



Contents lists available at ScienceDirect

Journal of Autoimmunity

journal homepage: www.elsevier.com/locate/jautimm

Tick-borne diseases and autoimmunity: A comprehensive review

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ARTICLE INFO

Article history:

Received 14 September 2017

Received in revised form

20 November 2017

Accepted 20 November 2017

Available online xxx

Keywords:

Autoimmune diseases

Autoimmunity

Infection

Ticks

Tick-borne diseases

Autoimmune ecology

ABSTRACT

Tick-borne diseases (TBDs) are emerging and reemerging diseases transmitted by ticks, which portray wide heterogeneity and global distribution. TBDs may present acute clinical pictures that resemble those of autoimmune diseases (i.e., musculoskeletal symptoms, cutaneous involvement, neurologic impairment, renal failure, etc.), and in some cases infection is considered a triggering factor for autoimmunity (e.g., rheumatoid arthritis, autoimmune thyroid disease, vasculitides). The clinician should consider TBDs among the differential diagnoses when approaching autoimmune-like signs in areas of tick infestation. Epidemiological setting (e.g., endemic areas, seasons) and an accurate diagnostic approach (i.e., clinical history, physical examination and laboratory tests) are necessary to confirm TBDs. Further, control and prevention of TBDs is warranted. Research in the fields of ticks microbiome and vaccination (i.e., wildlife and humans) are ahead to control vector transmission and bacterial infection. This review offers a comprehensive update on TBDs and their relationship with autoimmunity.

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Contents

| | |
|--|----|
| 1. Introduction | 00 |
| 2. Ticks | 00 |
| 3. Infectious diseases and ticks | 00 |
| 3.1. Bacteria | 00 |
| 3.1.1. Borrelioses | 00 |
| 3.1.2. Rickettsioses | 00 |
| 3.1.3. Ehrlichiosis and anaplasmosis | 00 |
| 3.1.4. Q fever | 00 |
| 3.1.5. Tularemia | 00 |
| 3.2. Parasites | 00 |
| 3.2.1. Babesiosis | 00 |
| 3.3. Viruses | 00 |
| 3.3.1. Tick-borne encephalitis virus | 00 |
| 3.3.2. Hemorrhagic fever virus and tick-borne coltivirus | 00 |
| 4. Tick borne diseases and autoimmunity | 00 |
| 4.1. Tick-borne diseases and ADS | 00 |
| 4.2. Systemic sclerosis | 00 |
| 4.3. Sarcoidosis | 00 |
| 4.4. Dermatomyositis | 00 |
| 4.5. Rheumatoid arthritis | 00 |
| 4.6. Ankylosing spondylitis | 00 |
| 4.7. Polymyalgia rheumatica | 00 |

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<https://doi.org/10.1016/j.jaut.2017.11.007>

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| Abbreviations | | | |
|---------------|---------------------------------------|------------|--|
| TBD | Tick-borne disease | BD | Behçet's disease |
| TBDs | Tick-borne diseases | TNF | Tumor nuclear factor |
| ADs | Autoimmune diseases | Osp | Outer surface protein |
| RA | Rheumatoid arthritis | aPL | Antiphospholipid antibodies |
| GBS | Guillain-Barré syndrome | TLR | Toll-like receptor |
| CNS | Central nervous system | PNS | Peripheral nervous system |
| LD | Lyme disease | LFA | Lymphocyte function-associated antigen |
| RF | Relapsing fever | EC | Endothelial cells |
| US | United States | RMSF | Rocky mountain spotted fever |
| BBB | Blood-brain barrier | TSH | Thyroid-stimulating hormone |
| STARI | Southern-tick-associated rash illness | GD | Grave's disease |
| SSc | Systemic sclerosis | aCL | Anti-cardiolipin |
| AS | ankylosing spondylitis | Anti-β2GP1 | anti-β2-glycoprotein-1 |
| GCA | Giant-cell arteritis | LAC | Lupus anticoagulant |
| MS | Multiple sclerosis | ANCA | Anti-neutrophil cytoplasmic antibody |
| GBS | Guillain-Barré syndrome | TA | Thromboangiitis obliterans |
| TM | Transverse myelitis | HME | Human monocytic ehrlichiosis |
| HT | Hashimoto thyroiditis | HGA | Human granulocytic anaplasmosis |
| APS | Antiphospholipid syndrome | AHA | Autoimmune hemolytic anemia |
| GPA | Granulomatosis with polyangiitis | IT | Immune thrombocytopenia |
| PBS | Primary biliary sclerosis | Th1 | T-helper cell type 1 |
| SLE | Systemic lupus erythematosus | TBEV | Tick-borne encephalitis virus |
| PMR | Polymyalgia rheumatica | ADEM | Acute disseminated encephalomyelitis |
| AITD | Autoimmune thyroid disease | ASMA | Anti-Smooth-Muscle Antibody |
| | | AMA | Antimitochondrial antibodies |
| | | HFVs | Hemorrhagic fever viruses |

| | | |
|-------|---|----|
| 4.8. | Reactive arthritis | 00 |
| 4.9. | Vasculitides | 00 |
| 4.10. | Uveitis | 00 |
| 4.11. | Multiple sclerosis | 00 |
| 4.12. | Guillain-Barré syndrome | 00 |
| 4.13. | Transverse myelitis | 00 |
| 4.14. | Autoimmune thyroid disease | 00 |
| 4.15. | Autoimmune hemolytic anemia | 00 |
| 4.16. | Immune thrombocytopenia | 00 |
| 4.17. | Antiphospholipid autoantibodies and antiphospholipid syndrome | 00 |
| 4.18. | Autoimmune liver disease | 00 |
| 5. | Tick borne diseases and likely associations with autoimmunity | 00 |
| 5.1. | Systemic lupus erythematosus-like syndrome | 00 |
| 5.2. | Fibromyalgia | 00 |
| 5.3. | Morphea | 00 |
| 5.4. | Crohn's disease | 00 |
| 5.5. | Addison's disease associated with celiac autoantibodies | 00 |
| 5.6. | Protein S deficiency | 00 |
| 5.7. | Other autoimmune diseases | 00 |
| 6. | Tick borne diseases prevention | 00 |
| 7. | Conclusion | 00 |
| | Funding | 00 |
| | Acknowledgement | 00 |
| | Supplementary data | 00 |
| | References | 00 |

1. Introduction

Tick-borne diseases (TBDs) are emerging and re-emerging pathogens [1]. Recently, several emerging infections such as Zika and Chikungunya viruses have been associated with autoimmune phenomena [2,3]. TBDs may present acute clinical pictures that resemble those of autoimmune diseases (ADs) (i.e., musculoskeletal

symptoms, vasculitis, cutaneous involvement, neurologic impairment, renal failure, etc.) [4,5]. Further, the association of some ADs with TBDs (i.e., rheumatoid arthritis [RA], Guillain-Barré syndrome [GBS]) have increased the suspicion of induced autoimmunity through mechanisms of bystander activation, epitope spreading, molecular mimicry and original antigenic sin [6–8]. In addition, apoptosis induced by bacteria promoting self-peptides

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