

Malignancy masquerading as food hypersensitivity

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Key words: acquired angioedema; food hypersensitivity; non-Hodgkin's lymphoma.

• A 54-YEAR-OLD woman was referred to the allergy unit of the department of dermatology at University Hospital Zurich for a diagnostic work-up after she had emergency treatment for an episode of angioedema of the tongue and throat. Angioedematous symptoms occurred 30 min after she ate a spaghetti dinner with clam and tomato sauce. Otherwise, the personal history was noncontributory, except for the mild pancytopenia reported in the referral letter. In particular, no previous food allergies/intolerance reactions were reported. Angioedema and the patient's complaint of persistent gastrointestinal pain prompted the assessment of complement C4 and the regulatory protein C1 inhibitor (C1-INH). Both proteins were undetectable (C4 <0.01 g/l, normal range 0.1–0.4; C1-INH concentration <0.03 g/l, normal range 0.2–0.36; C1-INH function <18%, normal range 70–135%).

A preliminary diagnosis of hereditary (HAE) or acquired angioedema (AAE) was made, and treatment with the attenuated androgen danazol (400 mg daily for 2 weeks; then 200 mg per day for a total duration of 3 weeks) was initiated. Ten

days after initiation of danazol therapy, a rise in the international normalized ratio (INR) for coagulation was noted. A subsequent coagulation work-up revealed the presence of antiphospholipid antibodies (anticardiolipin-IgM 520 IU/l, normal <15 IU/l). Serology for antinuclear and antinative DNA antibodies was unremarkable, excluding the diagnosis of systemic lupus erythematosus (SLE). The initial diagnosis was revised in favor of acquired C1-INH deficiency in association with antiphospholipid antibody syndrome. AAE was confirmed in two individual samples collected 1 day apart by low C1q and C1r values (C1q: 0.014 g/l, normal range 0.046–0.116 g/l; C1r 37%, normal range 75–125%, respectively). Finally, a bone-marrow biopsy specimen allowed us to diagnose AAE in conjunction with B-cell non-Hodgkin's lymphoma (NHL, IgG κ).

This particular case seems to be very instructive for various reasons:

- 1) Complement determinations were crucial to replace the initial diagnosis of food allergies with that of HAE or AAE.
- 2) Determination of proteins of the first complement component was helpful in the immediate differentiation between HAE and AAE.
- 3) The underlying causes of AAE must be aggressively pursued and may include a bone-marrow biopsy.

Recent studies suggest that the majority of acquired C1-INH deficiency patients have anti-C1-INH autoantibodies that appear to be responsible for the development of the C1-INH deficiency. Future progress in understanding these diseases may help to elucidate the mechanism and develop a

more specific treatment of autoantibody generation (1–6).

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Accepted for publication 27 November 2000

Allergy 2001; 56:349

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ISSN 0105-4538

References

1. CICARDI M, BERGAMASCHINI L, CUGNO M, et al. Pathogenetic and clinical aspects of C1 inhibitor deficiency. *Immunobiology* 1998; **199**:366–376.
2. ZURAW BL. Urticaria, angioedema, and autoimmunity. *Clin Lab Med* 1997;**17**: 559–569.
3. HEYMANN WR. Acquired angioedema. *J Am Acad Dermatol* 1997;**36**:611–615.
4. CICARDI M, BERETTA A, COLOMBO M, GIOFFRE D, CUGNO M, AGOSTONI A. Relevance of lymphoproliferative disorders and of anti-C1 inhibitor autoantibodies in acquired angio-oedema. *Clin Exp Immunol* 1996;**106**:475–480.
5. SPÄTH PJ, WÜTHRICH B. Inherited and acquired deficiencies of C1 esterase in humans. In: ROTHER K, TILL GO, HÄNSCH GM, editors. *The complement system*. 2nd ed. Berlin: Springer Verlag, 1998:353–402.
6. BERETTA KR, SPÄTH PJ, PEDRAZZINI A, MARTINELLI G, CAVALLI F. Angioödem durch erworbenen Komplement-C1-Inhibitor-Mangel bei einer Patienten mit Non-Hodgkin-Lymphom und autoimmun-hämolytischer Anämie [Angioedema due to acquired complement C1-inhibitor deficiency in a patient with non-Hodgkin's lymphoma and autoimmune hemolytic anemia]. *Schweiz Med Wochenschr* 1991;**121**:943–947.