

Correspondence on 'Jan Gösta Waldenström and rheumatology'

I read with great interest the article 'Jan Costa Waldenström and Rheumatology' written by the eminent colleague Wollheim.¹ In the late seventies, I had the unique privilege and opportunity to meet, exchange clinical and scientific information and discuss with this giant of medicine, during his visit at the clinical centre of the National Institutes of Health (NIH) in Bethesda, Maryland, USA, in the spring of 1978. I would like to share this inimitable experience with the readers of your distinguished journal. The announcement that the renowned Waldenström will visit us, spread around the NIH campus, with the speed of the wind. He was supported by the International Fogarty Center to visit the clinical centre of the NIH for a month, as a senior visiting medical scientist. His programme included several meetings with investigators in person, particularly with those working in areas close to his interest 'γ-globulin abnormalities' in order to discuss with them recent findings, the progress of their research and carefully listen to planned experiments. Moreover, he would participate in outpatient and inpatient rounds and deliver a lecture in the central 'Masur' auditorium. All of us, from senior to junior investigators were excited to meet a prominent physician-scientist with great contributions to Medicine-Immunology: *Macroglobulinemia and hyperglobulinemic purpura*, both of which bear his name. I remember, very vividly, my first encounter with Waldenström in my small office, adjacent to my laboratory. It is like it happened a couple of days ago. At first glance, his nobility, build, posture, appealing look and professional European style, in addition to his fame made me feel like a schoolboy meeting a famous teacher. I presented the findings of two ongoing projects, at that time; the presence of circulating Interferon(s) α/γ in the blood of active systemic autoimmune patients² and the occurrence of activated polyclonal and monoclonal B-lymphocytes in the blood and bone marrow of Sjögren's syndrome patients; a disease with a clinical spectrum expanding from a benign to a truly malignant lymphoproliferative disorder.^{3 4}

Waldenström's interest focused on the activation of B lymphocytes in systemic autoimmune disease. His participation in the presentation of our study results and his very pertinent questions revealed a physician with well-rounded knowledge not only in clinical medicine but also in the pathogenetic mechanisms accounting for the development of the autoimmune diseases. He posed an argument on the ongoing theory at that time, which was proposing that chronicity of B-lymphocyte activation, in a genetically predisposed individual, was leading to malignant B-lymphocyte transformation. Indeed he asked: 'if the chronic B-lymphocyte activation is the leading cause of transformation in patients with Sjögren's syndrome, why then only a small fraction of these patients develop lymphoid malignancy and not the majority?' It took decades of research to provide an answer to his question. Indeed, subsequent studies have confirmed that Sjögren's syndrome patients which will develop lymphoid malignancy have clinical, laboratory, immunological and molecular characteristics from the early days of the disease diagnosis.⁵⁻⁸

Waldenström's clinical skills together with interpersonal communication with the patients were unparalleled during the inpatient clinical rounds on the ninth floor, as well as on the grand rounds, where seriously ill or difficult outpatient cases were discussed.

I had the luck, at the time of his visit, to be the attending physician for the in-house patients of the ninth floor. These patients suffered from systemic autoimmune diseases and were hospitalised either to be evaluated in order to participate in a therapeutic protocol or to treat unwanted sequelae either from the treatment or disease progress itself. Our director, another great clinician, the Late John L. Decker Jr, suggested that we should present to Waldenström patients C and J. The whole team (two physicians in training and me) prepared the presentation of the cases with great details. We were ready to respond to any and every question. The cases were presented one after the other. Our visitor asked questions, spotted quickly the patients' problem and made necessary recommendations. It was evident in his facial expression that the answers he got to his comments or questions satisfied him. What did we gain from the inpatient and outpatient presentations to Waldenström?

- The empathic approach to the patient. This tall, elderly clinician was kneeling in order to be on the same level with the patient lying in the bed. In order to ask questions or examine the patient he was requesting his permission.
- He showed a great example of how up-to date (diagnostically-therapeutically) an academic physician should be, even in his retirement years.
- The emphasis he placed on the value of immunologic tests in diagnosis, prognosis and as tools for follow-up of the patients' response to therapy.
- He reiterated the value of the double blinded controlled therapeutic trials and application of therapies based on the disease pathogenetic process.

Virtually every moment of his visit offered world class medical education. This is the great opportunity a famous medical institute can provide to junior and the senior staff members.

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REFERENCES

- 1 Wollheim FA. Jan Gösta Waldenström and rheumatology. *Ann Rheum Dis* 2019;78:583–5.
- 2 Hooks JJ, Moutsopoulos HM, Geis SA, *et al.* Immune interferon in the circulation of patients with autoimmune disease. *N Engl J Med* 1979;301:5–8.
- 3 Fauci AS, Moutsopoulos HM. Polyclonally triggered B cells in the peripheral blood and bone marrow of normal individuals and in patients with systemic lupus erythematosus and primary Sjögren's syndrome. *Arthritis Rheum* 1981;24:577–84.
- 4 Moutsopoulos HM, Steinberg AD, Fauci AS, *et al.* High incidence of free monoclonal lambda light chains in the sera of patients with Sjögren's syndrome. *J Immunol* 1983;130:2663–5.
- 5 Skopouli FN, Dafni U, Ioannidis JP, *et al.* Clinical evolution, and morbidity and mortality of primary Sjögren's syndrome. *Semin Arthritis Rheum* 2000;29:296–304.
- 6 Tapinos NI, Polihronis M, Moutsopoulos HM. Lymphoma development in Sjögren's syndrome: novel p53 mutations. *Arthritis Rheum* 1999;42:1466–72.
- 7 Fragkioudaki S, Nezos A, Souliotis VL, *et al.* Mthfr gene variants and non-MALT lymphoma development in primary Sjögren's syndrome. *Sci Rep* 2017;7:7354.
- 8 Fragkioudaki S, Mavragani CP, Moutsopoulos HM. Predicting the risk for lymphoma development in Sjögren syndrome: an easy tool for clinical use. *Medicine* 2016;95:e3766.