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MINI REVIEW

Swiss Amyloidosis Network (SAN): Objectives and Challenges

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Systemic amyloidoses are chronic diseases with important consequences for patients' quality of life, thus presenting a major medical and socioeconomic burden. This article discusses the current diagnostic challenges and therapy options for systemic amyloidosis and summarizes the activities of the Swiss Amyloidosis Network (SAN) which aims to increase awareness of these rare diseases, include patients in the Swiss Amyloidosis Registry for research purposes and develop interdisciplinary guidelines for diagnosis and therapy of systemic amyloidosis in Switzerland.

PEER REVIEWED ARTICLE

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Introduction

Systemic amyloidoses are a heterogeneous group of disorders caused by the accumulation of misfolded proteins in various organs and tissues that may lead to vital organ failure and even death.[1,2] Systemic amyloidoses are chronic diseases with important consequences for patients' quality of life, thus presenting a major medical and socioeconomic burden. Despite recent advances in diagnosis and treatment, systemic amyloidoses continue to be detected late and are probably still undertreated. The Swiss Amyloidosis Network (SAN) aims to increase awareness of these rare diseases, to include patients in the Swiss Amyloidosis Registry for research purposes and to develop interdisciplinary guidelines for diagnosis and therapy of systemic amyloidosis in Switzerland.

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Diagnostic challenges and therapy options

Early diagnosis prior to irreversible organ damage, as well as correct amyloid typing, is critical for initiating appropriate therapy to prevent morbidity and improve survival in patients with systemic amyloidosis. However, establishing the diagnosis of amyloidosis can be challenging.[3-6]

Systemic amyloidosis is a group of rare diseases. Understandably, many healthcare providers are not familiar with the clinical symptoms, diagnostic criteria, and treatment options of these diseases. Clinical symptoms of systemic amyloidosis are often non-specific, vary significantly depending on the affected organ, and may overlap with manifestations of other, more prevalent disorders. Together with systemic wild type transthyretin Amyloidosis (ATTRwt), systemic light chain (AL) amyloidosis are the most common types of amyloidoses. AL amyloidosis is caused by accumulation of immunoglobulin light chains produced by clonal plasma cells or mature B-cells in the bone marrow or in lymph nodes, respectively. Moreover, certain paraproteinemic diseases, such as multiple myeloma or Waldenströms Macroglobulinaemia, can coexist with AL amyloidosis and disguise its presence. In addition, AL amyloidosis can coexist with other types of amyloidosis, for instance ATTR amyloidosis, which can make diagnosis challenging.

There are many subtypes of amyloidosis other than AL amyloidosis, each related to deposition of a different protein and requiring its own unique diagnostic and therapeutic approach. Mutated transthyretin for instance leads to variant transthyretin Amyloidosis (ATTRv) (hereditary) with involvement of the nervous system, whereas wild-type transthyretin is the cause of ATTRwt amyloidosis, both types of ATTR amyloidosis can lead to heart involvement.

Unspecific presenting symptoms of this rare disease are the main drawback hampering early diagnosis of amyloidosis, and to include amyloidosis in the differential diagnostic considerations in routine clinical practice is challenging. Finding the right specialist for further diagnostic work-up and treatment can aggravate the problem of a clinically significant diagnostic and therapeutic delay.

This highlights the need for raising awareness about systemic amyloidosis and for a multidisciplinary support in dedicated amyloidosis excellence centers.

The therapeutic armamentarium has considerably extended during recent years. It starts with the monitoring of N-terminal pro–B-type natriuretic peptide (NT-proBNP), albuminuria and alkaline phosphatase in patients with monoclonal gammopathy of undetermined significance (MGUS), multiple myeloma or Non-Hodgkin Lymphomas presenting with a monoclonal gammopathy and a pathological free light-chain ratio. This screening should help to detect systemic AL amyloidosis at an early stage in

patients at risk. Considering AL amyloidosis, in low-risk disease autologous stem cell transplantation after high-dose chemotherapy is still the mainstay of therapy, whereas intermediate-risk patients will usually receive a combination-therapy containing daratumumab, cyclophosphamide, bortezomib and dexamethasone (Dara-CyBorD). In high-risk patients, there is still no established standard therapy, and the treatment has to be individualized based on comorbidities and toxicity.[4,5]

In ATTRwt amyloidosis with cardiomyopathy, stabilizing tetramer therapy with tafamidis can be prescribed in patients that fulfill the treatment criteria, whereas the genetic silencers patisiran, inotersen and vutrisiran are used in ATTRv with polyneuropathy. Supportive treatments such as salt restriction and diuretics to treat heart failure, fitted elastic stockings to help with hypotension, pacemaker implantation in patients with recurrent arrhythmic syncope, nutritional support to ensure adequate caloric intake, and many others, are very important tesserae in this treatment mosaic.

International amyloidosis networks

There are several international societies and organizations dedicated to amyloidosis. They focus on raising awareness on amyloidosis among the medical community, facilitating research on molecular mechanisms of amyloidosis emergence and progression, developing novel diagnostic and therapeutic guidelines and recommendations, delivering educational resources, and providing support to patients and their families.

Among them are the Amyloidosis Foundation established in the United States in 2007 by joined efforts of healthcare professionals and patients through; a global Amyloidosis Research Consortium (ARC) and the International Society of Amyloidosis (ISA) that promote scientific collaboration and knowledge exchange among researchers and clinicians from around the world; European Network for Rare and Congenital Anemias (ENERCA) that includes studies on certain types of amyloidosis; Amyloidosis Support Groups in the UK and the United States that provide information and emotional support for affected individuals and families; EURORDIS (the Voice of Rare Disease Patients in Europe), a non-profit alliance of over 1000 rare disease patient organizations from 74 countries that aim to improve the lives of millions of people suffering from a rare disease globally.

The Swiss Amyloidosis Network (SAN)

The SAN has been created in 2020 as an initiative to improve care of amyloidosis patients throughout Switzerland. The SAN includes many specialists involved in the care of patients with amyloidosis, among them hematologists, oncologists, cardiologists, gastroenterologists, neurologists, nephrologists, rheumatologists, pathologists, and basic scientists from all university hospitals and major tertiary care centers in Switzerland.

The Swiss Amyloidosis Network organized a first consensus conference in Zurich in January 2020. Its main goal was to define a consensus statement regarding the diagnostic work-up and treatment for systemic amyloidosis, tailored to the Swiss healthcare system. In the same year SAN published an extensive review[7] that covers information on clinical considerations, diagnostic work-up, prognostic factors, treatment options and response assessment in AL amyloidosis. In 2021, SAN published a review on the management of ATTR amyloidosis.[8] Over the years, research activity has increased in Switzerland, with several groups working in basic or translational research, and with the creation of single-center and collaborative clinical projects.

SAN is aiming at including patients with amyloidosis in the Swiss Amyloidosis Registry for research purpose and at opening multinational trials with promising novel drugs in Switzerland.

In summary, the joined efforts of the interdisciplinary amyloidosis excellence teams are aimed to raise awareness of this complex life-threatening condition and will hopefully lead to the deeper understanding of the mechanisms of emergence of amyloidosis, the initiation and acceleration of the diagnostic work-up, the study of efficient treatment approaches, and the improvement quality of life and outcome of patients with systemic amyloidosis in Switzerland.

Conflict of interest

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