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Review

The histophysiology and pathophysiology of the peritoneum

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ABSTRACT

The peritoneum is an extensive serous organ with both epithelial and mesenchymal features and a variety of functions. Diseases such as inflammatory peritonitis and peritoneal carcinomatosis can induce disturbance of the complex physiological functions. To understand the peritoneal response in disease, normal embryonic development, anatomy in healthy conditions and physiology of the peritoneum have to be understood. This review aims to summarize and discuss the literature on these basic peritoneal characteristics.

The peritoneum is a dynamic organ capable of adapting its structure and functions to various physiological and pathological conditions. It is a key element in regulation of inflammatory responses, exchange of peritoneal fluid and prevention of fibrosis in the abdominal cavity. Disturbance of these mechanisms may lead to serious conditions such as the production of large amounts of ascites, the generation of fibrotic adhesions, inflammatory peritonitis and peritoneal carcinomatosis.

The difficulty to treat diseases, such as inflammatory peritonitis and peritoneal carcinomatosis, stresses the necessity for new therapeutic strategies. This review provides a detailed background on the peritoneal anatomy, microenvironment and immunologic responses which is essential to generate new hypotheses for future research.

Contents

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1. Introduction

The peritoneum is the largest serous membrane of the human body. It has a unique structure and function. The peritoneum is of importance in facilitating the movements of intraabdominal organs and in maintaining an equilibrium in the abdominal cavity. In case of disease, these balances are disrupted leading to a variety of symptoms.

It can be argued that the peritoneum is involved in almost all intraabdominal conditions. For example, it is highly active in inflammation, it contributes to fibrotic adhesion formation subsequent to infection or surgery and it is a preferred localization for metastases of several types of epithelial malignancies, including ovarian, colon and gastric cancer. This last condition, called peritoneal carcinomatosis is often difficult to treat because it is characterized by numerous miliary tumor depositions throughout the abdominal cavity. Complete removal by surgery is difficult and often not feasible. Recurrent disease often presents on the peritoneum leading to obstructive or paralytic ileus of the bowel, with high morbidity and mortality rates. To understand how the peritoneum is affected and to generate new hypotheses for therapeutic strategies, for example strategies that interfere with the immune response of the peritoneum, fundamental knowledge of the histophysiology and pathophysiology of the peritoneum is essential. Therefore, this review of literature describes the embryology, the anatomy and the functions of the peritoneum.

2. Embryology

Embryonal development of the peritoneum starts in the fifth week of gestation at the gastrulation stage. During this stage, a trilaminar embryo develops with the innermost endoderm, the outermost ectoderm and in between the mesoderm (Sadler and Langman, 2012; Hesseldahl and Larsen, 1969; Langemeijer, 1976) (Fig. 1A). The mesoderm differentiates into the lateral plate mesoderm, the intermediate mesoderm and paraxial mesoderm (Fig. 1B). The lateral plate mesoderm separates into the parietal plate and the visceral plate, covering the amnion and the yolk sac, respectively. The parietal plate mesoderm together with the ectoderm form the embryonic body wall, including the future parietal peritoneum. The visceral plate mesoderm and endoderm form the embryonic gut wall and this will become the visceral peritoneum.

Between the visceral and the parietal plate mesoderm a body cavity develops which forms the embryonic coelome (intra-embryonic cavity) (Fig. 1C, D). The coelome is covered completely by the mesothelial membrane. The parietal layer of the mesothelial membranes lines the outside of the peritoneal, pleural and pericardial cavities and secretes serous fluid. The visceral layer of the mesothelial membranes covers the intra-abdominal organs including liver, spleen, stomach, bowels, and, in females, the reproductive organs. Double layers of peritoneum form mesenteries that suspend the gut tube from the abdominal wall and provide a pathway for vessels, nerves and lymphatics to and from the organs. In the fifth to the seventh gestational week, the embryonic coelome is further compartmentalized by a septum transversum and pleuroperitoneal membranes, separating the cavity in pericardial, pleural and peritoneal cavities (Fig. 1E). Simultaneously, in the fifth gestational week, thickening of the parietal coelomic peritoneum, in combination with the intermediate mesoderm gives rise to the bilateral gonadal ridges. During the sixth gestational week, proliferation of the gonadal ridges and migration of epithelial cells through the underlying mesenchyme, results in indifferent sex cords or gonads. The parietal mesothelium forms the surface epithelium of the future ovaries or testes, whereas the stroma develops from subcoelomic intermediate mesoderm (Fig. 1F). In females, after splitting of the future ovaries, the gonads enlarge until they fuse and eventually develop into the urinary bladder and the reproductive organs including uterus, fallopian tubes and the upper part of the vagina. In males, the gonads proliferate and form the future testes. During this development, the parietal mesothelium of the gonads folds continuously with the underlying developing organs, resulting in a perfectly covering layer of peritoneum (Larsen and Sherman, 2002).

3. Anatomy

3.1. Macroscopic anatomy

The peritoneum is the largest serous membrane of the human body. The peritoneum has a surface area of approximately 1.8 m^2, which is of similar size as the surface of the human skin. The parietal peritoneum lines the inner surface of the abdominal walls, whereas the visceral peritoneum integrates with the outer serosal layers of organs, thereby covering the visceral organs. The blood supply of the parietal peritoneum is derived from arteries of the abdominal wall and from parietal pelvic arteries. The blood supply of the visceral peritoneum is derived from the mesenteric, coeliac and visceral pelvic arteries. Venous blood of the visceral peritoneum drains into the portal vein, whereas the parietal peritoneum drains into systemic veins returning to the vena cava (Khanna and Krediet, 2009). Approximately 80% of all the lymphatic drainage of the abdominal cavity is regulated by the thoracic duct and the right lymphatic duct (Aguirre and Abensur, 2014). The innervation of the parietal peritoneum of the upper abdomen is supplied by the phrenic nerve, the thoraco-abdominal nerve, and the subcostal and lumbosacral nerves, whereas the obturator nerve innervates the parietal peritoneum in the pelvis (Aguirre and Abensur, 2014). The nerves that innervate the visceral peritoneum have not been clearly identified, but sensations are possibly supplied by splanchnic nerves, the celiac plexus superior and the mesenteric plexus (Snell, 2011; Skandalakis et al., 2004). The parietal peritoneum is sensitive to pressure, pain, temperature, and laceration. The visceral peritoneum is not susceptible for these sensations, but is sensitive to stretch and chemical irritation (diZerega, 2000). Thus, the visceral and parietal peritoneal surfaces have different sensibilities, despite similar embryonic development.

The peritoneum adjacent to the female reproductive organs forms deep supportive parallel folds over the entire length of the fallopian tube. The thus formed ligament stretching out from pelvic wall to the uterus is collectively called the broad ligament. In accordance with the embryonic development, the peritoneum lining the abdominal walls and the visceral organs is similar throughout the abdomen, but is slightly different around the ovaries. It is composed of the mesovarium, the mesosalpinx and the mesometrium (Miller