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Wegener's granulomatosis: changing perceptions of a once-fatal disease

WE HAVE learned a great deal about Wegener's granulomatosis since Heinz Klinger and Friedrich Wegener made their original observations 60 years ago. In this minisymposium on Wegener's granulomatosis, we will look at how the disease was discovered, examine clues to its etiology, and discuss its current clinical management.

Dr. Ulises Mercado provides an opportunity to revisit Heinz Klinger, who as a young medical student in 1931 first described a systemic granulomatous vasculitic disease that included the respiratory tract.[1] In 1936 and 1939, Dr. Friedrich Wegener provided detailed information about three patients quite similar to those seen by Klinger.[2,3] With the help of Dr. Wegener's widow, Mrs. Ursula Wegener, Dr. Mercado enriches our sense of medical history by sharing a bit of the private lives of both men.

Klinger and Wegener were struck by the unusual distribution of disease in their patients. Involvement of the upper and lower airways was quite unlike the pattern seen in what had then been recognized as "periarteritis nodosa." Klinger suggested that an inhaled sensitizing agent or various "noxa" may have precipitated "...a particular reactivity of the vessels..."[1] Wegener was so impressed with upper airway involvement in his patients that he entitled his 1939 paper "Rhinogenic granulomatosis with special involvement of the arterial system and kidneys."[3]

Over the next 40 years, Wegener's granulomatosis was recognized as a uniformly fatal disease.[4] During the 1960s, glucocorticoid therapy improved mean survival time only slightly, from 5 months to 1 year.[5] In 1973, Fauci and Wolff[6] at the National Institutes of Health (NIH) unequivocally demonstrated that combination therapy with cyclophosphamide and glucocorticoids could induce remission and perhaps even cure. The NIH vasculitis group extended these observations to over 200 patients who have been followed for up to 24 years. The experience includes a recent report of 158 patients comprising over 1220 patient-years.[7]

Clearly, cyclophosphamide and glucocorticoid therapy is often lifesaving in Wegener's granulomatosis. However, it is also clear that the predisposition to disease expression remains, and at least 50% of patients will have at least one relapse. Almost all patients will suffer permanent morbidity from the disease or its treatment, or both. This has led to numerous attempts to identify more effective, safer therapy.

Ideally, a better understanding of pathogenesis will lead to improved treatment or cure. In 1985, antibody to neutrophil cytoplasmic antigen (ANCA) was recognized to be commonly associated with Wegener's granulomatosis.[8] During the past 8 years, a variety of ANCAs have been identified, target antigens have been characterized, and the effects of ANCA on in vitro systems and animal models have been studied.

Dr. Galperin and I review the evolving story of ANCA in this minisymposium, and in another brief article I describe the current treatment of Wegener's granulomatosis. We hope that the juxtaposition of Dr. Mercado's historical vignette and our reviews

will provide a glimpse of the progress that has occurred since the seminal reports by Klinger and Wegener.

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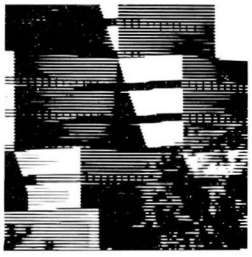

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