

April 2001 • Volume 107 • Number 4

Hereditary angioedema type III: An additional French pedigree with autosomal dominant transmission

- [Previous article](#) in Issue
- [Next article](#) in Issue
- [Drug links](#) from Mosby's DrugConsult
- [Genetic information](#) from OMIM
- Citation of this Article
 - View on [PubMed](#)
 - Download in [citation manager format](#)
 - Download in [Medlars format](#)
- [Related articles](#) in PubMed

To the Editor:

Binkley and Davis¹ recently identified a third variant of hereditary angioedema (HAE) in a family of Italian origin. Clinical presentation was indistinguishable from HAE type I or II except for the unique occurrence in women, notably during pregnancy or use of exogenous estrogens. More particularly, C1-inhibitor (C1inh) functional deficiency or ponderal abnormality was excluded in this family. This condition is probably identical to that described simultaneously by Bork et al² in women from unrelated German families and might also be called "HAE type III." Bork et al suggested X-linked dominance in their 10 pedigrees because the condition was restricted to women and there was an excess of female offspring from affected women.² In contrast, Binkley and Davis postulated that this disorder was transmitted in an autosomal dominant fashion. In this debate we would add a French family with HAE type III, in which X-linked dominance is excluded, that is also evocative of autosomal dominant inheritance.

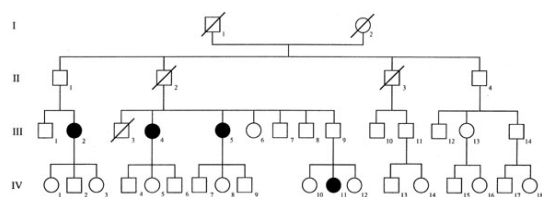
The proband is a 46-year-old woman whose medical history included multiple spontaneous or posttraumatic attacks of facial or acral edema, upper-airway obstruction,

and episodes of abdominal pain. On one occasion laparotomy demonstrated exudative ascites and an ovarian cyst. All of her symptoms had started after she took contraceptive pills for the first time at the age of 22 years and recurred during her 3 pregnancies. C4 levels, plasma C1inh protein concentration, and C1inh activity (chromogenic method, Berichrom C1inh; Dade Behring, Marburg, Germany), repeatedly measured during symptom-free intervals and during attacks over a period of 16 years, were always normal. Use of a contraceptive intrauterine device did not provide complete remission, which is in striking contrast with the report of Binkley and Davis.¹ Her condition finally improved when she was treated with danazol 200 mg every other day. The dosage was progressively tapered to 200 mg/wk without relapse after 2.5 years.

Familial exploration disclosed a similar condition in 3 other female patients in 2 successive generations (Fig 1). Episodes of swelling in these female patients were limited to times of oral estrogen contraceptive use or pregnancy. Ponderal and functional C1inh levels were also consistently normal. The clinical and biologic presentation in our family is very similar to that reported by Binkley and Davis¹ and Bork et al,² and the diagnosis of HAE type III is highly probable. X-linked dominant inheritance, with or without lethality in the hemizygotes, is excluded in our family. The affected women had no miscarriages evocative of lethality in male fetuses, and there was no excess of females over males in the pedigree. Moreover, the condition was transmitted through clinically normal men 3 times in 2 generations. The mutated gene was transmitted at least once from a man to his son, which is definite evidence against X-linked heredity.

We therefore think that in our family, as in that of Binkley and Davis,¹ autosomal dominant inheritance with reduced penetrance is the most likely explanation. However, one cannot easily admit that all HAE type III families in the Bork et al² article were evocative of X-linked inheritance only by chance. These discrepancies could be explained by genetic heterogeneity in HAE type III. Restriction of HAE type III to women is actually puzzling, even considering the likely influence of sex hormones. Digenic inheritance with a second gene located on one of the sex chromosomes might be discussed.

Fig. 1. Pedigree.



Click on Image to view full size

1/8/114242

doi:10.1067/mai.2001.114242

Ludovic Martin, MD
Danielle Degenne, PharmD
Annick Toutain, MD
Denise Ponard, MD
Hervé Watier, MD, PhD

^aDepartment of Dermatology ^bLaboratory of Immunology ^cDepartment of Genetics
University Hospital 37044 Tours Cedex 01, France ^dLaboratory of Immunology University
Hospital BP 185 38042 Grenoble Cedex 09 France

References

TOP

1. Binkley KE, Davis A 3rd. Clinical, biochemical, and genetic characterization of a novel estrogen-dependent inherited form of angioedema. *J Allergy Clin Immunol* 2000;106:546-50.

MEDLINE

ABSTRACT

FULL TEXT

2. Bork K, Barnstedt SE, Koch P, Traupe H. Hereditary angioedema with normal C1-inhibitor activity in women. *Lancet* 2000;356:213-7.

MEDLINE

CROSSREF

Articles with References to this Article

TOP

This article is referenced by these articles:

Hereditary angioedema with normal C1 inhibitor gene in a family with affected women and men is associated with the p.Thr328Lys mutation in the *F12* gene

Journal of Allergy and Clinical Immunology, The
October 2007 • Volume 120 • Number 4

Ludovic Martin, Nadia Raison-Peyron, Markus M. Nöthen, Sven Cichon, Christian Drouet

FULL TEXT

Hereditary and acquired angioedema: Problems and progress: Proceedings of the Third C1 Esterase Inhibitor Deficiency Workshop and beyond

Journal of Allergy and Clinical Immunology, The
September 2004, Supplement • Volume 114 • Number 3

Angelo Agostoni, Emel Aygören-Pürsün, Karen E. Binkley, Alvaro Blanch, Konrad Bork, Laurence Bouillet, Christoph Bucher, Anthony J Castaldo, Marco Cicardi, Alvin E Davis, Caterina De Carolis, Christian Drouet, Christiane Duponchel, Henriette Farkas, Kálmán Fáy, Béla Fekete, Bettina Fischer, Luigi Fontana, George Füst, Roberto Giacomelli, Albrecht Gröner, C. Erik Hack, George Harmat, John Jakenfelds, Mathias Juers, Lajos Kalmár, Pál N. Kaposi, István Karádi, Arianna

Kitzinger, Tímea Kollár, Wolfhart Kreuz, Peter Lakatos, Hilary J. Longhurst, Margarita Lopez-Trascasa, Inmaculada Martinez-Saguer, Nicole Monnier, István Nagy, Éva Németh, Erik Waage Nielsen, Jan H. Nuijens, Caroline O'Grady, Emanuela Pappalardo, Vincenzo Penna, Carlo Perricone, Roberto Perricone, Ursula Rauch, Olga Roche, Eva Rusicke, Peter J Späth, George Szendei, Edit Takács, Attila Tordai, Lennart Truedsson, Lilian Varga, Beáta Visy, Kayla Williams, Andrea Zanichelli, Lorenza Zingale

[ABSTRACT](#)

[FULL TEXT](#)

Hereditary and acquired angioedema: Problems and progress: Proceedings of the Third C1 Esterase Inhibitor Deficiency Workshop and beyond

Journal of Allergy and Clinical Immunology, The

September 2004, Supplement • Volume 114 • Number 3

Angelo Agostoni, Emel Aygören-Pürsün, Karen E. Binkley, Alvaro Blanch, Konrad Bork, Laurence Bouillet, Christoph Bucher, Anthony J Castaldo, Marco Cicardi, Alvin E Davis, Caterina De Carolis, Christian Drouet, Christiane Duponchel, Henriette Farkas, Kálmán Fáy, Béla Fekete, Bettina Fischer, Luigi Fontana, George Füst, Roberto Giacomelli, Albrecht Gröner, C. Erik Hack, George Harmat, John Jakenfelds, Mathias Juers, Lajos Kalmár, Pál N. Kaposi, István Karádi, Arianna Kitzinger, Tímea Kollár, Wolfhart Kreuz, Peter Lakatos, Hilary J. Longhurst, Margarita Lopez-Trascasa, Inmaculada Martinez-Saguer, Nicole Monnier, István Nagy, Éva Németh, Erik Waage Nielsen, Jan H. Nuijens, Caroline O'Grady, Emanuela Pappalardo, Vincenzo Penna, Carlo Perricone, Roberto Perricone, Ursula Rauch, Olga Roche, Eva Rusicke, Peter J Späth, George Szendei, Edit Takács, Attila Tordai, Lennart Truedsson, Lilian Varga, Beáta Visy, Kayla Williams, Andrea Zanichelli, Lorenza Zingale

[ABSTRACT](#)

[FULL TEXT](#)