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The omentum

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INTRODUCTION

The word omentum derives from the ancient Egyptians who, when embalming human bodies, used to assess their "omens" by looking at the variations in what we recognise today as the omentum[1]. Galen (128-199 AD)thought that the role of the omentum was to warm the intestines. This was on the basis of a gladiator who had an omental resection after a stab injury and suffered greatly from cold for the rest of his life[2]. A more conventional view of the omentum is that it plays a central role in peritoneal defence by adhering to sites of inflammation, absorbing bacteria and other contaminants, and providing leukocytes for a local immune response[3]. This review details current knowledge on the origins, structure, and function of the omentum, and discusses its role in the peritoneal cavity during various disease states.

ORIGINS

The omentum appears to have evolved as a primitive effector organ in lower vertebrates. It develops as a loose mesothelial sheet of tissue from the yolk sac ans is capable of basic immune functions such as allorecognition, natural cytotoxic reactions and the elaboration of cytokines. This area resides in lower vertebrates within a region delineated by the anterior limbs, foregut and mesonephros. That region is analagous to the boundaries of the developing omentum in mammals[4]. The immune system in humans has evolved from these origins to a very sophisticated level, yet the omentum has retained an important role in immune defence within the peritoneal cavity.

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DEVELOPMENT AND STRUCTURE

The greater omentum develops in the eighth week of gestation from the dorsal mesogastrium[5]. It is composed of two mesothelial sheets which enclose predominantly adipocytes embedded in a loose connective tissue, and also aggregates of mononuclear phagocytic cells. The omentum has a rich vascular supply with numerous characteristic capillary convolutions which are termed omental glomeruli due to their similarity to renal glomeruli. These capillary beds lie directly under the mesothelium[6]. The size of the omentum varies from 300 gm to 2000 gm with a surface area of 300 cm^2 to 1500 cm^2.

In the omentum, the leukocytes aggregate in the perivascular area to form what is termed milky spots. These structures were first described by the French anatomist Ranvier in 1874[7]. The cells derive their origin from the mononucl ear phagocyte system[8] and are arranged around the omental glomeruli that lie directly beneath the mesothelium[9]. These structures are supported by delicate networks of reticular fibres which constitute the framework of the organ[10]. In humans, milky spots comprise of macrophages (70%), B-lymphocytes (10%), Tlymphocytes (10%), mast cells, and stromal cells. On an ultrastructural level, it has been found that the macrophages are present in different stages of maturation, and that they can readily enter or leave the milky spots[11]. The mean number of cells in one milky spot is approximately 600[12] (Figure 1). Milky spots develop as specific structures in the greater omentum between the 20th and 35th week of gestation[5]. The number of milky spots is highest in infancy and gradually decreases with age[13].

Both the endothelium lining the omental capillaries and the mesothelium overlying the milky spots are specially adapted to facilitate transmigration of leukocytes[14], and for rapid fluid shifts. The endothelial lining of the blood vessels in the milky spots is either discontinuous or contain fenestrations[15]. Similarly, there are intercellular pores (the classical stomata of von Recklinghausen) between the mesothelial cells overlying milky spots, and there is an absence of the associated basal lamina in the submesothelial connective tissue[16] (Figure 1).

The macrophages in the mature omentum are essentially scavengers. They appear to differentiate from monocytic precursors in the milky spots and are not dependent on precursors derived from the bone marrow[17]. They are dendritic in shape and

have marked phagocytic abilities. They avidly phagocytose intraperitoneally injected carbon particles and bacteria. When activated, the macrophage precursors in the milky spots proliferate, migrate to the mesothelial surface , and transform into dendritic-shaped macrophages. This process in mice is dependent on macrophage colony stimulating factor (MCSF) being locally produced in the milky spots[17]. Interestingly, the omental macrophages, despite their dendritic shape, lack many specific features of true dendritic cells.

The omentum contains large numbers of B and T lymphocytes which are usually located in the periarteriolar area. Following antigen challenge of the peritoneal cavity, the number of lymphocytes in the milky spots may increase up to 40-fold. Although it is unclear whether this increase represents local proliferation or an influx of cells. With such stimulation, the B and T-lymphocytes are found to segregate into distinct areas *in situ*, and the lymphocytes appear to be associ ated with stromal cells. Nonetheless, these aggregates do not represent secondary lymphoid organs, because they do not contain interdigitating cells or follicular dendritic cells[11,18]. The omentum appears to be a primary site of B-lymphocyte development[19,20]. In experimental animals, the omentum is a source of unique B-lymphocytes that demonstrate specific surface markers. These B-lymphocytes are predominantly CD5+(Lyl+), and are common in not only the omentum but also the peritoneum. However, they are rare in the blood, spleen and lymph nodes. Conventional B and T-lymphocytes are not found in the omentum. The CD5+B lymphocytes develop in the omental milky sopts independ ently from the thymus or bone marrow[19,20]. Hence, the fetal omentum, like the fetal liver and bone marrow, acts as a primary site of B-lymphocyte development[21] and may be considered as a sort of intestinal thymus[4,22]. The function of these CD5+ B lymphocytes remains obscure, nontheless, they are most likely a remnant of a more primitive immune system which is in keeping with the evolutionary origins of the omentum.

Mesothelial cells lining the peritoneal cavity and endothelial cells lining blood vessels share the same mesodermal origin[23]. Human omental microvascular endothelial (HOME) and mesothelial (MESO) cells share many phenotypic propertis. In distinguishing between the two cell types, HOME and not MESO cells express a number of specific surface markers (i.e. E-selectin, P-selectin (CD62), and Le-y) and form tube-like structures when cultured on Matrigel. MESO cells differ from HOME cells based upon the expression of cytokeratins; their rapid proliferation in response to platelet-dervied growth factor, and a change from an epitheloid to fibroblast-like morphology in response to tumour necrosis factor and epidermal growth factor. Both HOME and MESO cells express tissue plasminogen activator and plasminogen activator inhibitor, form typical cobblestone monolayers, and are immunor eactive to von Willebrand Factor and Ulex europaeus I lectin[23,24]. Urokinase activity is only expressed by MESO cells[24].

OMENTAL MIGRATION

In 1896, Stichler placed snails into the peritoneal cavity of dogs and observed that they were walled off by omentum[25]. A few years later(1910), in his text entitled “Introduction to Surgery”, Rutherford Morrison referred to the omentum as “a special protective agency the abdominal policeman. It travels around the abdomen with considerable activity, and is attracted by some sort of inflammation in neighborhoods in which mischief is brewing”. These observations lead to a study in dogs where it was revealed with fluoroscopy that there is no movement of the omentum following the insertion of enterobacteria into the peritoneal cavity[25]. In 1926, Florey and others[26] conducted a series of experiments and concluded that there was no intrinsic omental movement, but rather passive movement. This movement resulted from both the general activity and the position of the animal, and also from the peristalsis of the gut and the action of the diaphragm. This allowed the omentum to move about the abdminal cavity and adhere either foreign bodies or areas of inflammation. It was also noted that the omentum was limited in its ability to attach to foreign bodies in the pelvis and above the liver because it was unable to make physical contact with them[27]. This lead Sir Charles Sherrington[28] to comment “that the doubled-up posture of the acute abdominal case is precisely that which will cause the omentum to be moved low dowm in the abdominal cavity”.

OMENTAL FUNCTION

Foreign bodies

Most surgeons have observed the ability of the omentum to adhere to intra abdominal foreign bodies such as drains and catheters. In dogs it has been noted that following the placement of various types of drains into the peritoneal cavity, that within seven days all tubes are surrounded and occluded by omentum[27]. This may lead to drainage problems in patients requiring long term catheters placed in the abdominal cavity, such as those for peritoneal dialysis. In such patients, removing the omentum has been found in a number of retrospective and uncontrolled studies to reduce the incidence of catheter blockage and to improve drainage[28-32]. In addition, omentectomy does not appear to alter the peritoneal diffusion capacity[33]. Because of this, it has been advocated that partial omentectomy is integral to the surgical technique of peritoneal catheter placement[28-32]. In contrast,

Lewis *et al*.[34] argued that the absolute risk reduction with omentectomy in preventing catheter blockage was only 0.18 in a series of 38 patients undergoing 66 catheter placements. It also remains to be clarified whether omentectomy has other deleterious side effects such as an increased incidence of peritonitis. None of the reported trials have adequately addressed this issue.

Peritonitis

The omentum performs a number of functions during episodes of peritonitis. The first of these is the rapid absorption and clearance of bacteria and foreign material from the peritoneal cavity. The omentum is the only site, other than the diaphragmatic stomata, that has a documented ability to absorb particles from the peritoneal cavity[35]. But unlike the stomata, the omentum contains potent local effector mechanisms that are mediated by especially macrophages(and probably also B lymphocytes) contained within the milky spots. These macrophages appear to be the principal site for the phagocytosis of particles and bacteria from the peritoneal cavity[13].

The second function of the omentum is to supply leukocytes to the peritoneal cavity. In experimental animals with peritonitis, the omentum appears to be the principal site by which firstly macrophages and then neutrophils migrate into the peritoneal cavity[36,37]. The macrophages are derived from the milky spots which provide the correct microenvironment and growth factors for macrophage proliferation and maturation. The correct microenvironment and growth factors for macrophage proliferation and maturation. The structure of the milky spots and their associated capillary structures aids this process (Figure 1). Because the mesothelium is absent over the milky spots, and the basement membrane is discontinuous, there is rapid exposure of the resident macrophages to intraperitoneal stimulants. this activates the macrophages which then demonstrate marked surface membrane activity and migrate through the stomata of the milky spots into twe peritoneal cavity[37].

The omentum also allows for the easy migration of neutrophils from the circulation[7]. Due to the structure of the milky spots, there is direct exposure of the postcapillary venules to inflammatory stimuli from the peritoneal cavity[38]. The neutrophils are then recruited from the circulation and extravasate via the post-capillary venules in the glomerular tufts into the milky spots and then via the mesothelial stomata into the peritoneal cavity. In one study on mice with peritonitis, the post capillary venules in the milky spots of the omentum were the only abdominal sites detected where plasma extravasation occurred, and the omental milky spots were the major route through which leukocytes migrated into the peritoneal cavity[38]. In addition, the omentum was the only abdominal organ which showed an increase in blood flow during peritonitis[38]. Milky spots do not seem to serve as a source of dendritic cells[7].

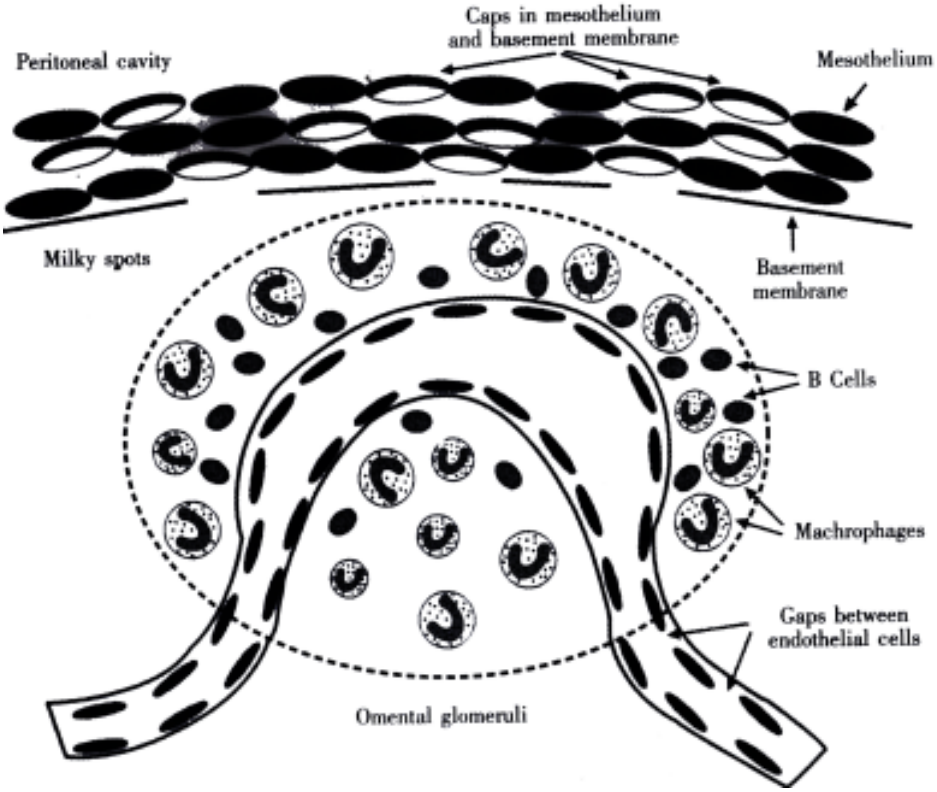

Figure 1 The basic structure of a milky spot in the omentum.

The third function of the omentum is to adhere to and attempt to seal off areas of contamination. The omentum can rapidly produce a layer of fibrin by which to adhere to the contaminated area at the point of contact. In the course of a few days, the fibrin begins to organise with the development of new blood vessels and fibroblasts. In the long term, if the host survives, the contaminated area will be walled of with collagen, and thereby forming dense adhesions[46].

Removal of the omentum impairs peritoneal defence mechanisms[3]. In experimental peritonitis, omentectomy has been found to reduce survival[40], and influence a number of peritoneal defence mechanisms[41]. In particular, there is a reduction in the total intra peritoneal cell counts, with macrophages being the most effected. There is also a reduction in neutrophil chemotaxis, although their phagocytic activity appeares unchanged[41]. In humans, omentectomy also appears to impair the peritoneal defence mechanisms[42,43]. One retrospective analysis compared a group of 406 patients having omentectomy with proctocolectomy and ileoanal anastomosis with a group of 239 patients having a similar procedure without omentectomy[42]. The patients were followed up for a mean of 4.3 years. The results showed that the omentectomy group had a significantly higher incidence of postoperative sepsis (4% *vs* 10%, $P<0.01$) and sepsis requiring reoperation (3% *vs* 8%, $P<0.01$) when compared with patients retaining their omentum. In addition, there was no difference in the incidence of partial or complete small bowel obstruction due to adhesions between the two groups.

Neovascul arisation

It has long been recognised that the human omentum can promote angiogenic activity in adjacent structures to which it is applied. Indeed, lipid material obtained from the omentum has been found to induce angiogenesis in rabbit corneas after only a single injection. This angiogenic material obtained from the omentum is abundant in supply[44]. Further evaluation of the factors involved in this process have found that the human omental microvascular endothelial cells (HOME cells) express the angiogenic peptide 'basic fibroblast growth factor'[39]. This process of neovascularization allows the omentum to provide vascular support to adjacent tissues such as the gut and promote function and healing in ischaemic or inflammed tissue[45,46]. Another example of the angiogenic activity of the omentum has been its ability to support splenic autotransplantations. Although the clinical practice of re implantation of splenic remnants following splenic injuries has largely been abandoned by surgeons, it is interesting to note that such implants are supported by the omentum and function to a limited capacity[47]. The omentum has also be found to be capable of supporting free structures such as the trachea, segments of intestine, sciatic nerve grafts. Such structure can then be used for reconstructive purposes[48-50].

CLINICAL ISSUES

Primary pathology

In contrast to its numerous advantages, the omentum is rarely a site of primary pathologic change. The have been several case reports of primary omental torsion in both children and adults, and primary omental infarction in adults. Patients usually present with an acute abdomen and have localized signs of peritonism plus or minus a palpable mass. They are readily treated by partial omentectomy[51-53]. In addition, both benign (lipoma, fibroma) and malignant (liposarcoma, fibrosarcoma, angiosarcoma) soft tissue tumours may occur in the omentum, although they are very rare.

Reconstruction

Surgeons have long exploited the unique structure and function of the omentum[54]. In paricular, its rich blood supply that supports a high absorptive capacity, its pronounced angiogenic activity which may support local tissues (and ischaemic tissues), its innate immune function, its ability to adhere to local structures, and finally its high concentration of 'tissue factor' which promotes haemostasis[2,55]. In 1927, Perrotti[56]used free and pedunculated flaps of omentum to enhance intestinal suture lines in dogs. Omentum has also been used: to close perforations in the gastro-intestinal tract; to reinforce gastro-intestinal anastomoses; to aid haemostasis during liver resections; to line the bed of hydatid cysts in the liver; as a pedicled graft to cover defects or to reconstruct areas from the chest wall to the perineum; to protect exposed carotid arteries; as free vascularized grafts in head and neck surgery; to repair bronchopleural fistula; and others[54,57,58].

There are several reports of the use of an omental flap to reconstruct the mediastinum in patients with mediastinitis secondary to open heart surgery[59-61]. These reports are retrospective and not adequately controlled. Nevertheless, they all comment that omental flaps are associated with fewer septic complications than pectoralis major flaps, and are associated with high rates of healing and lower mortality when compared with debridement. Similarly, there have been reports on the use of the omentum as a free transfer graft for the treatment of chronic ulcers, progressive hemifacial atrophies, and contused wounds. The transferred omentum appears to maintain its volume and nature under normal circumstances[62].

Gastrointestinal anastomoses

There have been numerous studies evaluating the use of the omentum to support gastrointestinal anastomoses. In animals, there have been conflicting results as to whether reinforcing a compromised (i.e., ischaemic or technically inadequate) anastomosis with well vascularized omentum improves healing[1,63,64]. However, the clinical relevance of studying anastomotic healing of grossly ischaemic segments of bowel is, I believe, questionable. In contrast, Carter *et al*[65]. evaluated the ability of omental wrapping to improve the healing of anastomoses using non compromised large intestine. They observed no improvement in fatal leak rates.

There has been one large clinical trial evaluating this issue in humans. This included 705 patients undergoing elective resections from the caecum to the midrectum with a mean age of 66 years. Patients were randomized after colectomy to undergo either omental reinforcing of the colonic anastomosis or no reinforcing. The intraoperative findings were similar between the two groups, except that there were significantly more septic operations performed in the control group. When comparing the omental reinforcement group with the controls, there was no significant difference in either anastomotic leakage (4.7% *vs* 5.2%) or deaths (4.9% *vs* 4.2%). The authors concluded that omental reinforcement of colorectal anastomosis was of no clear benefit *et al*[66].

Neurosurgery

Placing the omentum on the brain surface by surgical transposition or transplantation has been found to result in the development of numerous neovascular connec tions between these two structures. This phenomenon occurs even in the absence of cerebral ischemia. In a series of 30 children with moyamoya disease, aged from 2 to 17 years, omental transplantation was used to improve vascularity in either the anterior or the posterior cerebral artery territory. All 19 patients treated with omental transplantation to the anterior cerebral artery and 11 (84.6%) of the 13 treated with omental transplantation to the posterior cerebral artery showed improvement in their neurological state[67].

Vascular synthetic grafts

Synthetic vascular grafts lined with HOME cells appear to remain patent for longer periods[23]. However, HOME cells remain difficult to extract and culture. In contrast, MESO cells can be readily harvested in large numbers from the omentum, and by culturing them in specific conditions their natural tendency to express tissue factor which is thrombogenic can be inhibited. Such cells are an excellent alternative to HOME cells in seeding synthetic grafts[68]. This technique has been used to line the luminal surface of small diameter prosthetic bypass grafts, thereby lowering the grafts thrombogenicity. These grafts were then implanted into the carotid artery of dogs and have been found not to develop neointimal hyperplasia or stenosis when compared with controls[69].

Malignancy

The omentum has been observed to be a frequent site of metastatic disease for many malignancies. In animals, malignant cells inoculated into the peritoneal cavity preferentially infiltrate the milky spots in the omentum and grow into distinct metastic[70,71]. The omentum appears capable of supporting not only malignant cells in the milky spots but free intraperitoneal cells. It achieves this due to its intrinsic angiogenic properties. In animals, removing the omentum impacts on the survival of free intraperitoneal malignant cells and there by reduces the rate of local recurrence[72,73]. Because of these observations, the omentum is frequently removed as part of resections for malignancies of various intra abdominal organs[74].

Ovarian cancers, in particular, are characterized by their tendency to spread intraperitoneally and involve the omentum. Hence, there has evolved a general consensus that surgical management of ovarian cancer should include optimal cytoreduction[75-78]. The minimum surgical requirements of this are to perform a total abdominal hysterectomy, bilateral salpingo-oophorectomy, and omentectomy. The apparent value of performing an omentectomy is that it provides staging information and selects patients for adjuvant chemotherapy[79,80]. In addition, in patients with advanced disease, there appears to be a survival advantage in debulking tumour deposits[81]. Nonetheless, with borderline ovarian tumours, omentectomy is also frequently advocated but the evidence to support this remains limited[82].

The removal of the omentum in patients with ovarian cancer is not universal. In 1993, a United states national survey of the treatment of patients with ovarian cancer concluded that out of a total of 12, 316 patients with ovarian cancer, the requirements for what were defined as a minimum surgical resection were met in only around 60% of patients (bilateral salpingo-oophorectomy 67%; abdominalhy sterectomy 55%; and omentectomy, 59%)[83]. Another analysis of omentectomy in patients with ovarian cancer found that the mean omentectomy size was only 203.5cm^2 (normal omentum = 792 cm^2), and secondary ovarian cancer was present in 61%. Thus the optimal extent of omental resection and histological examination remains to be clearly defined[80].

The omentum is intimately associated with the stomach and the gastric lymphatic drainage. Therefore, it is invariably removed as part of a curative resection for gastric cancer[84,85]. Nonetheless, there is no clear evidence to provide guidance as to the extent of such a resection, and whether the entire omentum has to be removed[86,87]. Pseudomyxoma peritonei is a rare neoplasm characterized by mucinous ascites and the mucinous involement of peritoneal surfaces, omentum and bowel loops. Usually pseudomyxoma peritonei is associated with benign or malignant mucinous tumor of the appendix or ovary, and cytoreductive resections, including omentectomy, are advocated as the treatment of choice[88,89].

CONCLUSION

Our concept of the omentum as an abdominal policeman has obviously evolved since the days of Rutherford Morrison. We now understand that it occupies a central position in the peritoneal defence mechanisms. It achieves this by virtue of its innate immune function, its high absorptive capacity, and its ability to adhere to adjacent structures to both seal off gastrointestinal defects and promote their healing with its pronounced angiogenic activity. Because of these attributes, surgeons have utilised the omentum in a variety of settings, from reconstructing soft tissue defects, to supporting tissues to promote healing. In managing patients with intra abdominal malignancies, the role of omentectomy requires further evaluation to determine whether it is associated with a clear survival advantage, and to evaluate how much needs to be removed. In conclusion, the omentum needs to viewed as an important intra abdominal organ and hence careful consideration needs to be given before it is removed.

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