

Dendritic cells in the human ileum: A light microscopic zinc iodide-osmium study

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SUMMARY

The presence of dendritic cells in human and animal epithelium and subepithelial tissue is demonstrated. The present study used human ileal specimens, resected for carcinoma, and revealed zinc iodide-osmium positive dendritic cells in the crypts of Lieberkühn and throughout the lamina propria. There were more cells in the lamina propria than in the crypts. Dendritic cells were polygonal with multiple short, thick processes in the lamina propria and were triangular, often with a single long process directed toward the crypt lumen, in the crypts. The cells did not have a typical, mature phenotype.

Key words: Ileum – Crypt – Dendritic cell – Lamina propria – Zinc iodide-osmium

INTRODUCTION

Luminal antigens penetrate the intestinal lamina propria and interact with dendritic cells (DCs). DCs are bone marrow-derived, thymus-independent cells (Steinman and Nussenzweig, 1980); they are immunostimulatory cells (Steinman, 1991) and can take up and present both orally and intestinally administered antigens to naïve T cells (Liu and MacPherson, 1991). DCs are capable of presenting peptides to virgin T cells and initiating cell-mediated immunity to newly encountered antigens. The capture and presentation of antigens by DCs induces an immune

response (Colaco, 1999). DCs probably control T cell responses in the gut wall. DCs are present in organized lymphoid tissues and may also be present in gut epithelium (Maric et al., 1996).

Zinc iodide-osmium (ZIO) has been used to identify DCs in human and animal tissues (Mishima and Miller-Miniska, 1961; Crocker and Hopkins, 1984; Chandi et al., 1988, 1989; Dagdeviren et al., 1994; Breathnach and Goodwin, 1965; Niebauer et al., 1969; Rodriguez and Caorsi, 1978; Hart and Fabre, 1981; Sertle et al., 1986; Prickett et al., 1988; Steinman, 1991; Abraham et al., 1996, 2000; Indrasingh et al., 2001, 2002, 2003; Koshy et al., 2003a,b).

DCs have been found in human digestive tract tissues, oesophagus (Al Yassin and Toner, 1976), tonsil (Crocker and Hopkins, 1984; Chandi et al., 1988, 1989; Noble et al., 1996; Papadopoulos et al., 1999; Indrasingh et al., 2002), liver (Prickett et al., 1988), and colon (Pavli et al., 1996; Indrasingh et al., 2003).

Since human ileum has not been studied in detail and contains aggregated lymphatic follicles (Peyer's patches), the present study was carried out to demonstrate, using zinc iodide-osmium, the morphology and distribution of DCs in the human ileum.

MATERIALS AND METHODS

Full-thickness specimens of ileum were obtained from patients undergoing surgery for cancer (n = 2) at the Christian Medical College Hospital. The tissue pieces were immersed in a solution of

veronal-buffered zinc iodide-osmium tetroxide, pH 7.4 (Figueroa and Caorsi, 1980) for 48 hours at 4°C in the dark, washed in distilled water, dehydrated in graded ethanol, cleared in xylene, and embedded in paraffin wax. Serial sections of seven-micron thickness were cut and the sections were transferred to glass slides, deparaffinised, mounted in Canada balsam, without counter staining (Chandi et al., 1988; Abraham et al., 1996; Indrasingh et al., 2001), and viewed under a light microscope.

RESULTS

ZIO-positive DCs were located in the crypts of Lieberkühn and throughout the lamina propria. There were more DCs in the lamina propria than in the crypts (Fig. 1). The cells were polygonal in the lamina propria and had multiple short, thick dendritic processes, and were triangular in the crypts and showed a single long process directed toward the lumen of the crypt (Fig. 1). Where infiltration of lymphocytes from lymphoid

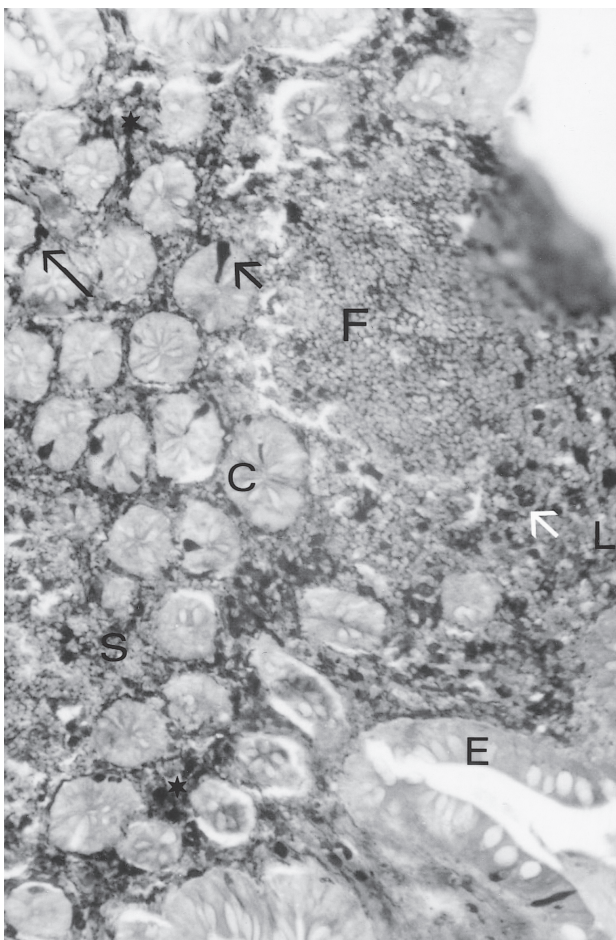


Fig. 1.- Triangular dendritic cell with a single long, thick process in the crypt (black arrow); polygonal dendritic cell with short, thick multiple processes in the lamina propria (long black arrow). ZIO; a few DCs (white arrow) at the site of infiltration of lymphocytes (L) from lymphatic follicles in the submucosa into the lamina propria; reticular framework pattern of the dendritic cells (*) x290.

follicles in the submucosa to the lamina propria occurred, a few ZIO-positive polygonal DCs with multiple processes, - possibly follicular dendritic cells (FDC) - were present (Fig. 1). DCs had a distinctive distribution pattern; they formed a reticular framework throughout the lamina propria and beneath the basement membrane of the crypts (Fig. 1).

DISCUSSION

ZIO has been extensively used to identify DCs. Cellular reactivity to ZIO is attributed to certain reducing substances such as catecholamines and ascorbic acid (Stockinger and Graf, 1965) and to lipid moieties unmasked from lipoprotein (Niebauer et al., 1969). The ZIO technique, with a marked deposition of reaction product in the mitochondrial granules, probably indicates the presence of lipids and/or precursor proteins (Taffarel et al., 1984).

DCs initiate immune reactions in lymphocytes and handle antigens (Nossal et al., 1968; Veerman and van Rooijen, 1975). Penetration of the gut mucosa by pathogens is believed to occur mainly through M cells located in Peyer's patches; bacterial uptake in the mucosal tissues of the gut is also mediated by DCs (Rescigno et al., 2001) by making intercellular adhesive links with epithelial cells, thereby preserving the integrity of the gut barrier. DCs can penetrate the epithelium to directly take up bacteria from the gut lumen without compromising the barrier function of the gut (Collins, 2002).

DCs form a reticular framework throughout the lamina propria and beneath the basement membrane of the crypts in the colon (Pavli et al., 1996). The reticular framework is present in skin (Hume et al., 1983) and in the large airways of the lung (Holt et al., 1989). A similar pattern was seen also in the human ileum in the present study. Indrasingh et al. (2002) differ from Pavli et al. (1996) in not finding the reticular framework pattern in human colon.

The stimulated release of DCs from intestine may be important in regulating antigen presentation in lymph nodes draining inflammatory sites (MacPherson et al., 1995). DCs were localized in the subepithelial dome region of Peyer's patches and are detectable in inflamed ileal mucosa in active Crohn's disease (de Baey et al., 2003). In Peyer's patches, DCs have been detected in the interfollicular regions and in clusters of cells in the subepithelial dome regions (Jameson et al., 2002). DCs may regulate intestinal immunity but remain poorly characterized (Bell et al., 2001). In human colon, polygonal DCs did not show processes and the triangular cells showed one or two processes; the processes were thin and short; the DCs did not have a typical, matu-

re phenotype (Indrasingh et al., 2002). The presence of triangular DCs, with their thick, long process directed toward the lumen of the crypt found in this study, as in the colon (Indrasingh et al., 2003) is probably a human characteristic.

The production of immunosuppressive factors is one of the mechanisms by which tumors evade immunosurveillance; primary tumors negatively impact DC development (Sombroek et al., 2002). DCs can be used as immunotherapeutic agents for cancer and in relation to the pathogenesis of human immunodeficiency virus (HIV) infection (Barratt-Boyes et al., 1996; Morse and Lyerly, 1998; Gilboa et al., 1998; Hermans et al., 1998; Nestle and Burge, 1999; Avigan, 1999; Timmerman and Levy, 1999; Melaro et al., 1999; Esche et al., 1999; Kershaw et al., 2001; Ikeda et al., 2001; Nair et al., 2002).

It is possible that the presence of DCs in the ileum is to respond to orally ingested antigens and commensal bacteria. DCs are probably the major antigen-presenting cells of the ileal lamina propria and play an important role in the immunological pathogenesis of ileal inflammation, as in the colon (Kimura and Morise, 1990; Pavli et al., 1996). The distribution of DCs in the mucosa of the ileum as seen in this study, is important because of the antigens that enter through mouth and because of the presence of intestinal bacteria. DCs are potent stimulators of primary T cell responses (Steinman, 1991). They reside in the interstitium of many tissues and the epithelium of mucosa, where they take up and process both soluble and particulate antigens. Following exposure to antigens, DCs mature and develop potent immunostimulatory activity whilst migrating to draining lymphatic follicles and nodes; there, they interact with T cells to initiate T cell responses (Pavli et al., 1996).

ACKNOWLEDGEMENTS

The authors thank Dr Aravindan Nair for providing and permitting us to use the ileum specimens resected during surgery for cancer from patients and the Fluid Research Committee of the Christian Medical College for funding this study.

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