MEDICAL IMAGE AT A GLANCE

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A case of follicular dendritic cell sarcoma with the expression of SRY-box transcription factor 9

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Abbreviations:
FDCS: follicular dendritic cell sarcoma
SOX9: SRY-box transcription factor 9

INTRODUCTION

Follicular dendritic cell sarcoma (FDCS) is a rare neoplasm that shows similar differentiation to non-neoplastic dendritic reticulum cells, the antigen-processing cells of normal germinal centers.[1] It usually present in adults as enlargement of a single lymph node, typically involving the cervical neck nodes; however, extranodal involvement, which includes the oral cavity, tonsil, and breast, has been reported.[2,3] Approximately 30% of cases present in extranodal sites. The tumor behaves as a low-grade sarcoma, usually with local recurrence; however, metastatic disease has also been reported.

Immunohistochemical studies are essential for the diagnosis of FDCS. The neoplastic cells of FDCS retain the staining pattern of normal follicular dendritic cells (FDCs), including reactivity to the complement markers CD21 and CD23, as well as the monocyte/macrophage lineage marker CD163. However, the nuclear markers of FDCS have not been well characterized.

SRY-box transcription factor 9 (SOX9) plays a key role in the successive steps of chondrocyte differentiation and skeletal development. Mutations in the human SOX9 gene cause campomelic dysplasia, a haploinsufficiency disease with several skeletal malformations that are frequently accompanied by 46, XY sex reversal.[4] Not only for bone and testicular development, SOX9 is also essential for the development of other organs, including the lungs, pancreas, intestine, heart and nervous system. I herein demonstrate that SOX9 is a possible nuclear marker of FDCS.

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PATIENT, MATERIALS AND METHODS

Patient and lymph nodes

The patient was a Japanese male in his 70s with a hemilateral tonsillar tumor measuring approximately 40 mm in maximal length. A biopsy was performed, and the patient was diagnosed with FDCS. Mesenteric lymph nodes dissected during gastric surgery in another patient were used as normal lymph nodes.

Antibodies

Primary antibodies against the following antigens were used: SOX9 (1:1000 dilution, ab185966, Abcam, USA) and CD21 (ready-to-use, 413771, Nichirei Bioscience, Japan).

Immunohistochemistry

Immunohistochemistry was performed on formalin-fixed paraffin-embedded tissue sections at 4 °C overnight in a humid chamber after antigen retrieval at 120 °C for 20 minutes. A mixture of peroxidase-labeled goat anti-mouse and anti-rabbit IgG (Histofine Simple Stain MAX-PO; Nichirei Bioscience, Japan) was used as the secondary antibody. Finally, a Histofine DAB substrate kit (Nichirei Bioscience, Japan) was used for color detection.[5] In single immunohistochemical staining, visualized SOX9-positive and CD21-positive cells appeared brown.

For immunohistochemical double staining, the sections were heat treated at 110 °C for 3 minutes after the development of the first color. Using the peroxidase and alkaline phosphatase double-staining method, SOX9-positive and CD21-positive cells were stained brown and red, respectively. A mixture of alkaline phosphatase-labeled goat anti-mouse and anti-rabbit IgG (Histofine Simple Stain AP; Nichirei Bioscience, Tokyo, Japan) was used.[6]

This study was reviewed and approved by Ethics Committee for Clinical Research of Showa Medical University (approval number, 2025-0173). The requirement for informed consent was waived by the ethics committee of Showa Medical University. Opt-out consent was approved by the committee and made available on our website. This study was conducted in accordance with the principles of the Declaration of Helsinki (1975).

RESULTS

The expression of SOX9 in lymph nodes

Immunohistochemical single staining of the lymph nodes showed that SOX9-positive cells were sparsely distributed in the lymphoid follicle (Fig. 1, upper left panel). CD21-positive FDCs were concentric (Fig. 1, upper right panel). Immunohistochemical double staining using 3,3'-diaminobenzidine (DAB) and the first red systems identified SOX9-positive (brown) and CD21-positive (red) FDCs (Fig. 1, lower panel) and indicated that SOX9-positive cells appeared to be CD21-positive cells.

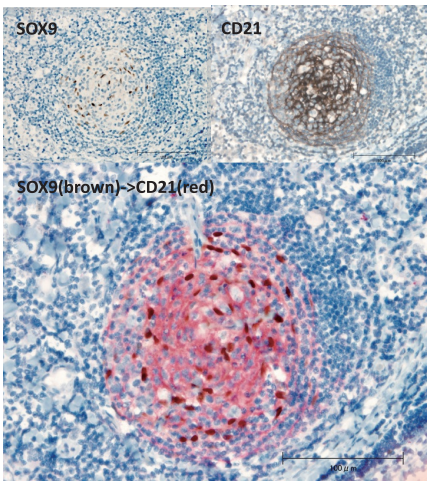

Fig. 1 The Immunohistochemical analysis of normal mesenteric lymph nodes
SRY-box transcription factor 9 (SOX9) immunohistochemistry showed that SOX9-expressed cells were observed in the lymphoid follicle (upper left panel), and follicular dendritic cells (FDCs) were positive for CD21 (upper right panel). Double immunostaining using the peroxidase and alkaline phosphatase method revealed that SOX9-positive nuclei (brown) appeared to be those of CD21-positive FDCs (red), which form a concentric meshwork within the follicle (lower panel). Scale bar: 100 μm.

The expression of SOX9 in FDCS

Figure 2 shows the case of an FDCS. Hematoxylin-eosin staining of FDCS showed that the neoplasm was composed of ovoid to spindle neoplastic cells with admixed reactive small lymphocytes scattered as single cells (upper left panel).

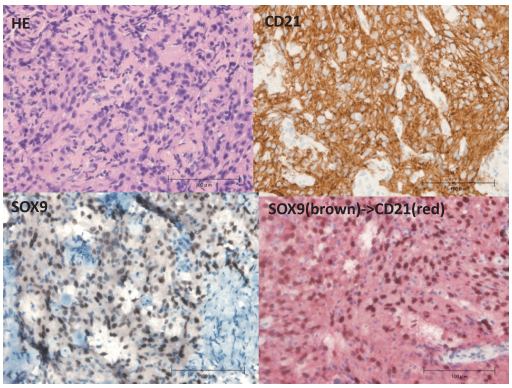

Fig. 2 Histopathological features of follicular dendritic cell sarcoma (FDCS) in the present case
Hematoxylin-eosin (HE) staining showed ovoid to spindle cell proliferation with admixed reactive small lymphocytes scattered as single cells, with neoplastic cells possessing a bland nucleus with an inconspicuous nucleolus. The cytoplasmic borders of the neoplastic cells are indistinct (upper left panel). The neoplastic cells showed strong membrane staining for CD21 (upper right panel). SRY-box transcription factor 9 (SOX9) staining revealed strong nuclear positivity in FDCS (lower left panel). Immunohistochemical double staining showed that the FDCS cells were positive for SOX9 (brown) and CD21 (red) (lower right panel). Scale bar: 100 μm.

Immunohistochemical staining revealed that the cell membrane of FDCS cells was positive for CD21 (upper right panel). The FDCS cells were also positive for CD23 and CD163 (data not shown). Immunostaining for C-X-C motif chemokine ligand 13 (CXCL13) was not performed in this case. The nuclei of FDCS cells showed a strong SOX9 expression (lower left panel). Immunohistochemical double staining revealed that the FDCS cells co-expressed SOX9 and CD21 (lower right panel).

DISCUSSION

The author previously reported the expression of SOX9 in human embryos and showed that SOX9 is expressed in the neural tube and notochord.[5] Here, I analyzed the SOX9 expression in adult human tissue using immunohistochemistry and found that SOX9-positive cells were limited in the lymph nodes and probably these cells were FDCs, a histiocyte/monocyte lineage. These findings are consistent with the notion obtained from the Human Integrated Protein Expression Database (HIPED), which revealed that SOX 9 is overexpressed in monocytes and testes. The present study included only one case because FDCS is a very rare disease. Further studies using several cases of FDCS are necessary to confirm the present findings on the expression of SOX9 in FDCS.

In conclusion, this study revealed that SOX9 is expressed in FDCS, thus providing the opportunity to use SOX9 as a new molecular marker to stain nuclei for the diagnosis of FDCS.

DISCLOSURE STATEMENT

The author declares no conflicts of interest.

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