hemoglobin dropped to 6.5 g/dl. When CAP was discontinued, the hematological values returned to normal. During the next years, no laboratory studies were performed. In 1973, he was admitted to a hospital because of diffuse hemorrhages. Severe hypoplastic anemia was observed. He underwent splenectomy without effect. The patient had since been pancytopenic and in need of blood transfusions and supportive antibiotic therapy. In 1979, anemia and thrombocytopenia aggravated. The white-cell count increased to 100,000/µl. Bone marrow and blood smears were consistent with acute myelo-monocytic leukemia (fig. la, b). In blood smears, some nucleated red cells were observed (fig. lc, d). Leukemic cells showed nuclear and cytoplasmic vacuolization. The patient died of profuse bleeding. At autopsy, replacement of hematopoietic precursors by leukemic cells staining for naphthol ASD chloracetate esterase (fig. le) and alpha-naphthyl acetate esterase (fig. lf) were demonstrated. Stainable iron was markedly increased in bone marrow and liver. Leukemic infiltrates were demonstrated in liver, lung, heart and testicle.

CAP is known to produce two different types of marrow toxicity, a brief erythroid suppression and an irreversible aplasia [9, 12], occurring in most cases several months after withdrawal of the drug [4, 11]. The question arises whether the pancytopenia observed in our patient in 1973 was induced by CAP. However, the exact time interval to development of aplastic anemia is not available and may have been much shorter than 5 years. Because no other toxic or hypersensitivity-related causes of aplastic anemia could be disclosed, CAP treatment may be implicated as a causative factor in marrow damage. The sequence of pancytopenia followed by leukemia after a period of many years has been described in secondary leu-
Fig. 1. a-d Peripheral blood smears. May-Grünwald-Giemsa. X 750. e, f Postmortem bone marrow imprints. e Naphthol ASD chloracetate esterase. X 300. f Alpha-naphthyl acetate esterase. X 1,000.

Our observation suggests that CAP may induce in some patients dose-related reversible marrow depression as well as irreversible aplasia progressing to overt leukemia.

References


