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Morphological features of the inflammatory response in molluscs

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ABSTRACT

Over the last few years, there has been a large increase in studying the biology and pathology of molluscs, predominantly in addressing the molecular patterns involved in their immune-mediated and inflammatory responses. Conversely, the literature-based diagnostic criteria concerning the morphology of the above phenomena still involves pathogenetic confusion and conflicting terminology. A comparison of bibliographic resources, such as the Abridged Glossary of Terms Used in Invertebrate Pathology and the National Status manual for molluscan histopathological examination and analysis from the NOAA, have revealed variability in the definitions of superimposable lesions, emphasising the need for further efforts in establishing standard terminology and methodologies in this field of study. This review suggests some possible solutions for overcoming the use of parallel terminologies in diagnosing inflammation in molluscs and also highlights conflicting features requiring further discussion.

1. Introduction

The inflammatory response occurring after pathogen invasion and/or cell injury is intended as a local defence reaction in host tissue (Cone, 2001). As a functional part of the immune response of an organism (Muller, 2003), vertebrate inflammation involves changes in local circulation (hyperaemia, increased vessel permeability) and the recruitment of immune cells (i.e., granulocytes, lymphocytes and macrophages) to injured foci to isolate or eliminate the causes of cell damage and eventually initiate tissue repair (Cone, 2001; Muller, 2003). This usually occurs via an integrated system of molecular signals (Hanada and Yoshimura, 2002) involving the release of regulatory/effector molecules (i.e., pro-inflammatory cytokines, such as interleukin (IL)-1β and TNFα, and chemokines, such as IL-8) and their binding to surface membrane receptors on immune and endothelial cells and the cross-membrane molecular transduction of the signals generated by ligand binding, usually involving a cascade of downstream chemical reactions starting from receptor phosphorylation. This ultimately directs the molecular signals described above to the nuclei of target cells via the phosphorylation of transcription factors, resulting in the induction of appropriate cellular responses (i.e., adhesion and motility, migration and extravasation, cytotoxic responses, phagocytosis and cell death induction, among others) (Cone, 2001; Humphries and Yoshino, 2003). According to Ottaviani et al. (2010), although the inflammatory response increased in complexity during metazoan diversification, its functional basis has not been substantially modified during evolution. Thus, similar functional events seem to occur in the inflamed tissue of molluscs as in vertebrates, though with obvious differences in some molecular features, the immune cells involved and their arrangement in injured tissues (Rowley, 1996; Humphries and Yoshino, 2003; Ottaviani et al., 2010). The molecular patterns involved in immune-mediated and inflammatory responses in molluscs have been increasingly investigated over the last few years, and excellent reviews are available on the topic (Tiscar and Mosca, 2004; Canesi et al., 2006; Koutsogiannaki and Kaloyianni, 2010; Loker, 2010; Ottaviani et al., 2010; Song et al., 2010). However, the literature-based diagnostic criteria addressing the morphology of the inflammatory response in these invertebrates (Onstad et al., 2006; Kim et al., 2006; Kim and Powell, 2004, 2007) still involves pathogenetic confusion and conflicting terminology among pathologists. Knowledge of the morphogenetic patterns involved in the mollusc inflammatory response not only has a comparative value for understanding the underlying mechanisms of tissue response to injury in these interesting animal models, it also has diagnostic relevance concerning their medical and veterinary interest (Canesi et al., 2006; Song et al., 2010; Loker, 2010) and their possible use as biomarkers in both acute and long-term sublethal exposure to pollutants (Garmendia et al., 2011). This brief review provides an overview of the terminology and diagnostic criteria related to different inflammatory responses in molluscs after a brief outline of their molecular pathogenesis.

2. Effector immune cells in mollusc inflammation

Molluscs possess only innate immunity, which involves both cellular and humoral effectors, the latter of which includes soluble lectins, hydrolytic enzymes and antimicrobial peptides (Canesi et al., 2006). Haemocytes (also called immunocytes) are the im-

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mune-effector cells in mollusc inflammation (Ottaviani et al., 2010; Ottaviani, 2011). In bivalves, which lack specific lymphoid organs, their differentiation and release occurs directly in the connective tissue adjacent to inflamed tissue (Hanselmann and Smolowitz, 2000; Ottaviani, 2006). Conversely, in some gastropods, immunocyte production appears to occur primarily in an "amebocyte-producing organ" (APO) located in the anterior pericardial wall separating the pericardial sac from the mantle cavity (Ottaviani, 2006; Yoshino and Coustau, 2011). There is no common system for classifying immunocytes (Ottaviani, 2006, 2011); however, two types are commonly described in molluscs: granulocytes and hyalinocytes (or agranulocytes) (Martin et al., 2007; Tiscar and Mosca, 2004; Ottaviani, 2011). Granulocytes contain cytoplasmic granules, have a low nuclear-to-cytoplasmic ratio and are effective in phagocytising foreign materials; in contrast, hyalinocytes are smaller cells, have a high nuclear-to-cytoplasmic ratio, few cytoplasmic granules and a poor capacity to phagocytose foreign materials (Martin et al., 2007; Tiscar and Mosca, 2004) (Fig. 1a; Table 1).

It is unclear if these two types of immunocytes represent distinct cell lineages or even differences in immunocyte maturation and/or physiology (Martin et al., 2007; Ottaviani, 2006, 2011). Immunocytes share many biological functions with vertebrate macrophages, the most relevant being phagocytosis of foreign particles, including particulate matter and biological pathogens (i.e., bacteria and parasites) (Ottaviani, 2006, 2011). Immunocytes secrete humoral factors that play a fundamental role in innate

Table 1
Summary of the main characteristics of immunocytes.

Hyalinocytes	High nucleus:cytoplasm (N:C) ratio
	Dimension:6–7 μM
	Agranular-hyaline cytoplasm
	No phagocytic activity
	Round form
Granulocytes	Low nucleus:cytoplasm (N:C) ratio
	Dimension:10–15 μM
	Granular cytoplasm (neutral, basophile, acidophile granules)
	Phagocytic activity (*Involved in recognition, chemotactic migration, adhesion, ingestion, destruction and elimination of foreign cells*)
	Form pseudopodia
	Contain hydrolytic enzymes and peroxidase

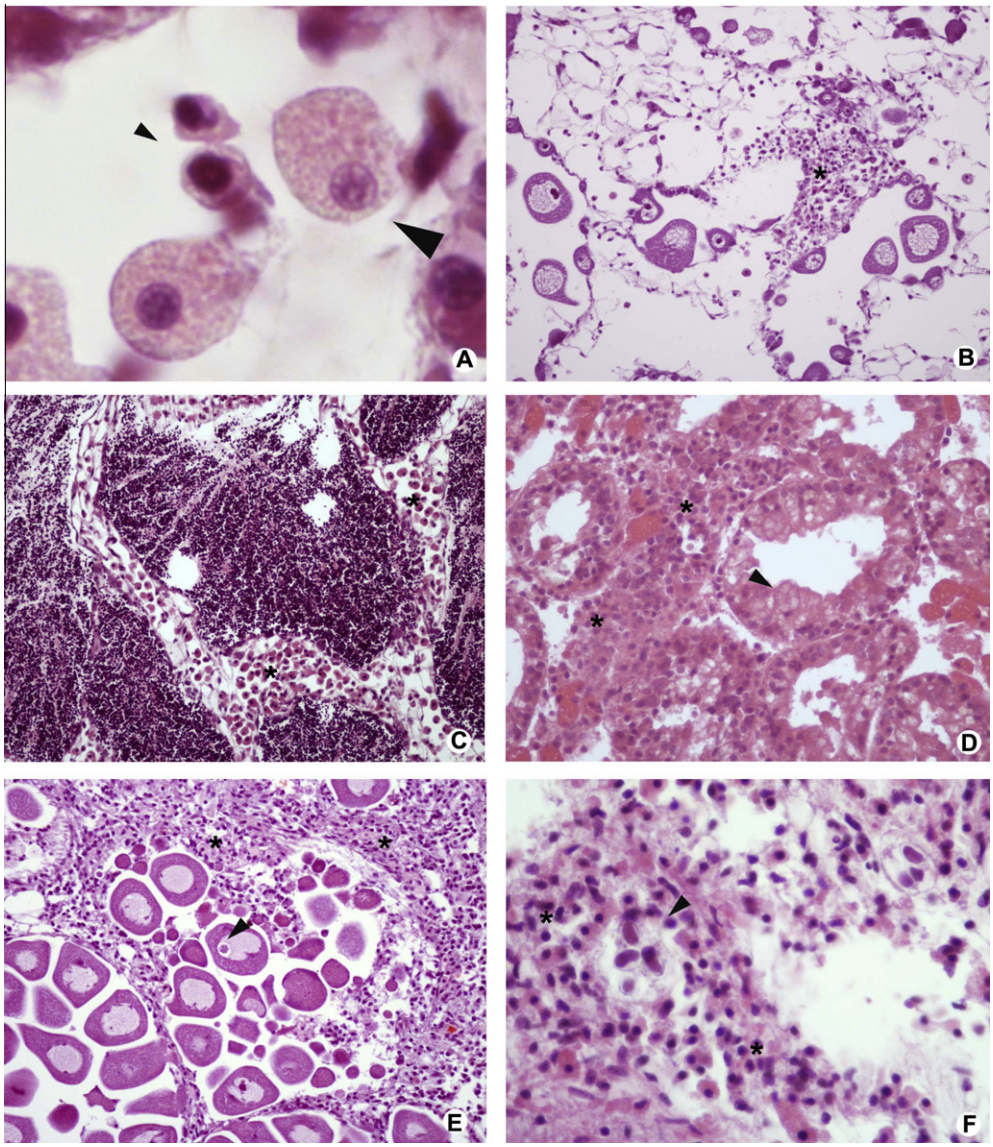

Fig. 1. (A) Haemocyte typology: hyalinocyte (little arrowhead), granulocyte (big arrowhead) (150×). (B) Ovarian focal inflammation (20×). (C) Testicle: diffuse-type inflammation (25×). (D–F) Infection with *Marteilia refringens* (arrowhead), *Steinhausia mytilovum* (arrowhead) and *Nematopsis* sp. (arrowhead) showing diffuse inflammation in the digestive gland, ovary and mantle, respectively (50×, 40×, 40×). *Haemocytes.