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Research Article

Development Expression of CD3 ε Epitope in the Human Cerebellar Purkinje Cells from Fetuses, Neonates, Infants to Adults: An Immunohistochemical Study

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Abstract

Background: Soma of human cerebellar Purkinje cell in adults has been reported to be positive for CD3, which is a surface marker only present on the cell membrane of T lymphocyte that recognizes antigen. Morphological development of Purkinje cell from fetus to infant stage is remarkable. Therefore, we examined CD3-immunoreactive development process of Purkinje cells from fetus, neonate, infant, to adult stage along with the morphological development.

Methods: This retrospective study was carried out on autopsy specimens of fetuses, neonates, infants, and adults. Paraffin sections of autopsied cerebella were immunostained with polyclonal antibody against CD3 epsilon (ε) epitope.

Results: In human fetal cerebellum from 16-20 weeks, there was no positive finding for CD3 ε epitope. At the gestation age of 21-27 weeks, soma of Purkinje cell became positive for CD3 ε epitope. From 29 weeks of gestation to one year and six months after birth, the arborization areas positive for CD3 ε epitope gradually extended in the order from primary, secondary, to tertiary dendrites of Purkinje cell. From one year and six months to adulthood, Purkinje cell showed that positive finding for CD3 ε epitope was confirmed in soma as well as primary, secondary, and tertiary dendrites.

Conclusions: We show that there are new developmental changes in immunohistochemical staining pattern of CD3 ε epitope in Purkinje cells from fetus to adult stage. Chronological changes in expression of CD3 ε epitope in Purkinje cells that we discovered are different from previously-reported markers of Purkinje cells. It is indicated that expression of CD3 ε epitope in human Purkinje cells is involved with morphogenesis and morphological maintenance of developmental stage of Purkinje cells.

ABBREVIATIONS

CD3: Cluster of Differentiation 3; TCR: T Cell Receptor; MHC: Major Histocompatibility Complex; ITAM: Immunoreceptor Tyrosine-Based Activation Motif; H&E: Hematoxylin and Eosin; ABC: Avidin-Biotin-Immunoperoxidase Complex; PBS: Phosphate-Buffered Saline; DAB: 3,3'-Diaminobenzidine Tetrahydrochloride; IP_3R1: Inositol 1,4,5-Triphosphate Type 1 Receptor; MAP2: Microtubule-Associated Protein 2; MCP-1: Monocyte Chemoattractant Protein-1; GDNF: Glial Cell Line-Derived Neurotrophic Factor; CCS: Copper Chaperone for Superoxide Dismutase; SOD1: Cytosolic Cu/Zn-Superoxide Dismutase; CNS: Central Nervous System

INTRODUCTION

Cluster of differentiation 3 (CD3) is a membrane protein of T lymphocytes that is generally well known. CD3 forms a T cell receptor (TCR) complex on the surface of T lymphocyte. This TCR complex consists of six types of subunits (alpha (α), beta (β), gamma (γ), delta (δ), epsilon (ε), zeta(ζ)), and ε subunit examined in this study is one of them. On the cell surface, T cells having α and β subunits first recognizes antigens bonded with major histocompatibility complex (MHC). The recognition causes the structural changes of the ε subunit itself, and the signals of the structural changes are transmitted to immunoreceptor tyrosine-based activation motif (ITAM) in the intracellular region; and in turn, signals from the antigens are transmitted into cells [1].

In 1981, a monoclonal antibody that reacts with the ε chain of this T lymphocyte—clone UCHT1—was reported to positively stain not only human T lymphocytes but also human adult cerebellar Purkinje cells at the same time [2].

However, subsequently, there has been no detailed study of expression of CD3 ε epitope in human cerebellar Purkinje cells. Morphological development of cerebellar Purkinje cells is especially remarkable from fetus stage to childhood [3]. To date, there have been many reports of both silver impregnation methods [4] and immunohistochemical methods using molecules that positively stain cerebellar Purkinje cells [5-15] to depict developmental changes in cerebellar Purkinje cells. Since CD3 ε epitope that we presently examined is a surface marker only present on the cell membrane of T lymphocyte that recognizes antigen, it is completely different from traditional molecules as the human cerebellar Purkinje cell markers. However, the significance of CD3-ε-epitope expression on morphological development of human cerebellar Purkinje cell is completely unknown. Therefore, we focused on human cerebellar Purkinje cells, and examined development expression of CD3 ε epitope in Purkinje cells along with the morphological development of Purkinje cell. As a result, unlike molecules that are considered traditional cerebellar Purkinje cell markers, development exchanges in a positive finding of immunostaining of CD3 ε epitope that indicates the morphological development process of human cerebellar Purkinje cell have been obtained. We could proclaim that developmental changes in the staining pattern of CD3 ε epitope from fetus, neonate, infant, to adult stage may be reflecting morphogenesis and morphological maintenance of human cerebellar Purkinje cells.

SUBJECTS AND METHODS

This retrospective study was carried out on autopsy specimens of 19 fetuses (from 16 to 40 weeks gestation), three neonates (from three days to one month after birth) and eight infants (from three months to one year and six months of age). Autopsy specimens of 10 individuals (9 males and 1 female; aged 41 to 72 years) were also examined as normal adult cases (Table 1). All cases showed no neurological sign, and had no chromosomal abnormality and no malformation. All cases were examined within postmortem 24 hours. Formalin-fixed, paraffin embedded cerebellar cortices were used. Several serial 6-μm-sections were prepared from each of the specimens. All paraffin sections were the sagittal sections which intersected cerebellar folia at an angle of 90 degrees. One section was stained with hematoxylin and eosin (H&E) and others were used for immunohistochemical analyses. Avidin-biotin-immunoperoxidase complex (ABC) method was employed for CD3 ε epitope detection. Sections were deparaffinized, endogenous peroxidase activity was quenched by incubation for 30 min with 0.3% H_2O_2 and then washed with phosphate-buffered saline (PBS). Normal rabbit serum served as the blocking reagent. The polyclonal antibody against CD3 ε epitope was used for the immunohistochemical study (Dako, Glostrup Denmark, 1:100 dilution). The appropriate Vectastain ABC kit (Vector Laboratories, Burlingame, CA, USA) was used to detect bound polyclonal antibody. 3,3'-diaminobenzidine tetrahydrochloride (DAB) was the final chromogen. The protocols

Table 1: Immunohistochemical development expression of CD3 ε epitope in the human cerebellar Purkinje cells.

Subjects		CD3 immunoreactivity				
Age	No.of cases	Cell Body	Primary dendrites	Secondary dendrites	Tertiary dendrites	Spiny branchlets
Fetus						
16 g. w.	1	-	-	-	-	-
18 g. w.	2	-	-	-	-	-
20 g. w.	1	-	-	-	-	-
21 g. w.	1	±~+	-	-	-	-
22 g. w.	1	+	-	-	-	-
23 g. w.	1	+	-	-	-	-
24 g. w.	1	+	-	-	-	-
25 g. w.	1	+	-	-	-	-
27 g. w.	1	+	-	-	-	-
29 g. w.	2	+	±~+	-	-	-
30 g. w.	2	+	+	-	-	-
33 g. w.	1	+	+	-~±	-	-
38 g. w.	1	+	+	-~±	-	-
39 g. w.	1	+	+	-~±	-	-
40 g. w.	2	+	+	-~±	-	-
Neonate/infant						
3 days - 1 m	3	+	+	-~+	-	-
3 ms - 9 ms	4	+	+	+	-~±	-
1 y 1 m - 1 y 6 ms	4	~+	+	+	±~+	-
Adult						
41ys - 72ys	10	+	+	+	+	-

Abbreviations: g. w.: Gestational Weeks; m(s): Month(s); y(s): Year(s); -: Negative, ±: Weakly Positive; +: Positive Staining

were approved by the Ethics Committee in Tottori University Faculty of Medicine (No. 1246).

RESULTS AND DISCUSSION

Since regional differences in the some degree of the maturation of the human cerebellar Purkinje cells were evident, the central lobules of the anterior lobe were mainly used for our experiments. The chronological development change of the immunostaining pattern of CD3 ε epitope in cerebellar Purkinje cells from fetuses, neonates, infants, to adults was summarized in Table.

At 16 weeks of gestation, the Purkinje cells were difficult to recognize definitely in H&E staining (Figure 1A). From 16 to 20 weeks of gestation, the three-layered structures of the external granular layer, the molecular layer, and the internal granular layer were observed in cerebellar cortices in H&E staining. The cellularity of the molecular layer between the external granular layer and the internal granular layer was low. The internal granular layer was composed of many migrating neuroblasts. Immunohistochemical study of CD3 ε epitope of fetal cerebellum from 16 to 20 weeks of gestation demonstrated that the no cells in the external granular layer, the molecular layer, and the internal granular layer expressed CD3 ε epitope (Figure 1B).

At 21 weeks of gestation, the width of the molecular layer of the cerebellum was increased and the cellularity of the internal granular layer consisting of the migrated neuroblasts was decreased in H&E staining. The layer of Purkinje cells was observed in H&E-stained sections: the cell bodies of Purkinje cells had somewhat abundant cytoplasm and were moderately elongated in shape (Figure 1C). Purkinje cells with somewhat abundant cytoplasm locating between the molecular layer and the internal granular layer were positive for CD3 ε epitope (Figure 1D). The CD3-ε-epitope stainability of Purkinje cells from 22 to 27 weeks of gestation was similar to that at 21 weeks of gestation (data not shown).

From 29 to 30 weeks of gestation, the four-layered structures (the external granular layer, the molecular layer, the layer of Purkinje cells, and the internal granular layer) were observed in cerebellar cortices in H&E-stained sections (Figure 1E). In addition, the lamina dissecans as a relatively acellular band appeared in the zone below the layer of Purkinje cells (Figure 1E). By this lamina dissecans, Purkinje cell layer and the internal granular layer were separated: this lamina dissecans disappeared around gestation age of 33-38 weeks. In the cerebellar cortices during 29th to 30th week of gestation, the cell bodies and the short dendrites suggesting the primary dendrites of Purkinje cells were observed in H&E-stained sections (Figure 1E). The cell bodies and the primary dendrites of Purkinje cells in the Purkinje cell layer expressed CD3 ε epitope (Figure 1F). From 33 to 40 weeks of gestation, a layer of Purkinje cells was recognized in H&E-stained sections. Similar to the gestation age of 29-30 weeks, the cell bodies and the primary dendrites of Purkinje cells at the gestation age of 33-40 weeks were positive for CD3 ε epitope. In addition, the secondary dendrites were sometimes weakly-positive for CD3 ε epitope (data not shown).

In neonates from three days to one month after birth, there was the external granular layer. The cell body size of Purkinje cell increased and showed the form of the pear type in H&E staining (Figure 2A). CD3-ε-epitope immunoreactivity was detected in the soma and the primary dendrites as well as often in the secondary dendrites (Figure 2B).

In infants from three months to nine months postnatal age, the cell number in the external granular layer decreased and the width of the molecular layer of the cerebellum increased. A significant single Purkinje cell layer was readily able to be recognized (Figure 2C). The cell body, primary dendrites, and secondary dendrites of Purkinje cells expressed immunoreactivity to CD3 ε epitope: the tertiary dendrites sometimes weakly expressed (Figure 2D).

From one year and one month to one year and six months of age, the external granular layer disappeared and a significant single Purkinje cell layer was readily observed (Figure 2E). Significant immunoreactivity to CD3 ε epitope was detected in the cell body, the primary dendrites, and the secondary dendrites, as well as often the tertiary dendrites of cerebellar Purkinje cells (Figure 2F).

Cerebellar Purkinje cells in the adults at the age of 41 to 72 years showed significant large cell bodies and well-developed dendritic arborization (Figure 2G). The cell bodies, the primary dendrites, the secondary dendrites, and the tertiary dendrites of Purkinje cells expressed CD3 ε epitope (Figure 2H): spiny branchlets branching from the tertiary dendrites did not express. Therefore, human cerebellar Purkinje cells at one year and six months of age revealed almost the same immunohistochemical expression pattern of cell bodies and dendritic arborization as seen in adults.

In this study, human adult cerebellar Purkinje cells were confirmed to be positive for CD3 ε epitope in immunostaining. It was already reported by Garson et al., [2] that CD3 monoclonal antibody (UCHT1) that recognizes T lymphocyte labels human adult cerebellar Purkinje cells in1982. Since the report by Garson et al., excluding our present study, there has been no other report on expression of CD3 ε epitope in human cerebellar Purkinje cells. Furthermore, this study is first to show that there are developmental changes in expression of CD3 ε epitope in human cerebellar Purkinje cells from infant to adult stage. From the gestation age of 16 to 20 weeks, there was no expression of CD3 ε epitope in cerebellum cells of fetus. A positive finding for CD3 ε epitope was first observed at the gestation age of 21 weeks in soma of cerebellar Purkinje cell. From 29 weeks of gestation to one year and six months after birth, the dendritic arborization areas positive for CD3 ε epitope gradually expand in the order from primary dendrites, secondary dendrites, to tertiary dendrites in Purkinje cells. From one year and six months after birth to adulthood, CD3 ε epitope was expressed in soma as well as primary, secondary, and tertiary dendrites of Purkinje cells. We are first to show that as the morphological structure of Purkinje cells develops, the expression area of CD3 ε epitope extends in the order from soma, primary dendrites, secondary dendrites, to tertiary dendrites of Purkinje cell.

To date, a number of molecules have been reported as markers of human cerebellar Purkinje cells, such as inositol 1,4,5-triphosphate type 1 receptor (IP_3R1) [5,11-13], calbindin [7], microtubule-associated protein 2 (MAP2) [6], monocyte

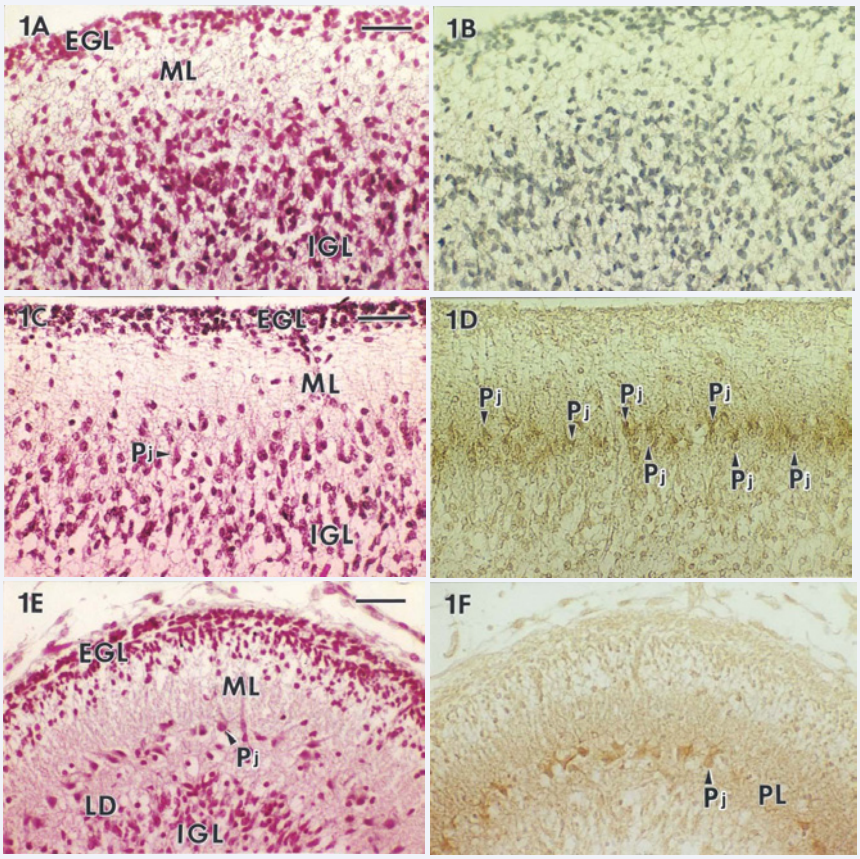

Figure 1 Hematoxylin and eosin (H&E) staining and CD3-ε-epitope immunostaining of human cerebellar Purkinje cells of fetuses.

1A) H&E staining of fetal cerebellum at 16 weeks of gestation. The external granular layer (EGL), the molecular layer (ML), and the internal granular layer (IGL) are distinguishable. The cellularity of the molecular layer between the external granular layer and the internal granular layer is low. The internal granular layer is thick and is comprised of many migrating neuroblasts. The Purkinje cells are not clearly identified.

1B) Serial CD3-ε-epitope immunostained section of H&E staining (Figure 1A) of fetal cerebellum at 16 weeks of gestation. The external granular layer, the molecular layer, and the internal granular layer do not express CD3 ε epitope, respectively.

1C) H&E staining of fetal cerebellum at 21 weeks of gestation. The external granular layer (EGL), the molecular layer (ML), and the internal granular layer (IGL) are distinguishable. Purkinje cells with somewhat abundant cytoplasm (arrowhead and Pj) are arranged in the layer between the molecular layer and the internal granular layer.

1D) Serial CD3-ε-epitope immunostained section of H&E staining (Figure 1C) of fetal cerebellum at 21 weeks of gestation. The Purkinje cells (arrowhead and Pj) with somewhat abundant cytoplasm locating between the molecular layer and the internal granular layer are positive for CD3 ε epitope.

1E) H&E staining of fetal cerebellum at 29 weeks of gestation. The external granular layer (EGL), the molecular layer (ML), the Purkinje cell layer, and the internal granular layer (IGL) can be observed. The lamina dissecans (LD) as a relatively acellular band is also able to be seen in the zone above the internal granular layer. By this lamina dissecans, the layer of Purkinje cell and the internal granular layer are separated. Purkinje cells with cell bodies and short dendrites are observed in H&E-stained sections (arrowhead with Pj).

1F) Serial CD3-ε-epitope immunostained section of H&E staining (Figure 1E) of fetal cerebellum at 29 weeks of gestation. The cell bodies and the primary dendrites of Purkinje cells (arrowhead and Pj) in the Purkinje cell layer (PL) express CD3 ε epitope.

1A, 1C, 1E: Scale Bar = 50 μm.

chemoattractant protein -1 (MCP-1) [14], glial cell line-derived neurotrophic factor (GDNF) [8], synaptojanin [9], aldolase C [15], and copper chaperone for superoxide dismutase (CCS)[10].

IP_3R1 is a glycoprotein that is present in large amounts in cerebellar Purkinje cells. The cerebellar Purkinje cell in normal brain at the age of 1-74 years clearly expressed the cell body, the primary dendrites, the secondary dendrites, and the tertiary dendrites as well as spiny branchlets [11-13]. With respect to development of cerebellar Purkinje cells in IP_3R1 staining, soma of immature Purkinje cell in fetus of 16 weeks postconceptional age presented a positive finding. Subsequently, positive arborization areas in Purkinje cells expanded, and Purkinje cells at 40 weeks postconceptional age showed first positive reaction in spiny branchlets branching from the tertiary dendrites of Purkinje cells [5]. The localization of CD3 ε epitope was mainly from soma to tertiary dendrites, and the expression in spiny branchlets was unclear. Soma of cerebellar Purkinje cell became positive for CD3 ε epitope in fetus of 21 weeks postconceptional age, and later in comparison with IP_3R1. In other words, localization and timing

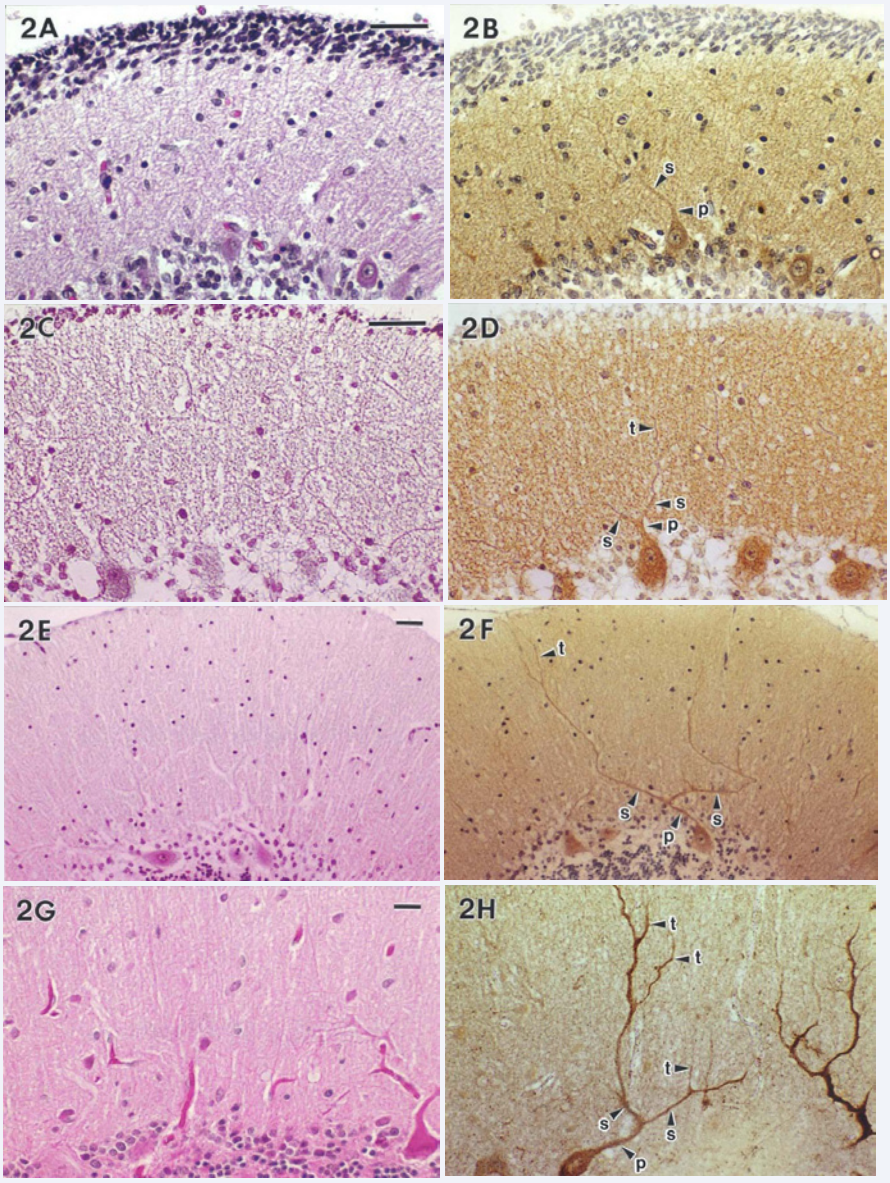

Figure 2 Hematoxylin and eosin (H&E) staining and CD3-ε-epitope immunostaining of human cerebellar Purkinje cells from neonates to adults.

2A) H&E staining in an one-month-old neonate, there is the external granular layer. The cell body size of Purkinje cell increases and shows the form of the pear type. A single layer of Purkinje cells can be seen.

2B) Serial CD3-ε-epitope immunostained section of H&E staining (Figure 2A) in an one-month-old neonate, immunoreactivity is detected in the soma and the primary dendrites (arrowhead and p) as well as in some secondary dendrites (arrowhead and s) of Purkinje cells.

2C) H&E staining at the age of three months after birth, the cell number in the external granular layer decreases and the width of the molecular layer of the cerebellum increases. A Purkinje cell layer can be seen.

2D) Serial CD3-ε-epitope immunostained section of H&E staining (Figure 2C) at the age of three months after birth, the cell body, primary dendrites (arrowhead and p), and secondary dendrites (arrowhead and s) of Purkinje cells express CD3-ε-epitope immunoreactivity: the tertiary dendrites weakly-positive for CD3 ε epitope (arrowhead and t) are also seen.

2E) H&E staining at the age of one year and six months after birth, the external granular layer disappears and a significant single Purkinje cell layer is readily seen.

2F) Serial CD3-ε-epitope immunostained section of H&E staining (Figure 2E) at the age of one year and six months after birth, CD3-ε-epitope immunoreactivity is detected in the cell body, primary dendrites (arrowhead and p), secondary dendrites (arrowhead and s), and tertiary dendrites (arrowhead and t) of cerebellar Purkinje cells.

2G) H&E staining in an adult, a large cell body and dendritic arborization are seen in Purkinje cells.

2H) Serial CD3-ε-epitope immunostained section of H&E staining (Figure 2G) in an adult, the cell bodies, the primary dendrites (arrowhead and p), the secondary dendrites (arrowhead and s), and the tertiary dendrites (arrowhead and t) of Purkinje cells express CD3 ε epitope.

2A,2C,2E,2G: Scale Bar = 50 μm.

of expression of CD3 ε epitope and IP_3R1 in Purkinje cells were different. Spiny branchlets received afferent information from parallel fibers of granule cells in the internal granular layer. The fact that there was no staining of spiny branchlets for CD3 ε epitope indicates that unlike IP_3R1, it is not involved with the function of input information from parallel fibers.

Calbindin is a calcium-binding protein, and at the gestation age of 11-12 weeks, immunoreactivity is already confirmed in human cerebellar Purkinje cells [7]. From the gestation age of 11 weeks to adulthood, calbindin is expressed in Purkinje cells. However, there was no detail statement about the development of the Purkinje cell dendrites. The significance of calbindin being expressed in Purkinje cells is that it plays an important role in regulating Ca^{2+}-dependent activity. However, CD3 ε epitope in Purkinje cells was still not expressed at the gestation age under 21 weeks: the expression of CD3 ε epitope in Purkinje cells of fetus was much later compared to calbindin, and was shown to be first expressed at the gestation age of 21 weeks. These findings indicate that the functional role of CD3 ε epitope is different from that of calbindin.

With regard to expression of MAP2, the neuronal cell bodies suggesting human cerebellar Purkinje cells at 18 weeks of gestation were immunostained [6]. However, there was no detail description about the development of the Purkinje cell dendrites. Function of MAP2 is that it is a protein associated with the transport of intracytoplasmic materials. When the fact that CD3 ε epitope is expressed later than MAP2 is taken into consideration, CD3 ε epitope and MAP2 have different roles.

Staining of Purkinje cells for MCP-1 is transient [14]. At the gestation age of 27 weeks, it becomes positive, and at the gestation age of 36 weeks, staining intensity peaks. At one month after birth and later, staining intensity is weakened, and staining is completely disappeared by one to two years after birth. However, there was no detail description about the development of the dendritic arborization of Purkinje cells. MCP-1 is assumed to be involved with maturity of synaptic function in Purkinje cell dendrites. CD3 ε epitope is expressed earlier than MCP-1, and is positive in adult Purkinje cells; therefore, it is assumed that CD3 ε epitope has a different function from MCP-1.

Strong immunoreactivity of GDNF was confirmed in Purkinje cells at the gestation age of 12-19 weeks, and expression of GDNF continued up to the gestation age of 39 weeks [8]. However, only human brains of ranging from 7 to 39 weeks in gestation were examined. Positive reaction for aldolase C was found in Purkinje cells at the gestation age of 35 -36 weeks and later [15]. Synaptojanin was strongly expressed in human cerebellar Purkinje cells at the gestation age of 23-37 weeks [9]. Its intensity decreased in infants between three months and two years of age, and was maintained until 70 years old [9]. As for each expression of GDNF, aldolase C, and synaptojanin, there was no detail description about the development of the dendritic arborization of Purkinje cells. Expression timings for CD3 ε epitope and each molecule of GDNF, aldolase C, and synaptojanin are different; and thus, functions of CD3 ε epitope and each molecule mentioned above are assumed to be different.

With respect to CCS, the Purkinje cells of the normal cerebella at the age of 1-59 years were positive for CCS [10]. Immunostaining of the cell bodies, the primary dendrites, the secondary dendrites, the tertiary dendrites, and the spiny branchlets was clearly detected. However, only human cerebella at the age of 1-59 years were examined. CCS specifically transfers copper ions to cytosolic Cu/Zn-superoxide dismutase (SOD1). Since there are no free copper ions *in vivo*, SOD1 cannot obtain copper without CCS and cannot be activated, so the delivery of copper to SOD1 by CCS is essential for the normal activity of SOD1in the cerebellar Purkinje cells. CD3 ε epitope is not copper chaperone.

In this study, immunostaining for CD3 ε epitope showed different timing and staining pattern from traditional cerebellar molecular markers: IP_3R1 [5,11-13], calbindin [7], MAP2 [6], MCP-1 [14], GDNF [8], aldolase C [15], synaptojanin [9], and CCS [10]. CD3 ε epitope is assumed to be involved with signal transduction due to antigen stimuli in immune response of T cell lymphocyte against various antigens. Expression of CD3 ε epitope in human cerebellar Purkinje cells is found in the intracytoplasmic region, but expression of CD3 ε epitope in T cell lymphocytes is limited in cell membrane only. Therefore, functions of CD3 ε epitope in Purkinje cells are considered to be different from functions of CD3 ε epitope in T cells. Since there is a blood-brain barrier in the central nervous system (CNS) including human cerebellar Purkinje cells, human cerebellar Purkinje cells never have a direct contact with antigen outside of CNS. Therefore, functions of CD3 ε epitope in Purkinje cells are different from functions of antigen recognition that CD3 ε epitope has in T lymphocytes. In CD3-ε-epitope knockout mouse, it has been reported that there is a morphological abnormality in cerebellar Purkinje cell [16]. In addition, based on the facts that expression of CD3 ε epitope in human cerebellar Purkinje cells continued on from the gestation age of 21 weeks to adulthood and that the expression area of CD3 ε epitope extended in the order of the soma, the primary dendrites, the secondary dendrites, and the tertiary dendrites, functions of CD3 ε epitope in human cerebellar Purkinje cell are assumed to be involved with morphogenesis and morphological maintenance of developmental stage of Purkinje cells.

CONCLUSION

1. This retrospective study was carried out on autopsy specimens of 19 fetuses, 3 neonates, 8 infants, and 10 adults, in order to elucidate the functions of CD3 ε epitope in human cerebellar Purkinje cells.

2. In human fetal cerebellum from 16 -20 weeks, there was no positive finding for CD3. At the gestation age of 21-27 weeks, soma of Purkinje cell became positive for CD3. From 29 weeks of gestation to one year and six months after birth, the arborization areas positive for CD3 extended in the order from primary, secondary, to tertiary dendrites of Purkinje cell. From one year and six months to adulthood, Purkinje cell showed that positive finding for CD3 was confirmed in soma as well as primary, secondary, and tertiary dendrites.

3. Chronological changes along with the morphological development could indicate that the function of CD3 ε epitope in human cerebellar Purkinje cells is involved with morphogenesis and morphological maintenance of developmental stage of Purkinje cells.

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