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Very Late Relapse in Hodgkin's Disease

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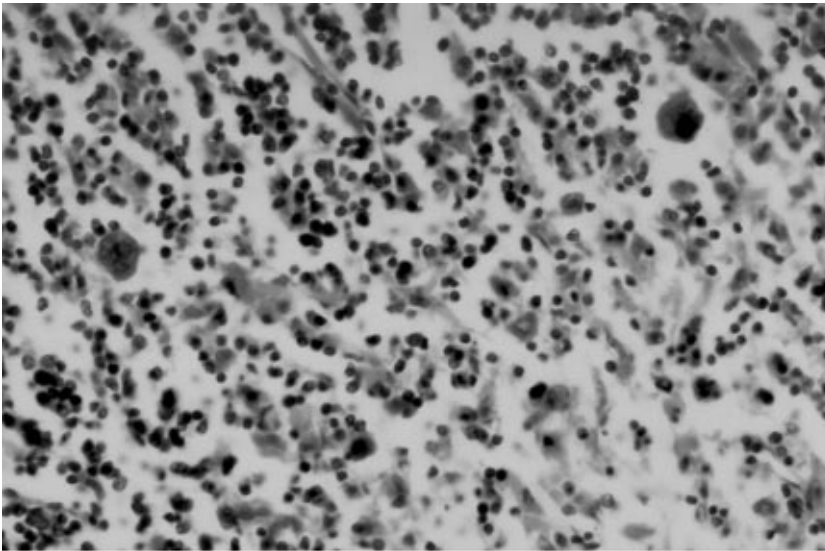
The use of modern therapeutic modalities in the treatment of Hodgkin's disease (HD) has led to a high rate of long-term survivors in complete remission (CR) (1–8). The great majority of relapses after treatment for early-stage HD are observed within 4 to 5 years after completion (2). The occurrence of late relapse is significantly related to stage I disease and nodular sclerosis histologic subtype (9). The occurrence of late relapse is extremely rare after 25 years of CR (4,6). Here we report a case of HD relapsing 29 years after the initial radiotherapy. The first diagnosis was made in 1969 and the patient was observed until April 1997 at the Department of Hematology–Oncology at the University of Ankara, İbn-i Sina Hospital.

A 50 year-old male patient was admitted to the hospital. He complained of night sweating for one month. When he was 20 years old, he was presented with a left cervical lymphadenopathy in 1969. He had no other symptoms, and other physical findings were unremarkable at that time. The histopathologic diagnosis of the biopsy specimen taken from the enlarged lymph node was lymphocyte predominant (LP) type HD. Histopathologic examination showed the lymph node architecture to be effaced. Numerous mature lymphocytes, scattered L&H cells and atypical mitosis, rarely mummified cells and Hodgkin cells were observed in the lymph node (Fig. 1a). The clinical stage was IA, and the patient received regional irradiation and achieved CR with this radiotherapy. He remained in CR until April, 1997.

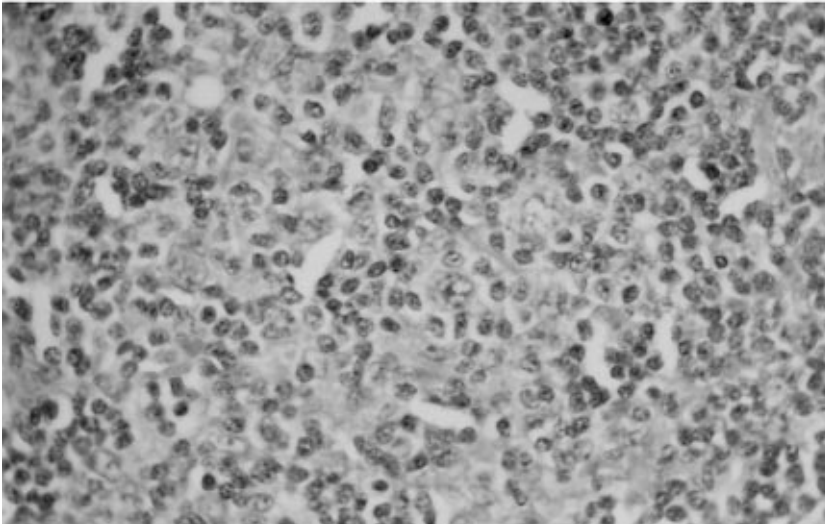
During this recent admission, a physical examination revealed hepatosplenomegaly. The liver and spleen were palpable below the costal margin. Pulmonary x-ray radiography showed mediastinal enlargement. A CAT scan examination of the abdomen and thorax revealed an enlarged spleen and liver, and periaortic, subcarinal, paraesophageal and periportal lymphadenopathies. The hematocrit was 37 percent, and other blood parameters, urine and bone marrow biopsy were normal. At this time, mediastinoscopic biopsy was done and the histopathologic diagnosis was LP type HD after light microscopic (Fig. 1b) and immunohistochemical examination. In immunophenotyping examination of both biopsy specimens of neoplastic cells (L&H cells and Hodgkin cells), a positive reactivity was found for CD20, CD45 and CD30 (Fig. 2), but a negative reactivity for CD15 and CD45RO. With a systemic chemotherapy (MOPP) regimen, the patient achieved a second CR.

Patients who are presented with early-stage HD are likely to achieve a complete remission, and can be cured with current modern therapies (2). Late recurrences of HD 10 years after the achievement of CR are very uncommon and few cases have been reported in the literature (1, 3–6, 8). Our patient relapsed 29 years after the achievement of CR.

The early stage disease and histology of nodular sclerosis at initial diagnosis are reported to be significantly correlated with the risk of late relapse (9). Three other factors in addition to initial treatment are



a)



b)

Figure 1. (a) The first biopsy was lymphocyte predominant HD diagnosed in 1969 (H.E.X100). (b) The second mediastinal biopsy also diagnosed as lymphocyte predominant HD diagnosed in 1997 (H.E.X100).

correlated with an increased risk of late relapse: male gender, presence of B symptoms, and mediastinal involvement (1). In 1969, our patient apparently had early stage disease with no B symptoms, male gender and the LP subtype.

The administration of radiotherapy may have favored the local control of the disease more successfully. Most patients with stage I and II disease have late relapse primarily in unirradiated nodes, whereas patients with stage III and IV disease have late relapse in previously irradiated nodes or extranodally (9). The tendency of patients treated with chemotherapy alone to relapse at the sites of previous involvement has been described by

Young et al. (7). The patient reported by Hung et al. was treated with initial regional radiotherapy and relapsed from a different site, as did our case (6). Although the presentations of both our patient and theirs were early stage (IA) LP type HD. Their patient relapsed with lymphocyte depletion subtype, but our patient relapsed with LP type HD, which was confirmed histopathologically and immunohistochemically.

Whether these very late recurrences in patients treated for HD represent a reappearance of the primary disease or a neoplasm has not yet been established (1). The clinical characteristics and the data on sporadic cases of very late relapses in the literature are shown in Table

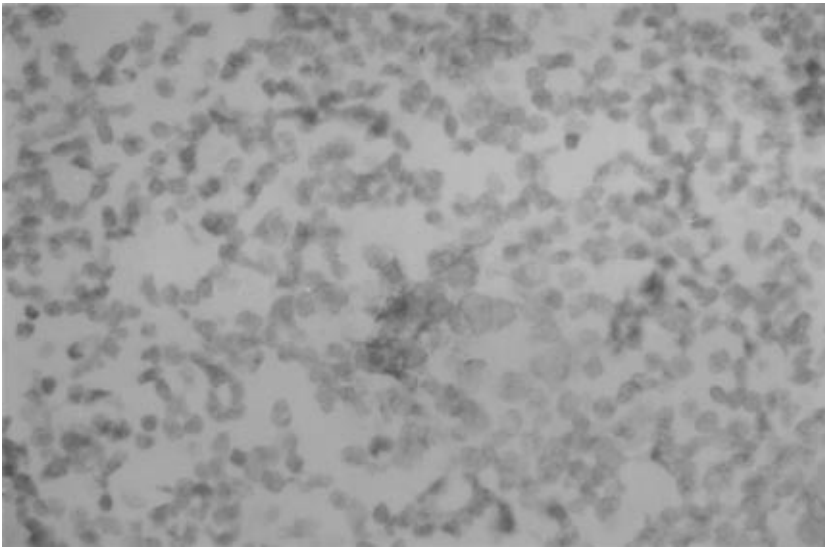


Figure 2. CD30 positivity on atypical Hodgkin's cells which are making groups. X100 (ABC peroxidase).

1. Just as in our case, in the majority of patients with very late relapses after 25 years, the secondary histologic subtype was the same as the primary subtype (Table 1). This recurrence of the same histologic type may support the hypothesis of reappearance of the primary disease. In contrast, Lee and Spittle's patient had an early stage (IA) LP type HD relapsed with a different subtype (4). However, LP type HD may be associated with late relapse after radiotherapy. Five cases reported by Anselmo et al. were previously treated with combination

chemotherapies, and three of them relapsed at 120 months, one at 170 months and one at 191 months. All achieved a second CR with rescue therapy and none have relapsed since (1). Our patient was treated with combined chemotherapy (MOPP) and achieved second CR, and is still disease free at present.

In conclusion, extremely few reports demonstrate the necessity of prolonged follow-up of patients with HD, and early detection of recurrence may improve response to treatment for HD.

Reported by	Stage	Histology	Recurrent-histology	DFI-years
Green et al ⁸	IA	MC	MC	22
Hung et al ⁶	IA	LD	LD	29
Lee, Spittle ⁴	IA	LP	LBCL	32
Our case	IA	LP	LP	29

Table 1. Very late relapsing patient characteristics with HD.

MC= Mixed cellularity LD= Lymphocyte depletion; LP= Lymphocyte predominance; LBCL= Low grade B-cell lymphoma, DFI= Disease free interval.

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