

Letter to the Editor

The perifollicular zone of the spleen as a distributor and filter of blood components

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TO THE EDITOR

The splenic pulp consists of the red pulp, white pulp, and immediately surrounding the white pulp, the perifollicular zone (PFZ). These basic structures develop during gestation.¹ In the rat spleen, the PFZ is easily distinguished on light microscopic examination as the region between the white pulp and red pulp owing to the marginal sinus that divides the PFZ and the white pulp.² However, in conventional paraffin section of the human spleen, it is generally difficult to identify the PFZ on light microscopy as there are no vessels that correspond to the marginal sinus in the rat spleen.³ Steiniger *et al.*⁴ recommended calling the area between the follicular marginal zone and the red pulp, the PFZ. However, I consider that the PFZ coincides with the previously described marginal zone of the human spleen, although Steiniger *et al.* described the PFZ as a special compartment of the red pulp.^{4,5} I have demonstrated that the marginal zone of the human spleen has similar structure and function as that of the rat spleen except for differences in the forms of the termini of the arterioles; we also showed that no venous sinuses are found within the marginal zone.³ The term marginal zone of the spleen often also comprises parts of the lymph follicle,⁴ thereby mixing the area where the follicle marginal zone or marginal zone surrounds the white pulp. Therefore, to avoid misunderstanding, I used the term PFZ in the present report instead of the marginal zone, which immediately surrounds the white pulp. Recently, the PFZ has been described as a special partition that represents the bordering area between the red and the white pulp.⁵

In a recent autopsy, I clearly visualized the PFZ of the human spleen in a specimen with severe sepsis and disseminated intravascular coagulation (DIC). A 40-year-old Japanese man was treated for influenza at our hospital after complaining of fever and showing influenza-like signs. However, he died of renal insufficiency the next day. On autopsy, DIC due to sepsis caused by both gram-negative and gram-positive diplococcus was confirmed. The spleen weighed 55 g, showed microscopic congestion, and had a marked decrease in lymphocytes, especially the lymphocytes of the lymph follicle. The lymph follicle was filled with red blood cells instead of lymphocytes (Fig. 1A). The periarterial/periarteriolar lymphoid sheath (PALS) continued to maintain an accumulation of lymphocytes. The lymph follicle was surrounded by the PFZ (Fig. 1A and 1B), consisting

of an eosinophilic framework with eosinophilic materials containing neutrophils and red blood cells. Neutrophils were primarily found grouped in the PFZ (Fig. 1B). No lymphocytes were found in the PFZ. On phosphotungstic acid-hematoxylin (PTAH) staining, the PFZ framework was deep blue in color, forming a blue zone surrounding the lymph follicle (Fig. 1C). The PFZ was not found in the areas surrounding the PALS.

In the human spleen, the basic structure of the PFZ is a framework of stellate-shaped reticular cells in which many arterioles terminate and no venous sinuses are found.³ The terminal ends of these arteries dilate and open into the reticular framework of the PFZ, shown clearly in Figure 1D.³

At the terminal end of the arteries, arteriole blood flow branches and spreads across a wide area in the PFZ. These arterial termini in the PFZ function as a distributor, or an equalizer, similar to the function of the marginal sinus in the rat spleen.^{2,3} In the present case, fibrin was distributed throughout the PFZ via the arterioles and was deposited within the framework of the reticular cells. This was demonstrated by the blue color of the PFZ on PTAH staining. Focal aggregation of neutrophils in the PFZ in the present case also suggested that neutrophils responded to bacteria flowing into the PFZ at the terminals of arterioles.

In the present case, neutrophils were found in the PFZ, but not in the lymph follicle. These findings suggest that cells demarcating the PFZ from the lymph follicle may function as a barrier, preventing cells from migrating into the lymph follicle. The cells between the PFZ and the white pulp are flat reticular cells with pores through which the lymphocytes pass.³ On immunostaining, the cells bordering the white pulp show alpha-smooth muscle actin and expression of mucosal addressin cell adhesion molecule-1, suggesting its function in lymphocyte homing and segregation of the lymph follicle from the blood.^{4,6}

In the present case, the PFZ was visible on routine sections; it was a different and unique unit from the white pulp and red pulp, an important area of heavy blood flow and filtration and distribution of blood components to other pulps of the spleen.

CONFLICT OF INTEREST

The author has no conflict of interest to declare.

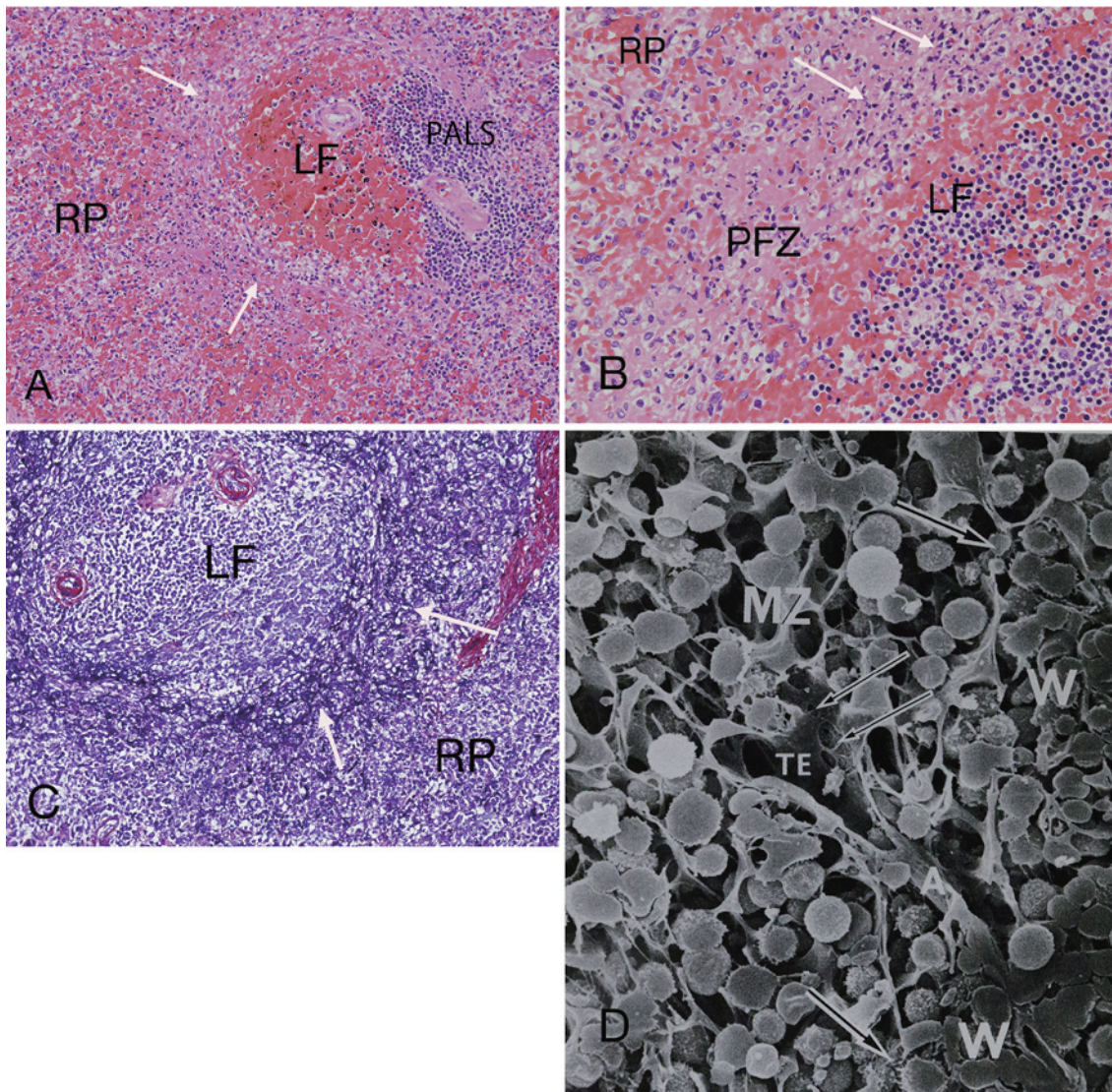


Fig. 1. (A) Low-power magnification of the spleen. The lymph follicle (LF) was filled with red blood cells instead of the lymphocytes. The perifollicular zone (PFZ, arrows) surrounded the lymph follicle. The PALS continued to maintain an accumulation of the lymphocytes. RP: red pulp. H and E stain.

(B) High-power magnification. The PFZ lies between the lymph follicle and red pulp, consisting of eosinophilic framework. Arrows show clusters of neutrophils. LF: lymph follicle, RP: Red pulp. H and E stain.

(C) The framework of the PFZ (arrows) stained blue with phosphotungstic acid-hematoxylin (PTAH) stain, which produced a blue color around the lymph follicle. RP: red pulp, LF: lymph follicle. PTAH stain.

(D) Scanning electron micrograph of the human spleen, quoted from reference No. 3. The basic structure of the PFZ is a framework of stellate-shaped reticular cells in which many arterioles terminate (TE) and no venous sinuses are found. The terminal ends of these arteries dilate and open into the reticular framework of the PFZ. In this figure, MZ is used synonymously with PFZ and WP with the lymph follicle.

In summary, I clearly visualized the PFZ in autopsy specimens of the human spleen under the condition of severe sepsis and DIC; it was a different and unique unit from the white pulp and red pulp, functioning as the distributor of blood components to other pulps.

REFERENCES

- 1 Satoh T, Sakurai E, Tada H, Masuda T. Ontogeny of reticular framework of white pulp and marginal zone in human spleen: immunohistochemical studies of fetal spleens from the 17th to 40th week of gestation. *Cell Tissue Res.* 2009; 336 : 287-297.
- 2 Sasou S, Satodate R, Katsura S. The marginal sinus in the perifollicular region of the rat spleen. *Cell Tissue Res.* 1976; 172 : 195-203.
- 3 Sasou S, Satodate R, Masuda T, Takayama K. Scanning electron microscopic features of spleen in the rat and human: a comparative study. *Scan Electron Microsc.* 1986; 3 : 1063-1069.
- 4 Steiniger B, Barth P, Hellinger A. The perifollicular and marginal zones of the human splenic white pulp : do fibroblasts guide lymphocyte immigration? *Am J Pathol.* 2001; 159 : 501-512.
- 5 Han J, van Krieken JM, Orazi A. Spleen. In: Mills SE (ed), *Histology for pathologist*, 5th edition, Philadelphia, Baltimore, New York, London, Buenos Aires, Hong Kong, Sydney, Tokyo, Wolters Kluwer. 2020; pp.799-812.

- 6 Satoh T, Oikawa H, Yashima-Abo A, Nishiya M, Masuda T. Expression of mucosal addressin cell adhesion molecule-1 on the reticular framework between white pulp and the marginal zone in the human spleen. *J Clin Exp Hematop*. 2019; 59 : 187-195.

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