Hereditary Angioedema, A National Study in Denmark

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Anette Bygum defended her doctoral thesis "Hereditary and acquired angioedema" at the University of Southern Denmark, Odense, Denmark on 23 January 2015. The dissertation is available in full in a recently published supplement (Forum Nord Derm Venereol 2014; 18 Suppl 17). For several years Anette Bygum dedicated herself to locating patients with this rare disease. A recent article in the Syddansk University Newsletter is highlighting her detective-work in locating patients with hereditary angioedema and her continuing work in diagnosing which rare disease is present in patients with diffuse symptoms. You can read the complete paper at http://www.medicaljournals.se/forum/Syddansk.pdf.

The rare disease hereditary angioedema (HAE) is found in approximately 100 Danish patients. These individuals lack the blood protein complement C1 inhibitor, resulting in painful and potentially life-threatening attacks of swelling of the skin and mucosa.

Anette Bygum started her research project in 2001, identifying 33 patients with HAE in Denmark. After establishing a national HAE Centre at the Department of Dermatology and Allergy Centre, Odense University Hospital, together with a public and healthcare personnel campaign, focused tracing of patients and family testing, more than 100 patients were identified. These patients were included in her dissertation, which focuses on prevalence, symptoms, heredity, treatment and quality of life measures.

Fig. 1. Anette Bygum and her family.

Since 2001 the mean time from symptom onset to diagnosis of HAE has been reduced from 18.6 to 1.7 years. Accurate diagnosis is necessary for the treatment of patients and avoidance of unnecessary surgery or occlusion of the upper


Fig. 2. The audience of the dissertation presentation.

airway. Treatment options have improved significantly in recent years, with new drugs being licensed for acute therapy of swelling attacks in HAE. Emergency treatments include subcutaneous icatibant or intravenous complement C1 inhibitor concentrates. Selected patients are treated with long-term prophylactic complement C1 inhibitor concentrates, which is an expensive therapy. Children and adults are trained in home therapy with emergency medication, which was previously administered in emergency departments or during hospitalization. Home therapy reduces the mean number of hospital visits by 84%. Patients on home therapy also have a more active part in their disease course, achieving greater independence and a better quality of life.

The HAE Centre at Odense University Hospital is collaborating with the University of Southern Denmark to develop a point-of-care test for immediate diagnosis of HAE in the emergency care setting. Also, pathophysiological mechanisms are being further explored. In collaboration with the Department of Biomedicine, University of Aarhus, the possibilities of gene therapy are being explored in cell and mouse model systems. Other ongoing research projects, in collaboration with physicians and researchers from HAE Centres in Frankfurt, Grenoble, Madrid, Milan and Charleston, support the necessity of international networks for research into rare diseases.

The dissertation was based on the following papers:

1. Bygum A. Hereditary angio-oedema in Denmark: a nationwide survey. Br J Dermatol 2009; 161: 1153–1158.
2. Bygum A, Vestergaard H. Acquired angioedema – occurrence, clinical features and associated disorders in a Danish nationwide patient cohort. Int Arch Allergy Immunol 2013; 162: 149–155.
3. Bygum A, Broesby-Olsen S. Rapid resolution of erythema marginatum after icatibant in acquired angioedema. Acta Derm Venereol 2011; 91: 185–186.
4. Bygum A. Hereditary angioedema – consequences of a new treatment paradigm in Denmark. Acta Derm Venereol 2014; 94: 436–441.
5. Bork K, Bygum A, Hardt J. Benefits and risks of danazol in hereditary angioedema: a long-term survey of 118 patients. Ann Allergy Asthma Immunol 2008; 100: 153–161.
6. Bygum A, Fagerberg CR, Ponard D, Monnier N, Lunardi J, Drouet C. Mutational spectrum and phenotypes in Danish families with hereditary angioedema because of C1 inhibitor deficiency. Allergy 2011; 66: 76–84.
7. Bygum A, Andersen KE, Mikkelsen CS. Self-administration of intravenous C1-inhibitor therapy for hereditary angioedema and associated quality of life benefits. Eur J Dermatol 2009; 19: 147–151.

The following poem and the illustration were used to support and strengthen Anette Bygum's message on the specific approach to rare diseases:
The Starfish:
A woman is walking along a beach where a storm has washed hundreds of starfish up on the shore. She goes and throws starfish back into the sea. A man comes up to her and says: What are you doing? You will never be able to save all starfish on this beach, not to mention all other beaches. Is this relevant? The woman takes a starfish up, throws it back into the sea and says: For this starfish it has immense importance!

[Modified after Dayle Ann Dodds 1952]