LETTER TO THE EDITOR

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HLA-genotyping and the historical naming process of an old disorder

Genotipagem de HLA e o processo histórico de nomenclatura de uma doença antiga

Cem Evereklioglu[1]

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Dear Editor,

I read the article by Metzger et al. entitled "*Endovascular treatment of aortic saccular aneurysms associated with Adamantiades-Behçet disease*" (BD, 2021). They reported a 49-year-old man with an abdominal aorta aneurysm treated with an inferior vena cava filter and endovascular repair. I thank the authors for their efforts. However, I have 2 questions to be clarified:

1) They stated that BD has associations with HLA-B51 and HLA-B27. However, BD is strongly associated with HLA-B51,[1,2] but weakly with HLA-B27[3] and there is no study linking BD strongly with HLA-B27. Indeed, an HLA-B27-related non-infectious entity is associated with ankylosing spondylitis uveitis.[4,5] I wonder whether the authors performed HLA analyses or did they demonstrate any link with HLA-B27 or HLA-B51?

2) This disorder was called by the authors "Adamantiades-Behçet". Investigators before Hulusi Behçet reported several Behçet findings since Hippocrates,[6] such as Planner and Remenovsky (1922)[7] and Pils (1925).[8] However, none indicated a novel disease with the "classical-triad". Adamantiades concluded that "hypopyon iritis" (not classical-triad) constitutes a distinct entity, which can occur in many disorders.[9] Hulusi Behçet was the first to realize and group dermato-ophthalmological findings into one disease (triple-symptom-complex; 1937-1940).[10-12] Metzger et al. used the "International Study Group Criteria for BD" (not Adamantiades-Behçet). The authors should respect the name of an established old disease and no-one should try to change it. Therefore, the authors should address the reason for preferring the eponym Adamantiades-Behçet. Why should only Dr. Adamantiades be honored? PubMed reveals 13,315 Behçet articles (1946-2022), and 175 Adamantiades-Behçet (1970-2022). Similarly, they used 17 articles in the reference and only one paper stated it as "Adamantiades-Behçet". It is the authors' responsibility to use the correct, accepted, and established international eponym because editors may not realize such a historical naming process. The "Jornal Vascular Brasileiro" published 5 articles, all using Behçet without exception. Moreover, the American BD Association, International BD Society, and Japan BD Committee all call the disease "Behçet" to honor the first describer of the "triple-symptom-complex". Furthermore, textbooks of dermatology, rheumatology, and ophthalmology, and international congresses call this entity BD, not Adamantiades-Behçet. Adamantiades himself named the syndrome "Behçet".[13] I think it is time to abandon efforts to change the name of an old syndrome.

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[1] Department of Ophthalmology, Division of Uvea-Behçet Unit, Erciyes University Medical Faculty, Kayseri, Turkey.
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Correspondence:
Cem Evereklioglu
Erciyes University Medical Faculty, Division of Uvea-Behçet Unit,
Department of Ophthalmology,
Talas
Kayseri, Turkey
Tel.: +90-530 5616306
E-mail: cemevereklioglu@gmail.com

Author information
CE - Professor of Ophthalmology from the Department of Ophthalmology, Division of Uvea-Behçet Unit, Erciyes University Medical Faculty, Kayseri, Turkey.

RESPONSE LETTER

Dear Editor,

We read the aforementioned letter to the editor about the article we published entitled: Endovascular treatment of aortic saccular aneurysms associated with Adamantiades-Behçet disease[1]. We thank the author for reading and for his well-founded questions. Below are the answers to clarify the questions:

1- In this study we did not perform HLA analysis. A large number of studies have shown a link between the disease and HLA-B51 and HLA-B27 antigen.[2-5] It has been shown that susceptibility to Adamantiades-Behçet disease or Behçet disease is strongly associated with the presence of HLA-B51 cells and the frequency within families has been shown to be up to 15%.[2] Environmental factors, such as infectious agents, have also been implicated in this pathogenesis.[2] However, the correlation with HLA-B27 is significant, although not strong, as demonstrated in the recent 2019 meta-analysis published by Khabbazi et al.,[6] in which they determined that the prevalence of "HLA-B27" in patients with Behçet disease compared with controls was 1.55 (95%CI 1.01-2.38), P = 0.04.

2- In 1930, Benediktos Adamantiades (1875-1962), Greek ophthalmologist from Prussa - Asia minor, presented a lecture with the title "A case of relapsing iritis with hypopyon", describing a 20-year-old male patient with the three cardinal signs of the disease. The disease had begun at the age of 18 with edema and ulcerations of the left leg diagnosed as thrombophlebitis. Over the following 2 years (1928-30), the patient developed recurrent iritis with hypopyon in both eyes that led to blindness and atrophy of the optic nerve, scrotal ulcers healing with scars, oral aphthous ulcers, and sterile arthritis of both knees. The last three signs were recurrent. Bacterial cultures of knee and anterior eye chamber punctures were sterile and inoculation experiments in animals were negative, whereas staphylococci grew in cultures from scrotal ulcers and a tonsillar abscess. The lecture was published in the Proceedings of the Medical Society of Athens[7] in the same year and in the French journal Annales d'Oculistique in the following year.[8] Adamantiades identified the genital ulcers, the arthritis, and the ocular signs in conjunction as signs of a single disease. In 1946, Adamantiades reported two further patients and defined thrombophlebitis as a fourth cardinal sign of the disease.[9] Later, he presented the first classification of the disease by describing the ocular, mucocutaneous, and systemic forms in a review article.[10] He pointed out that the disease can occur for years as a monosymptomatic or oligosymptomatic

disorder and that eye involvement and severe prognosis are more common in men than in women. In this paper he also proposed the first diagnostic criteria.

On May 11, 1937, Hulsi Behçet (1889-1948) presented a 34-year-old female patient with recurrent oral aphthous ulcers, genital ulcers, and ocular lesions for 7 years at the meeting of the Dermatological Association of Istanbul. This patient's case was published by Behçet the same year, together with a 40-year-old old man with a disease history of over 20 years.[11] The microscopic Giemsa preparation from an oral ulcer of the first patient showed structures whose size corresponded to smallpox elementary bodies and therefore Behçet initiated the hypothesis of the viral etiology of the syndrome.[12] Over the following 3 years he published articles on five further patients in different languages.[12-16] In these publications he added periodontitis, jaw cysts, acneiform skin lesions, erythema nodosum, and arthralgia to the so-called "triple symptom complex". He was convinced of the autonomy of this multisymptomatic illness and of its viral etiology and finally drew the attention of the scientific community to this puzzling disease.

The first description of the disease was neither by Adamantiades nor by Behçet. Hippokrates of Kos (460-377 BC) had already described an illness whose manifestations fit very well with the cardinal signs of Adamantiades-Behçet's disease in the fifth century before Christ in his third "Epidemion" book.[17]

The term "Adamantiades-Behçet's disease" honors both first describers of the several manifestations constituting an autonomous disease in modern times.

The intention of our article was not to discuss the merits of the nomenclature, nor to be little any of the authors who collaborated in recognition of the disease. We recognize as positive all contributions in the process of describing this old syndrome. Therefore, the objective of the article was to report and describe the interventionist approach to an inflammatory disorder with aortic involvement that is not prevalent.

We are glad that our article has generated scientific discussion.

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Patrick Bastos Metzger[1],
Kamilla Rosales Costa[1],
Simone Lessa Metzger[1,2,3],
Leonardo Cortizo de Almeida[4]

[1] Escola Bahiana de Medicina e Saúde Pública (EBMSP), Salvador, BA, Brasil.
[2] Universidade Salvador (UNIFACS), Salvador, BA, Brasil.
[3] Hospital Santo Antônio, Obra Sociais Irmã Dulce (OSID), Salvador, BA, Brasil.
[4] Hospital Geral Roberto Santos (HGRS), Salvador, BA, Brasil.

Correspondence:
Patrick Bastos Metzger
Escola Bahiana de Medicina e Saúde Pública (EBMSP)
Rua Professor Diógenes Rebouças, Pituba
CEP 41830-570 - Salvador (BA) - Brazil
Tel.: +55 (71) 99977-6356
E-mail: patrickvascular@gmail.com

Author information
PBM - PhD in Medicin from Universidade de São Paulo (USP); vascular and endovascular surgeon from Sociedade Brasileira de Angiologia e Cirurgia Vascular; interventional radiologist from Colégio Brasileiro de Radiologia.
KRC - Medical student from Escola Bahiana de Medicina e Saúde Pública (EBMSP).
SLM - Geriatrician from Sociedade Brasileira de Geriatria e Gerontologia; assistant professor at Escola Bahiana de Medicina e Saúde Pública (EBMSP); assistant professor at Universidade Salvador (UNIFACS). Assistant Geriatrician at Geriatric clinic, Obras Sociais Irmã Dulce.
LCA - Vascular and endovascular surgeon from Sociedade Brasileira de Angiologia e Cirurgia Vascular.

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