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Pathology of tissue loss (white syndrome) in *Acropora* sp. corals from the Central Pacific

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ABSTRACT

We performed histological examination of 69 samples of *Acropora* sp. manifesting different types of tissue loss (*Acropora* White Syndrome-AWS) from Hawaii, Johnston Atoll and American Samoa between 2002 and 2006. Gross lesions of tissue loss were observed and classified as diffuse acute, diffuse subacute, and focal to multifocal acute to subacute. Corals with acute tissue loss manifested microscopic evidence of necrosis sometimes associated with ciliates, helminths, fungi, algae, sponges, or cyanobacteria whereas those with subacute tissue loss manifested mainly wound repair. Gross lesions of AWS have multiple different changes at the microscopic level some of which involve various microorganisms and metazoa. Elucidating this disease will require, among other things, monitoring lesions over time to determine the pathogenesis of AWS and the potential role of tissue-associated microorganisms in the genesis of tissue loss. Attempts to experimentally induce AWS should include microscopic examination of tissues to ensure that potentially causative microorganisms associated with gross lesion are not overlooked.

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1. Introduction

Diseases such as white band (Aronson and Precht, 2001; Gladfelter, 1982) and white pox (Patterson et al., 2002) that cause tissue loss and partial to total colony mortality (Bythell et al., 2004) are believed to have been principal factors in the decline of the once dominant *Acropora palmata* and *A. cervicornis* in the Caribbean (Aronson et al., 1998). Tissue loss diseases termed "white syndromes" are also emerging as a problem for corals in the Indo-Pacific (Aeby, 2005; Willis et al., 2004).

The study of tissue loss in *Acropora* has proved challenging, in part, because this lesion is non-specific and probably has multiple causes (Work and Aeby, 2006). Some tissue-loss lesions are explained by factors such as predation, which is evidenced by presence of the predators directly associated with tissue loss or distinctive marks that can be identified in the field (Raymundo et al., 2008). However, in many cases, an explanation of the lesion is absent, and often the default assumption is that infectious agents are probably responsible. For example, several experimental transmission studies have implicated *Arantimonas coralicida* (Denner et al., 2003), *Vibrio* spp. (Gil-Aguledo et al., 2006; Sussman et al., 2008), and *Serratia marcescens* (Patterson et al., 2002) as bacterial causes of various types of tissue loss in *Acropora* in the Atlantic and Pacific. However, the morphologic end point for all these studies was replication of gross lesions with no microscopic confirmation of bacteria-induced pathology. Presumably, if bacteria (or any other microorganism larger than a virus) were the potential cause of tissue loss in *Acropora*, characteristic pathology (e.g., cell death associated with these organisms) should be evident at the microscopic level (Beckman et al., 1981).

To gain a greater understanding of *Acropora* White Syndrome (AWS), we systematically described gross and microscopic morphology of tissue-loss lesions in this genus in the Central Pacific.

2. Materials and methods

Tissue loss was documented as part of ongoing coral disease surveys at French Frigate Shoals (Hawaii), Johnston Atoll, and American Samoa between 2002 and 2006. Corals manifesting lesions were photographed and placed into categories based on distribution (diffuse, focal, multifocal) and type of tissue loss (acute, subacute). Acute tissue loss included lesions revealing bare white intact skeleton, whereas subacute tissue loss involved a gradual progression from bare white intact to alga covered skeleton giving it a green-yellow hue (Work and Aeby, 2006). Presence of predators directly associated with tissue loss was documented.

For microscopy, tissues were sampled with a bone shear carefully ensuring that the border between intact tissue and lesion was included. Coral fragments were fixed in Z-fix diluted 1:5 in seawater within 20–30 min of collection. Corals were decalcified

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in formic acid/formaldehyde (Cal Ex-II, Fisher Scientific), embedded in paraffin, sectioned at 5 μm, and stained with hematoxylin and eosin. If warranted, Gram's and Grocott's methenamine silver staining procedures were used to identify bacteria and fungi, respectively (Prophet et al., 1992). We sampled one fragment per colony ($n = 69$) and examined 1–2 histology sections from each fragment on histology.

At the microscopic level, host response was classified into three categories: (1) Tissue fragmentation characterized by loss of epidermis and exposure of basal body wall and mesenterial filaments; (2) Suspect wound repair characterized by fragmented tissues with evidence of epidermal regeneration (Work and Aeby, 2010) and (3) Necrosis characterized by cytoplasmic hypereosinophilia or fragmentation associated with nuclear karyolysis, karyorrhexis or pyknosis. Tissue samples with an absence of evident microscopic alterations were classified as "no lesion". Algae were identified by the presence of cell walls and sponges as metazoans consisting of connective tissue matrix with spicules and choanocytes (Hyman, 1940). Cyanobacteria were identified based on characteristic trichrome morphology (Stanier and Cohen-Bazire, 1977). Morphologic diagnoses were not always mutually exclusive, and in such cases (e.g. suspect wound repair and necrosis) the lesion or associated organism predominating was given nomenclatural priority.

3. Results

We found gross lesions of *Acropora* tissue loss fit into three general categories: Diffuse subacute (Fig. 1A), diffuse acute (Fig. 1B), and focal to multifocal acute to subacute (Fig. 1C). The most commonly sampled gross lesion was diffuse subacute tissue loss (40/69 or 58% of sampled corals) followed by diffuse acute tissue loss (25/69 or 36%), and diffuse to multifocal acute to subacute tissue loss (4/69 or 6%) (Table 1). At least nine species of *Acropora* were sampled with *A. cytherea* and plating morphs predominating (44/69 or 64%) (Table 2).

Table 1
Types of *Acropora* tissue loss sampled for histopathology partitioned by region.

	American Samoa	French Frigate Shoals	Johnston Atoll	Total
Tissue loss diffuse acute	11	4	10	25
Tissue loss diffuse subacute	24		16	40
Tissue loss focal to multifocal acute to subacute	2	1	1	4
Total	37	5	27	69

Table 2
Types of *Acropora* tissue loss sampled for histopathology partitioned by species.

Animal	Tissue loss diffuse acute	Tissue loss diffuse subacute	Tissue loss focal to multifocal acute to subacute	Total
A. abrotenoides	1		1	2
A. austera		2		2
A. branching	1			1
A. clathrata		4		4
A. crateriformis	3	1		4
A. cytherea	14	19	2	35
Acropora encrusting	4		1	5
A. hyacinthus	1	5		6
Acropora plating		9		9
Acropora sp.	1			1
Total	25	40	4	69

Any given gross lesion had within it multiple different microscopic changes. The most common host response was suspect wound repair (34/69 or 49%) followed by necrosis (23/69 or 33%) and fragmentation (7/69 or 7%); the remainder of samples showed no evident microscopic lesions. Significantly more necrosis was seen in corals manifesting gross evidence of acute tissue loss

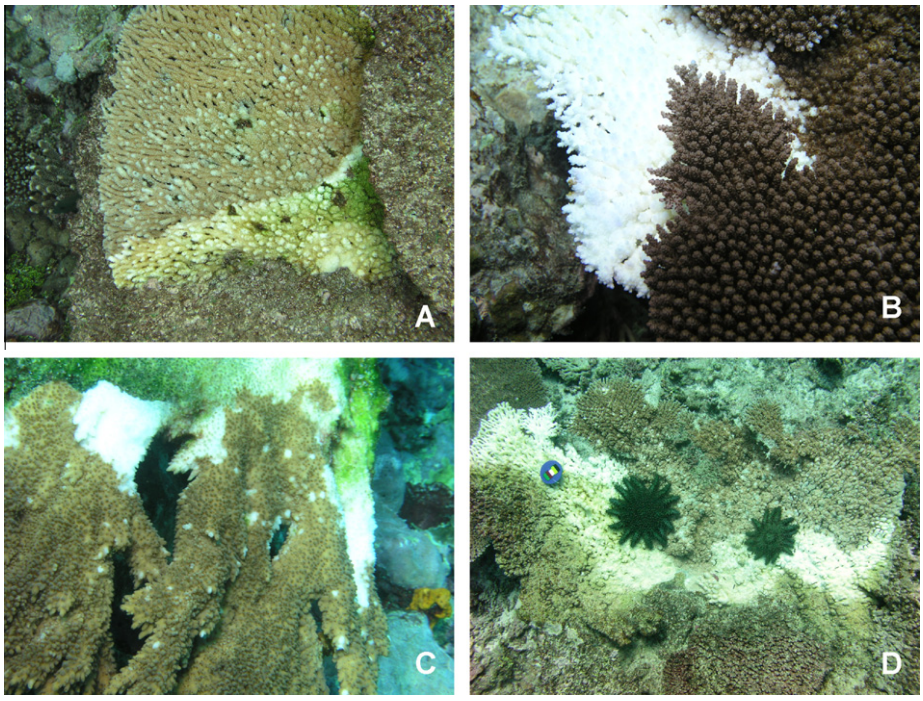

Fig. 1. (A) *A. clathrata* with diffuse subacute tissue loss, American Samoa. (B) *A. hyacinthus* with diffuse acute tissue loss, American Samoa (C) *A. abrotenoides* with multifocal to diffuse acute to subacute tissue loss, American Samoa (D) *A. cytherea* with diffuse subacute tissue loss associated with crown-of-thorns starfish, Johnston Atoll.

whereas significantly more wound repair was seen in corals manifesting gross evidence of subacute tissue loss (Chi square = 7.6, $p = 0.02$, $n = 69$).

Suspect wound repair in *Acropora* was characterized by areas of tissue fragmentation revealing exposed basal body wall and mesenterial filaments with localized areas of presumed epidermal regeneration (Fig. 2A). We based this morphologic diagnosis on its similarity to wound repair in another coral species (*Montipora capitata*) from the same family (Acroporidae) where this process has been systematically described (Work and Aeby, 2010). We acknowledge that wound repair has not been experimentally described in *Acropora*, hence our use of the qualifier "suspect". That said, given the limited data on pathogenesis of disease in corals, we judge this morphologic diagnosis to be a reasonable inference because host responses at the cellular level tend to be broadly similar among related classes of animals (Montali, 1988). Necrosis was usually exemplified by masses of eosinophilic debris mixed with zooxanthellae and nuclear debris (Fig. 2B) and occasionally associated with clumps of hyaline membranous material (Fig. 2B).

Numerous organisms were observed associated with lesions including algae, sponges, fungi, helminths, ciliates and cyanobacteria (Table 3). Of 24 cases with associated organisms, ciliates were most common (30%) followed by algae (25%), helminths (21%), sponges or fungi (12% each) and cyanobacteria (remainder) (Table 3). Ciliate infection was exemplified by invasion of ciliates replete with zooxanthellae into gastrovascular canals associated with clumps of bare mesoglea and cellular debris (Fig. 2C). Various morphologies and sizes of algae were present associated with necrosis or fragmentation (Fig. 2D). Helminths were often seen along with ciliates or fungi (Fig. 2E), but sponge-coral interactions were invariably associated with a leading front of mixed filamentous irregular walled branching structures some of which stained

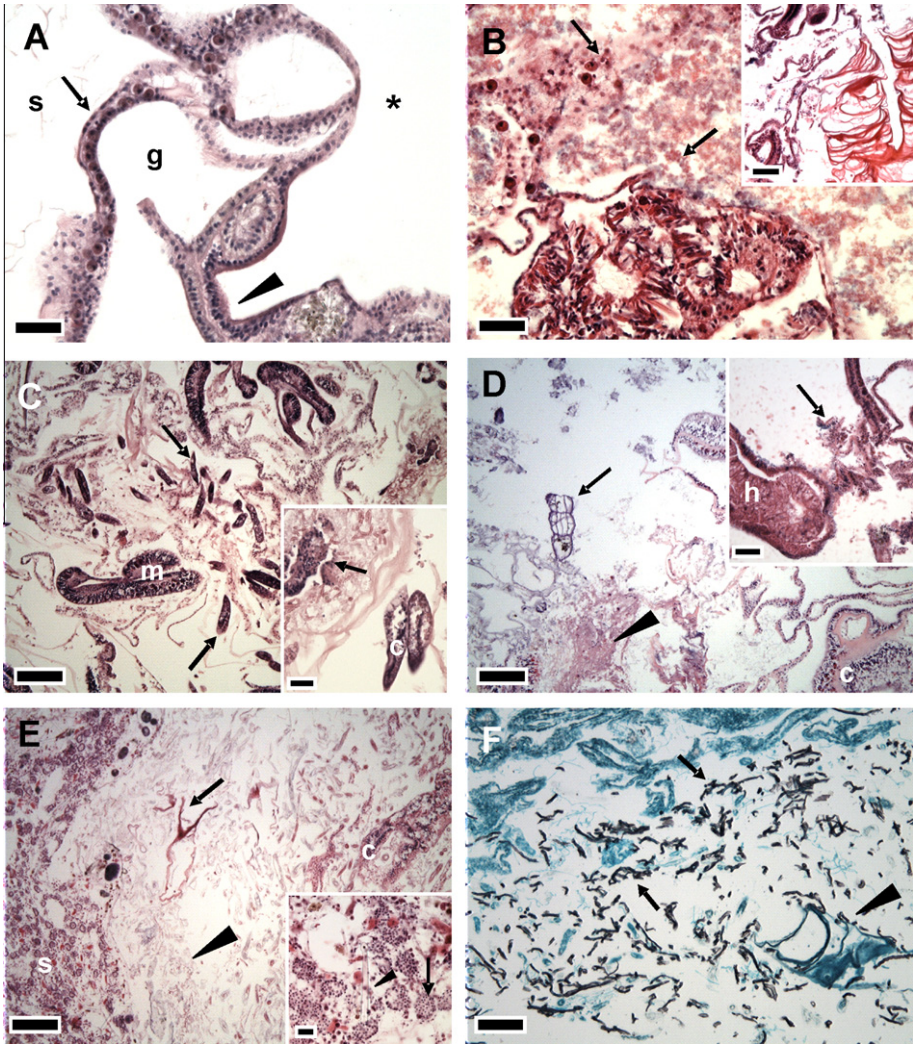

Fig. 2. (A) Suspect wound repair in plating *Acropora* with diffuse subacute tissue loss. Note exposed basal body wall (asterisk), skeleton (s), gastrovascular canals (g), simple squamous calicodermis (arrow) and epithelial regeneration characterized by cuboidal cells (arrowhead) bar = 20 μm. (B) Necrosis (cytoplasmic and nuclear debris with loss of cellular architecture) in *A. abrotenoides* with subacute to acute multifocal to diffuse tissue loss. Note mesenterial filament (m) adjacent to eosinophilic cellular debris (arrows); bar = 20 μm. Inset – necrosis in *A. clathrata* with diffuse subacute tissue loss. Note regular lamina of hyaline membranes (right) adjacent to fragmented and necrotic coral tissues (left), bar = 30 μm. (C) Ciliate invasion and necrosis in *A. cytherea* with diffuse acute tissue loss. Note ciliates (arrows) adjacent to fragments of mesoglea and eosinophilic debris; m = mesenterial filaments; bar = 60 μm. Inset-ciliates (c) adjacent to mesogleal and cellular debris (arrow); bar = 20 μm. (D) Necrosis (arrowhead) associated with algae (arrow) in *A. cytherea* with diffuse acute tissue loss; bar = 60 μm. Inset – helminth (h) associated with tissue fragmentation (arrow) in *A. clathrata* with diffuse subacute tissue loss; bar = 15 μm. (E) Sponge invasion in *A. crateriformis* with acute diffuse tissue loss. Note sponge (s) separated from necrotic coral tissue (c) by mats of invasive fungal hyphae (arrowhead) mixed with clumps of hyaline mesogleal fragments (arrow), bar = 60 μm. Inset – close up of sponge tissue-note choanocytes (arrow) mixed with granular red pigment cells and spicule (linear non-staining structure-arrowhead); bar = 10 μm. (F) Grocott's methenamine silver stain of E. Note silver positive fungal hyphae (arrows) invading coral tissue and clumps of mesoglea (arrowhead); bar = 30 μm.

Table 3
Morphologic diagnoses on microscopy partitioned by gross lesions.

	Tissue loss diffuse acute	Tissue loss diffuse subacute	Tissue loss focal to multifocal acute to subacute	Grand total
Fragmentation	1	1		2
Fragmentation and algae	1			1
Fragmentation and cyanobacteria		1		1
Fragmentation and Sponge	1			1
Necrosis	3	2	1	6
Necrosis and algae	2	2	1	5
Necrosis and ciliates	3	3		6
Necrosis and sponge	2			2
Necrosis and sponge and fungi	1			1
Necrosis, ciliates, helminths		1		1
Necrosis, fungi			1	1
Necrosis, fungi, helminthes	1			1
No remarkable lesion	2	5		7
Wound repair	7	19	1	27
Wound repair and helminths		1		1
Wound repair and necrosis		3		3
Wound repair and sponge	1			1
Wound repair, necrosis and helminth		2		2
Grand total	25	40	4	69

positive with silver and were judged based on this to be fungi (Fig. 2E–F). Invasive organisms observed in this study were most often associated with necrosis (17/23 or 74%), followed by fragmentation (2/4 or 50%) and wound repair (4/34 or 12%). No bacteria were visualized associated with lesions either on hematoxylin and eosin or Gram's stain.

4. Discussion

Acute tissue loss in *Acropora* manifests mainly as necrosis, an active process of cellular degeneration that is most often associated with various organisms. The role of these organisms has two interpretations. (1) Either they are the cause of the tissue loss or (2) Some other insult has allowed tissue necrosis to occur and these organisms are secondary scavengers or colonizers. The organisms seen here are capable of causing tissue necrosis in other species, so the first explanation is plausible. For example, fungi (Sexton and Howlett, 2006) and ciliates (Small et al., 2005) secrete proteases and other compounds that break down cell membranes and walls allowing them to invade animal and plant tissues. Algae are also known to cause invasive tissue disease in vertebrates (Stenner et al., 2007) and invertebrates (Shields et al., 2003) although the mechanisms of pathogenesis are not as defined as in fungi (Stenner et al., 2007). Whether the organisms we observed play a primary or secondary role in causation of tissue loss remains uncertain, but their presence certainly merits further investigations. Ciliates have been associated with tissue loss in *Acropora* (Bourne et al., 2008), helminths have caused tissue loss in *Montipora* in Hawaii (Jokiel and Townsley, 1974), algae (McCook et al., 2001) have been associated with gross or microscopic pathology in other corals, and so a precedent exists.

Necrosis, particularly those cases where no associated organisms were present on light microscopy, could also be caused by viruses or mycoplasma or some type of toxin or toxicant. Some viruses can form intracytoplasmic or intranuclear inclusions visible on light microscopy in vertebrates (Roberts, 2001) and invertebrates (Sparks, 1985); however we saw no evidence of this in the corals examined here. Confirming the role of viruses or mycoplasma would require examination of tissues at the ultrastructural level. Digestive enzymes from a predator could be one potential local toxicant that would explain some uncomplicated tissue necrosis; for example, crown-of-thorns starfish evert their stomach over tissues leading to localized lysis of cells (Hanscomb et al., 1976). Extracellular bacteria are also known to secrete toxins that kill cells (Hueck, 1998), however reconciling this mechanism as a cause of tissue loss in *Acropora* in this study with absence of bacteria on histology is problematic.

Subacute tissue loss in *Acropora* manifests mainly as wound repair confirming our field suspicions that this gross lesion indicates a more regenerative cellular process. Evidence of regeneration of lesions in *Montipora capitata* (an Acroporid coral) affected by white syndrome has been documented in field studies in Hawaii (Aeby et al., 2010). This impression is supported by the lack of invasive organisms associated with wound repair at the cellular level (in contrast to observations in necrosis). In some cases corals with subacute tissue loss were in proximity to known predators, crown-of-thorns starfish (Fig. 1D), suggesting that predators may have been the reason for subsequent wound repair or necrotic lesions of those samples. However, to be conservative, a diagnosis of predator-associated tissue loss was not made unless the predator was visibly associated with the lesions. Predation (such as by *Drupella* sp. or crown-of-thorns) can result in lesions of acute or subacute tissue loss in coral, therefore, it is advised when describing tissue-loss lesions, that the immediate scene is investigated for coral predators. Although some predators such as parrotfish can leave distinctive lesions (Raymundo et al., 2008), predation is a transient event with some predators being cryptic or nocturnal. Sorting this out may require continuous long-term monitoring of individual colonies over a 24 h period.

Ten percent (7/69) of samples with gross evidence of tissue loss had no microscopic lesions. Either we failed to trim the area of the tissue manifesting the lesion, or we were seeing completely healed tissues. Controlled studies of wound repair in *M. capitata* usually revealed complete wound repair and normal microscopic appearance of tissues long before the gross lesions regained completely normal fully pigmented appearance probably because of incomplete colonization of regenerating tissue by zooxanthellae (Work and Aeby, 2010).

We saw no evidence of bacteria-induced necrosis (microcolonies of bacteria associated with cell death) in the classical sense as seen in mammals (Cheville, 1988), birds (Randall and Reece, 1996), reptiles (Jacobson, 2010), fish (Roberts, 2001), crustacea (Sparks, 1985), plants (Nelson and Dickey, 1970), or wounds in vertebrates caused by marine *Vibrio* sp. (Beckman et al., 1981). Investigations of *Acropora* white syndrome in Australia using in situ hybridization revealed presumably symbiotic bacterial aggregates but not bacteria associated with lesions (Ainsworth et al., 2006); however, increased aggregates of bacteria were seen in *Acropora* manifesting white band diseases from the Atlantic but were also seen in normal tissues (Peters et al., 1983). A variety of bacteria are associated with diseased and healthy coral tissue, and in many cases, the flora between the two differ (Pantos et al., 2003; Pantos and Bythell, 2006). Manipulative studies have implicated bacterial infections as causing tissue loss in corals (Richardson et al., 1998; Patterson et al., 2002; Sussman et al., 2008); however, presence of bacteria associated with lesions at the microscopic level for these experimental transmissions awaits confirmation.

In contrast, in this study we saw a panoply of organisms associated with tissue loss in *Acropora*, which could plausibly cause cellular necrosis yet none of which were readily visible grossly. This study confirms a recurring pattern that any given gross lesion in corals can have multiple microscopic manifestations (Williams et al., 2010; Work and Rameyer, 2005) and illustrates the nonspecific nature of gross lesions in corals when it comes to changes

at the cellular level. Careful manipulative studies and monitoring of the development of coral lesions over time (pathogenesis) in captive and field situations coupled with descriptions of changes at the cellular and subcellular levels can go a long way towards shedding light on potential causes of coral disease. To avoid confounding interpretation of results, investigators wishing to experimentally replicate tissue loss in *Acropora* should ensure that experimental animals are free of these organisms grossly and at the light microscopy level prior to initiating experiments. Confirming presence of organisms associated with experimentally induced lesions at the light microscopy level is also particularly when infecting corals with organisms larger than viruses or mycoplasma that should be visible on light microscopy.

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