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CD7 Expression in Malignant Pleural Mesothelioma

Shigeyoshi Hibi,[1,7] Yoshiko Kataoka,[2] Naohisa Fujita,[3] Hidetoshi Okabe,[4] Kazuhiro Yoshikawa,[5,6] Masao Seto,[6] Ryuzo Ueda[6] and Shinsaku Imashuku[1]

[1]Division of Pediatrics in Children's Research Hospital, [2]Department of Pediatrics, and [3]Department of Clinical Laboratory and Medicine, Kyoto Prefectural University of Medicine, Kajii-cho, Hirokoji-Kawaramachi, Kamigyo-ku, Kyoto 602, [4]Clinical Laboratory, Shiga Medical College, Tsukinowa-cho, Seta, Ohtsu 520-21, [5]Department of Urology, Aichi Medical University, Nagakute, Aichi 480-11 and [6]Laboratory of Chemotherapy, Aichi Cancer Center Research Institute, 1-1 Kanokoden, Chikusa-ku, Nagoya 464

CD7 antigen was found to be expressed on malignant mesothelioma arising from the right pleura in a 15-year-old girl not only by immunostaining using monoclonal antibodies, but also by Northern blot analysis. The level of expression in this tumor was comparable to those in T-cell lines, Jurkat and CCRF-CEM. Cytogenetic analysis of the tumor showed hypodiploidy (n=43). CD7 has been regarded as one of the hematopoietic cell markers selectively expressed on the majority of T cells and multipotential stem cells. To our knowledge, this is the first report of a non-hematopoietic tumor expressing CD7.

Key words: CD7 — CD56 — Malignant pleural mesothelioma — Soft tissue sarcoma

CD7 antigen is a 40 kDa glycoprotein expressed on the surface of most T cells and thymocytes.[1-3] Because CD7 appears very early during T cell ontogeny, it is regarded as one of the most reliable T lineage markers.[4-6] Recent studies have shown that in addition to T cells and their precursors, CD7 is also present on multipotential hematopoietic stem cells in bone marrow which are capable of differentiating into both lymphoid and myeloid cells.[7] Since CD7 expression on non-hematopoietic cells has not been reported, it is thought to be a marker specific for hematopoietic cells. Here we report the first case of non-hematopoietic malignancy (malignant pleural mesothelioma) expressing CD7, which was confirmed not only by monoclonal antibodies, but also by Northern blot analysis.

A 15-year-old girl was referred to our hospital on February 14, 1991 with right chest pain. She had no history of exposure to asbestos. Chest X-ray showed a large round shadow in the right lower lung field, and pleural fluid collection. Computed tomography revealed a tumor mass arising from the pleura with widespread intrathoracic dissemination (Fig. 1). Blood examination showed a normal complete blood count, but elevation of serum lactate dehydrogenase (LDH) 1,792 U/liter (normal <600 U/liter), CA125 83 U/ml (normal <50 U/ml), and neuron-specific enolase 20 ng/ml (normal <10.0 ng/ml). Carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), human chorionic gonadotropin (HCG), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and electrolytes were all within the normal ranges. The pleural effusion showed protein 5.1 g/dl, glucose 89 mg/dl, and LDH 3,876 U/liter. There were no pathological cells by cytology.

The biopsied tumor tissue was highly cellular and comprised monotonous fusiform cells arranged in anastomosing fasciculus. Mitoses were more than 15/10 HPF (Fig. 2A). Vascular-rich areas were included in part of the specimen. Immunohistological analysis demonstrated that tumor cells were positive for vimentin, and CD56 (Leu 19, UJ13A), but were negative for desmin, alpha-smooth muscle actin, alpha-sarcomeric actin, cytokeratin, glial fibrillary acid protein (GFAP), neurofilament, S100 protein, CD15, and CD57. Finally a diagnosis of malignant pleural mesothelioma (localized fibrous, malignant)was made.[8] During the period before the final diagnosis, hematopoietic cell surface markers were also analyzed. The tumor cells were found strongly to express CD7, which was confirmed not only by two different types of monoclonal antibodies (3A1, T55) (Fig. 2B), but also by Northern blot analysis using total RNA isolated from the tumor tissue (Fig. 3). None of the other hemopoietic cell markers, such as CD2, CD3, CD4, CD5, CD8, CD10, CD19, CD20, HLA-DR, and CD45, was positive.

Cytogenetic analysis of the tumor showed 43,X,del(X)-(q11;q28), -1, -2, -3, -6, -10, -14, -19, -21, +der-(2)t(2;?)(p13;?), +der(6)t(6;?)(q13;?),del(9)(p22;p24),

[7] To whom correspondence should be addressed.

+der (19) t (?; 19;?) (?; p 13 q 13;?), + mar 1 (A-sized), +mar2(G-sized),(variable), indicating that hypodiploidy, reported a common chromosomal abnormality for malignant mesothelioma, was present in this case.[9, 10]

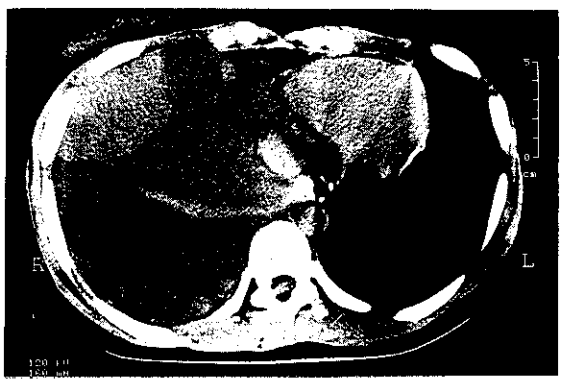

Fig. 1. Chest computed tomography of the present case on admission. Tumor mass arose from the right pleura with pleural fluid collection.

The patient was treated with 3 cycles of adriamycin (ADR) (45 mg/m^2, day 1)/cyclophosphamide (CPM, 50 mg/kg, day 2)/vincristine (0.05 mg/kg, day 1), 2 cycles of ADR/CDDP (30 mg/m^2, day 1–3)/VP-16 (150 mg/m^2, day 1–3), and finally 5 cycles of CPM (600 mg/m^2, day 1)/ADR/CDDP. In response to these chemotherapies, the tumor mass decreased in size and almost disappeared in ten months.

The function of CD7, which is a member of the immunoglobulin superfamily,[2, 11, 12] is still unknown though some investigators suggest that it is a kind of IgM receptor.[13] In the past, CD7 was regarded as pan-T cell marker. However, recent extensive studies unambiguously demonstrated that CD7 was expressed not only on a majority of immature and mature T cells, but also on some multipotential hematopoietic stem cells which have not made a lineage commitment.[7] The present study has further demonstrated the expression of CD7 in non-hematopoietic tumor cells.

Several hypotheses can be set up to explain this observation. One is that previously CD7 was not fully examined on non-hematopoietic tissues, including malignant mesothelioma. Neuroblastoma was reported to be

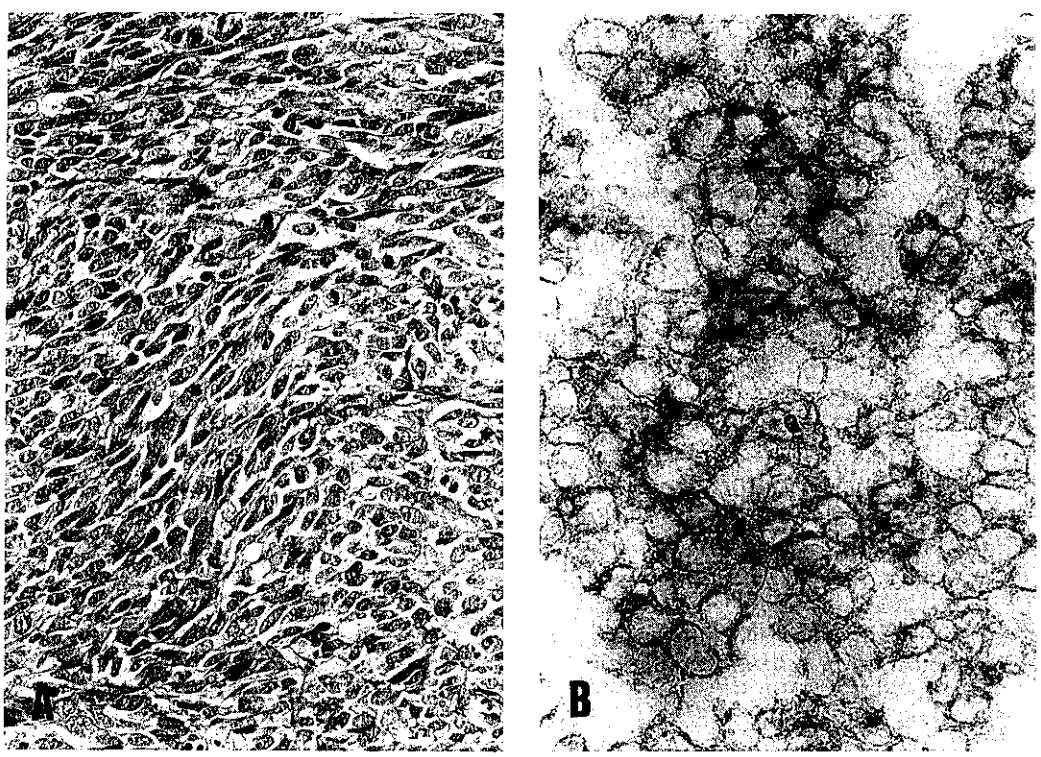

Fig. 2. (A) The biopsied tumor specimen comprised mostly fibrous tumors cells. (HE staining. Original magnification ×200). (B) CD7 was diffusely detected on tumor cells by peroxidase anti-peroxidase (PAP) methods using monoclonal antibody T55.

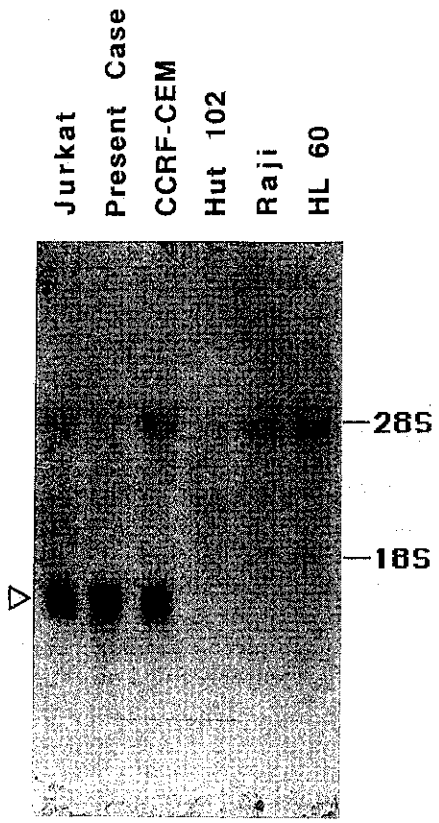

Fig. 3. CD7 gene expression detected by Northern blot analysis. Ten μg of total RNA isolated from a biopsy specimen by guanidium thiocyanate was electrophoresed in a 1% agarose-formamide gel, transferred to nylon membrane, and hybridized with random-labeled human CD7 cDNA probe.[16] A 1.3 kb band (shown by open triangle) was detected at a similar intensity in the present case to those in Jurkat and CCRF-CEM cells. Lanes: Jurkat (T cell line, CD7+); present case; CCRF-CEM (T cell line, CD7+); Hut-102 (T cell line, CD7−); Raji (Burkitt lymphoma cell line, CD7−); HL-60 (myeloid cell line, CD7−).

negative for CD7, though it expressed some B cell markers.[14] We could not find any literature in which CD7 expression was examined on any other solid tumors. CD7 might, therefore, have been detected in solid tumors, if they had been examined.

Secondly, the tumor cells in our case may have arisen from embryonic residues of T cell precursors. According to the precise studies of Haynes *et al.*,[6,7] the earliest T cell precursors during fetal development appear in the fetal yolk sac and liver. These cells were positive for CD7 as well as CD45, but did not express CD2 or CD3. These precursors then migrate into the mesenchyme throughout the upper thorax and neck area at 7–8 weeks of gestation, and thereafter into the thymus rudiment. Since CD7- and CD45-coexpressing cells during fetal life have multipotential character,[7] there is a possibility that malignant mesothelioma of the present case, which lacked CD45 expression, arose from T cell precursors left in the thoracic mesenchyme during fetal development.

Lastly, CD7 gene may have been activated during evolution of mesothelioma by gene alteration such as chromosomal translocation. Cytogenetic analysis, however, did not show any structural abnormality involving chromosome 17q25, where CD7 gene was mapped.[15] Furthermore, Northern analysis demonstrated the ordinary size of CD7 mRNA.

To our knowledge, this is the first report of a non-hematopoietic malignancy expressing CD7. It should be further elucidated whether CD7 is rather specifically expressed in malignant mesothelioma or whether it is widely expressed on other cells besides hematopoietic cells in normal as well as pathological states.

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