LETTER TO THE EDITOR

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Clinical terminology and biological mediators in allergology: why biomarkers do not define a syndrome

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To the Editor,

the present letter is prompted by the recent introduction in the scientific literature of molecular designations, such as "defensin syndrome" or "defensin-related allergy syndrome", to describe clinical presentations that are already well-characterized under established nosological categories. The term "defensin-related allergy syndrome" was first introduced by Cosi and colleagues to denote a novel type of cross-reactive IgE-mediated allergy involving plant defensin-like proteins (1). The terminological and methodological appropriateness of such designations warrants critical scrutiny.

Clinical medicine rests on a methodological principle that has accompanied the development of modern medicine since its origins: the precision of scientific language. Medical terminology is not merely a descriptive tool; it constitutes one of the fundamental elements through which medicine organizes knowledge, defines pathological entities, and ensures the coherence of clinical reasoning. In an era characterized by a remarkable expansion of biological and molecular knowledge, the relationship between clinical language and scientific understanding assumes even greater relevance.

Over recent decades, clinical allergology has benefited substantially from advances in molecular immunology. The structural characterization of allergens, the identification of novel allergenic protein families, and the development of molecular diagnostics have considerably deepened our understanding of the pathogenetic mechanisms underlying allergic diseases – achievements that represent a cornerstone of modern precision medicine.

At the same time, however, the growing availability of molecular information raises a methodological question of considerable importance: how biological knowledge can be correctly integrated into the language and conceptual categories of clinical medicine. In particular, it is essential to avoid the inappropriate transformation of biological mediators or biomarkers into clinical definitions.

Among the foundational terms in the tradition of internal medicine is the concept of syndrome, which denotes a recognizable cluster of signs and symptoms that tend to present with a degree of consistency, thereby constituting a defined clinical picture.

Although a syndrome may be associated with specific pathogenetic mechanisms or with particular laboratory findings, its definition remains intrinsically clinical, deriving from the systematic observation of the patient and from the integration of historical, clinical, and diagnostic data (2).

This distinction between clinical observation and biological description is particularly relevant in the era of molecular medicine. Biomarkers serve as indicators of biological or pathogenetic processes and may have diagnostic, prognostic, or therapeutic utility. Nevertheless, they do not automatically coincide with clinical entities. As emphasized in the translational medicine literature, biomarkers must be interpreted within the clinical context and cannot substitute for the clinical definition of disease (3).

An instructive example concerns defensins, a family of small cationic antimicrobial peptides that are principal effectors of innate immunity, produced by neutrophils and epithelial cells, with both direct antimicrobial and immunomodulatory properties (4-6). Defensin-like proteins are also present in the plant kingdom, where they serve defense functions and may act as allergens, participating in IgE-mediated sensitization in humans (7).

The clinically best-characterized syndrome involving plant allergenic proteins is the pollen-food syndrome, in which individuals sensitized to pollens develop allergic reactions upon ingestion of specific plant-derived foods through cross-reactive IgE epitopes (8); celery allergy associated with pollen sensitization, involving lipid transfer proteins and other plant defense proteins, is a well-documented example (9).

The fact that certain plant proteins belong to the defensin family constitutes an interesting and scientifically valid biological observation. It does not, however, justify the introduction of a clinical definition based solely on the presence of a specific biological molecule. The use of the expression defensin syndrome to describe clinical presentations of food allergy associated with pollen sensitization is therefore methodologically inappropriate. Such conditions are already clearly classified in the scientific literature under the well-established category of pollen-food syndrome – a clinically defined syndrome characterized by the relationship between pollen sensitization and allergic reactions to specific plant-derived foods.

This is not a matter of mere terminological detail. The clarity of scientific language is an essential component of the quality of scientific communication and of the methodological coherence of clinical medicine. Clinical allergology, having developed historically within the tradition of internal medicine, has always grounded its strength in the integration of clinical observation, laboratory data, and biological knowledge. In the era of precision medicine, preserving terminological precision and conceptual rigor becomes even more imperative: biological mediators are indispensable for understanding pathophysiological processes, but the definition of clinical entities continues to rest on the systematic observation of the signs and symptoms that characterize disease in the patient. We therefore propose that the naming of clinical syndromes in allergology should continue to be grounded in phenotypic and clinical criteria, reserving molecular nomenclature for the characterization of specific sensitization profiles within established diagnostic frameworks.

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GDL contributed entirely to this work.

Conflict of interests

The author declares that he has no conflict of interests.

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