

Adult T-cell Leukemia-lymphoma (ATLL) Associated with Acute Pancreatitis due to Hypercalcemia

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Summary: We have investigated the incidence of acute pancreatitis in adult T-cell leukemia-lymphoma (ATLL), and in the other diseases. ATLL, and acute pancreatitis cases were collected using the annual report of pathological autopsy cases in Japan in 1982-1989. Of the 317,325 autopsy cases in these years, 632 were ATLL; the numbers of the acute pancreatitis cases of them were 1,833 (0.58%) and 25 (4.0%), respectively. The odds ratio of the 2×2 table composed from these figures is 7.17 and Pearson's Chi-square statistics with one degree of freedom is 126, which is highly significant. Therefore, it was suggested that a correlation exists between acute pancreatitis and hypercalcemia in patients with ATLL. The reasons for the correlation between hypercalcemia and acute pancreatitis in patients with ATLL have not been clearly elucidated. A possible explanation may be that all the hypercalcemic patients exhibited high levels of nephrogenous cyclic adenosine monophosphate that stimulated pancreatic secretion in the extralobular ductal system of the pancreas, resulting in acute pancreatitis due to occlusion of the pancreatic duct.

Introduction

Human T-cell lymphotropic virus Type 1 (HTLV-1) infection causes adult T-cell leukemia-lymphoma (ATLL),^{1,2)} tropical spastic paraparesis,⁴⁾ and myelopathy.^{1,6)} The clinical and hematological characteristics of this disease are following: (i) onset in adulthood; (ii) appearance of pleomorphic leukemic cells that have markedly deformed nuclei and T-cell surface markers; (iii) acute and chronic leukemia with rapidly progressive terminal course; (iv) high incidence of skin involvement such as erythroderma and nodules formation due to the infiltration of neoplastic cells; (v) frequent accompaniment by lymphadenopathy, hepatosplenomegaly, hypercalcemia, and severe infections; (vi) absence of mediastinal tumor; (vii) some familial disposition; and (viii) exclusively limited location of patients' birth places, clustered in southwestern Japan and in the Caribbean region.^{3,12)} Since our university is in southwest Japan, ATLL cases frequently come to autopsy.

We reported a case of ATLL associated with acute pancreatitis due to hypercalcemia,¹⁷⁾ and we encountered three other cases of the same complication. On the other

hand, recently Dr Dazai and coworkers published such two cases.¹⁾ We investigated the incidence of acute pancreatitis in ATLL, and in the other diseases. This investigation was undertaken as an extension of our previous works,¹⁷⁻¹⁹⁾ and the summary of this paper was published in July 15, 1991 issue of the Lancet.¹⁹⁾

Materials and Methods

ATLL, and acute pancreatitis cases were collected from the annual report of pathological autopsy cases in Japan in 1982-1989.⁶⁻¹³⁾ Statistical calculation was performed. The statistical method for this study is the following: (1) Odds ratio to assess the degree of association between ATLL and acute pancreatitis in a 2×2 contingency table.²⁰⁾ (2) Pearson chi-square test for the significance of the odds ratio in the contingency table.²⁰⁾

Results

Of the 317,325 autopsy cases in these years, 632 were ATLL; the numbers of the acute pancreatitis cases of them 1,833 (0.58%) and 25 (4.0%), respectively. The odds ratio of the 2×2 table composed from these figures is 7.17 and Pearson's chi-square statistics with one degree of freedom is 126, which is highly significant. Table 1 shows ATLL associated with acute pancreatitis cases. The male to female ratio was 16:9 in ATLL with acute pancreatitis cases. The highest incidence of ATLL associated with acute pancreatitis cases was found in the 61-70 year-old age group (Fig. 1).

Discussion

A frequent complication of ATLL has been reported to be hypercalcemia, which is one of the most difficult conditions to treat and often is the direct cause of early death for

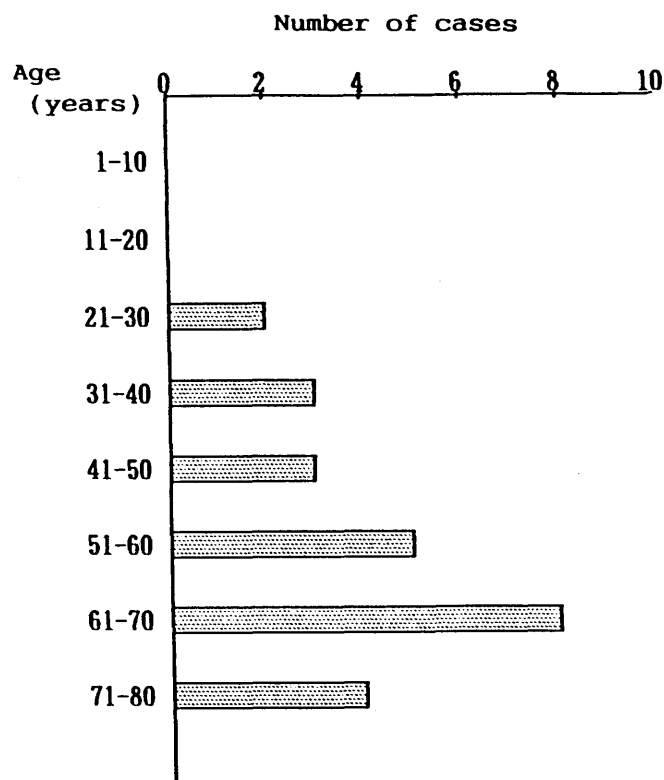
Table 1. Adult T-cell leukemia-lymphoma associated with acute pancreatitis

No.	Year/Sex	Hospital	Reference
1	63/M	Oita Med. Coll. Hospital	1983 [5, 7]
2	69/M	Koube Med. Coll. Hospital	1984 [8]
3	24/M	Kyushu Univ. Hospital	1984 [8]
4	57/M	Kyourin Med. Coll. Hospital	1985 [9]
5	71/M	Nagasaki Univ. Hospital	1985 [9]
6	71/M	Ekisaikai Maebashi Hospital	1985 [9]
7	58/F	Matsuyama Red Cross Hospital	1985 [9]
8	62/M	Nagasaki City Hospital	1985 [9]
9	59/M	Niigata Univ. Hospital	1986 [10]
10	68/F	Okayama Univ. Hospital	1986 [10]
11	28/F	Kumamoto Univ. Hospital	1986 [10]
12	64/M	Miyazaki Med. Coll. Hospital	1986 [10]
13	67/F	Asahikawa City Hospital	1986 [10]
14	77/M	Nagasaki Red Cross Hospital	1986 [10]
15	40/F	Miyazaki Med. Coll. Hospital	1987 [11]
16	50/F	Kushiro Red Cross Hospital	1987 [11]
17	39/M	Hamanomachi Hospital	1987 [11]
18	59/M	Kokura National Hospital	1987 [11]
19	73/F	Tohoku Univ. Hospital	1988 [12]
20	66/F	Akita Univ. Hospital	1988 [12]
21	55/F	Kumamoto National Hospital	1988 [12]
22	47/M	Kagoshima City Hospital	1988 [12]
23	37/M	Tohoku Univ. Hospital	1989 [13]
24	42/M	Sumitomo Hospital	1989 [13]
25	66/M	Nagasaki Red Cross Hospital	1989 [13, 17]

Med.: Medical; Coll.: College; Univ.: University

22% of ATLL patients.^{3,15} In hypercalcemic conditions, there may be a close correlation between hyperparathyroidism and occurrence of acute pancreatitis.¹⁴ Hypercalcemia is the major etiologic factor for acute pancreatitis in renal transplant recipients;² therefore, it is suggested that a correlation exists between acute pancreatitis and hypercalcemia in patients with ATLL. ATLL associated with acute pancreatitis due to hypercalcemia was first described by Hosokawa and coworkers in 1984,⁹ followed by the second report by myself and my colleagues,¹⁷ and the third by Dazai and coworkers in 1991.¹

The mechanisms of acute pancreatitis due to hypercalcemia in ATLL patients have not been clearly explained. However, the causes of acute pancreatitis due to hypercalcemia have been proposed from research of hyperparathyroidism. The most plausible theoretical speculation was proposed by Dr. Kelly that relationship between acute pancreatitis and hypercalcemia is caused through the following sequence of events: elevated serum calcium, increased pancreatic juice calcium, accelerated calcium-dependent conversion of trypsinogen to trypsin, and acute pancreatitis.¹⁴ Another possible explanation may be that all hypercalcemia in ATLL patients exhibited high level of nephrogenous cyclic adenosine monophosphate which stimulated pancreatic secretion in the extralobular ductal system of the pancreas,³ resulting in acute pancreatitis due to occlusion of pancreatic duct.²² We conclude that either or both of the above mechanisms should lead to

**Fig. 1.** Age distribution of adult T-cell leukemia-lymphoma with acute pancreatitis

acute pancreatitis under hypercalcemic conditions in ATLL.

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