6. Radiolabeled Antibodies in Hodgkin’s Disease

Stanley E. Order

The theoretical concept of a restrictive cytotoxic radiolabeled antibody administered cyclically for the treatment of malignancy has now become a clinical reality both with polyclonal and monoclonal antibodies [1–3]. Due to their relative radiosensitivity compared to other solid tumors, lymphomas (i.e., Hodgkin’s disease or others) make ideal tumors for clinical investigation of radiolabeled antibodies and for monitoring investigative clinical progress [4]. This chapter will summarize to date both laboratory and clinical data pertinent to the development and clinical use of radiolabeled antibodies in the treatment of Hodgkin’s disease.

Ferritin as a tumor antigen

The finding that ferritin is a tumor-associated protein in Hodgkin’s disease led to investigation of its cellular source and relevance to the disorder [5]. Assaying the least dense layers of bovine serum albumin gradients in cellular extracts from the tumor, our laboratory demonstrated that the lymphocytes contained ferritin both within the cell and on the cell surface [6]. Sarcione found that the T-lymphocytes from Hodgkin’s patients synthesized and secreted ferritin preferentially compared to normal lymphocytes, and in the same lymphocytes puramycin inhibited ferritin synthesis [7]. In contrast, protein synthesis was greater in normal lymphocytes than in Hodgkin’s lymphocytes, even though ferritin synthesis was greater in the Hodgkin’s lymphocytes [7]. Pretlow noted that T-lymphocytes in Hodgkin’s spleens showed surface ferritin and would form rosettes with Hodgkin’s cells [8]. More recently, Strauchen published a new observation that pre-AIDS patients with Hodgkin’s disease had T-suppressor cell dominance and a T-cell helper deficit, unlike other Hodgkin’s patients with both T-suppressor and T-helper cells infiltrates in the tumor [9]. Presently we are evaluating these observations in our study of ferritin distribution in Hodgkin’s disease.

In addition, in patients with acquired immunodeficiency and in Hodgkin’s patients after successful remission, the inexplicable observation remains that serum ferritin levels are elevated [10]. We observed increased ferritin content
in circulating lymphocytes, as well, in patients with active Hodgkin’s disease [11]. These initial limited observations have not been pursued further in our laboratory.

As an antigenic target, ferritin in Hodgkin’s disease is present on both the lymphocyte surface and, importantly, in a halo-like distribution surrounding the tumor in the stroma. The stromal ferritin provides an excellent zone of high concentration antigen for antibody targeting (figure 1) [12].

The isotype of ferritin in Hodgkin’s disease is similar to splenic ferritin [13]. One may ask, then, why the radiolabeled I-131 antiferritin does not target normal tissues containing ferritin such as muscle, bone marrow, heart, and spleen?

Biologic Window

There are no animal models for Hodgkin’s disease. The fundamental problem concerning the preferential targeting of ferritin tumors, as contrasted with normal tissue, has been explored in rodent hepatoma and in clinical hepat-

Figure 1. Gallium scan with positive Hodgkin’s tumor infiltrates (arrows) due to increased transferrin and ferritin activity in the tumors.