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Short Communication

Germinal matrix cells associate with veins and a glial scaffold in the human fetal brain

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Abstract

Germinal matrix (GM) in the subventricular zone (SVZ) includes progenitor cells of neurons and glia, which migrate from the SVZ to regions where they become integrated into the developing brain. In the human fetal brain, GM cells pack into high density clusters that encircle GM veins producing a profile we describe as a venous cuff. Venous cuffs are, in turn, encircled by GFAP-positive astrocytes that project processes through the cuff to the venous wall. The high cell density exhibited by cuffs, as well as their association with astrocytes, are reminiscent of features associated with chain migration. However, chain migration has not been associated previously with veins. We suggest that the GM cuff cells may represent a distinct subset of GM cells that migrate away from the GM on a pathway consisting of a vein and its associated astrocytic scaffold.

Theme: Development and regeneration
Topic: Cell differentiation and migration

Keywords: Brain; Germinal matrix; Astrocyte; Alkaline phosphatase; Vein; Migration

In the developing cerebrum, proliferating cells in the subventricular zone (SVZ) create a distinct accumulation of tissue, the germinal matrix (GM), which contains progenitor cells of neurons and glia [10,11,14,15,23,26,27]. In humans, GM tissue persists until term though its extent diminishes as gestational age increases as progenitor cells migrate away from the SVZ [18,25,28]. The signals, mechanisms, and structures that influence this migratory process are only partially characterized and are the focus of intense current research interest [4,19–21,29–31].

Neuropathologists have noted that GM cells persist longest in the vicinity immediately adjacent to large GM vessels [12,22]. The developmental significance of the affiliation between large GM vessels and the persistent GM cells is not immediately apparent. In the current report, we examine the association of GM matrix cells with GM vessels in the developing human brain. Sections were stained with alkaline phosphatase (AP) histochemistry, which stains afferent, but not efferent, blood vessels [2] and with antibodies to glial fibrillary acidic protein (GFAP), which labels astrocytes [3]. We report observations made on 29 brains from neonates born prematurely and describe an anatomically intricate structural relation between a subset of GM cells, a subset of GM veins, and vein-associated astrocytes and propose that this structure may facilitate the migration of GM cells.

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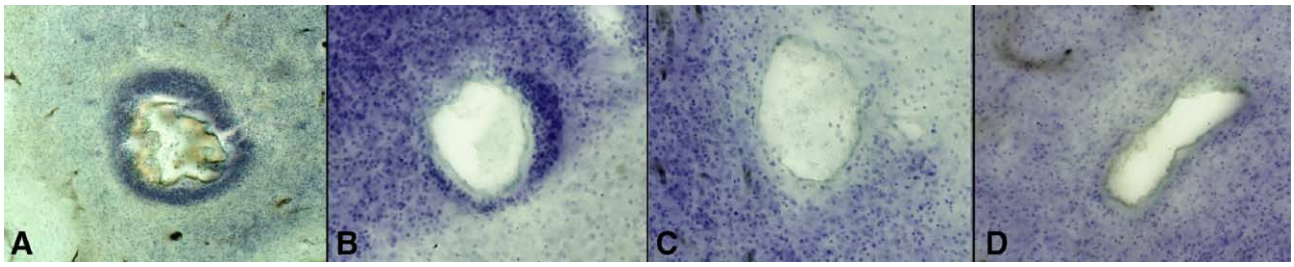

Fig. 1. Brain slices 100 μm thick stained with alkaline phosphatase enzyme histochemistry and counterstained with cresyl violet acetate/light green. GM progenitor cells are concentrated around the periphery of veins located within the germinal matrix. (A) 36 weeks post-conception. (B–D) 30.5 weeks postconception. One vein in the GM may have a cuff (B) while adjacent veins in the same GM will have no evidence of a cuff (C) or have only one layer (D) of GM cells.

consent from next of kin for the investigation of autopsy material. This study involved 29 neonates whose postconception age, taken from autopsy records, ranged from 23 to 56 weeks. Survival times in this group ranged from minutes to >100 days. The material was grouped according to postconception age, which was determined by adding together gestational age and survival.

1. Preparation and staining of tissue

Briefly, at autopsy, brains were fixed in cold 70% ethanol, dehydrated, embedded in celloidin and sectioned into 100 μm-thick sections. The sections were stained for native endothelial AP by Bell and Scarrow's modification of the Gomori method [2,6] and counterstained by either hematoxylin and eosin, cresyl violet acetate/light green, or trichrome. Other sections were immunostained with a mouse monoclonal antibody specific for GFAP (Chemicon, Inc., Temecula, CA). Floating sections were incubated overnight in the antibody (1:80,000; diluted in 2% normal goat serum), followed by incubation in biotinylated anti-mouse IgG visualized using streptavidin HRP and diaminobenzidine/H_2O_2 (DAB kit; Vector Labs, Burlingame, CA). Nuclei in some sections were counterstained with cresyl violet acetate. Slides were viewed with an Olympus

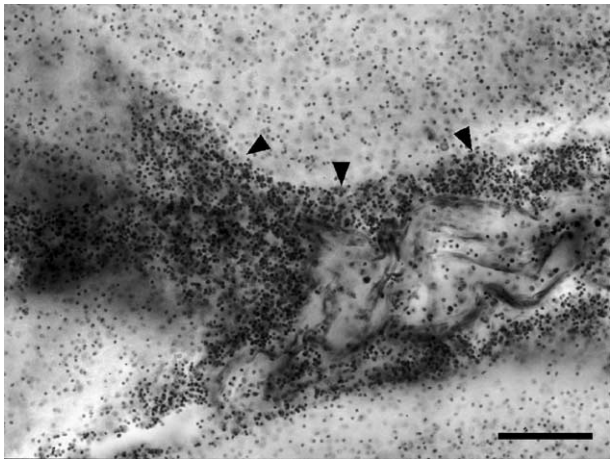

Fig. 2. Brain slice 100 μm thick stained with alkaline phosphatase enzyme histochemistry and counterstained with cresyl violet acetate/light green. Post-conception age is 35 weeks. The periphery of cuffs form a smooth, distinct boundary (arrowheads) that separates the cuff from the surrounding tissue. Scale bar = 200 μm.

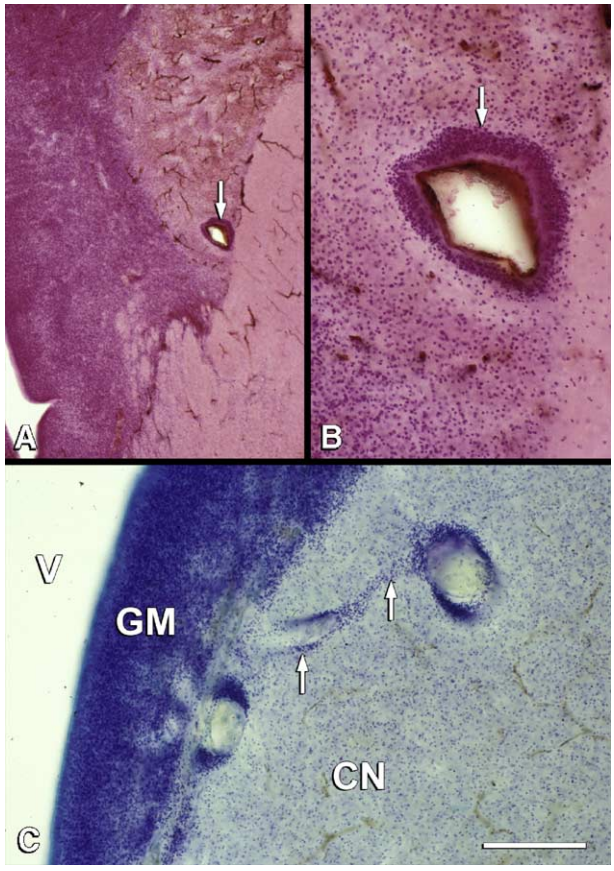

Fig. 3. Brain slices 100 μm thick stained with alkaline phosphatase enzyme histochemistry and counterstained with hematoxylin and eosin (A and B) or cresyl violet acetate/light green (C). Post-conception age is 26 weeks postconception (A and B) and 34 weeks postconception (C). (A) A venous cuff (arrow) is located within the caudate nucleus, beyond the limits of the GM tissue. (B) Higher magnification of the same cuff shown in A. (C) A cuff (arrow) can be identified around a vein at the boundary between the GM and caudate nucleus (CN). Due to the tangential plane of sectioning, a lateral extension of the cuff can be followed into the caudate nucleus where the vein, again appears in cross-section still associated with the cuff. Bar shown in panel C = 750 μm (A), 150 μm (B), and 400 μm (C).