Clinical Immunology (2015) xx, xxx–xxx

available at www.sciencedirect.com

Clinical Immunology

www.elsevier.com/locate/yclim

Characterization of patients with angioedema without wheals: The importance of *F12* gene screening

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Received 12 November 2014; accepted with revision 20 February 2015

KEYWORDS
Factor XII;
F12;
Normal C1-INH;
U-HAE;
C1 inhibitor;
Bradykinin

Abstract Sporadic and familiar forms of non-histaminergic angioedema and normal C1 inhibitor encompass a group of disorders possibly caused by bradikinin. We aimed to study the subgroups of hereditary angioedema with FXII mutation (FXII-HAE), unknown genetic defect (U-HAE) and idiopathic non-histaminergic acquired angioedema (InH-AAE). We screened the *F12* locus in our cohort and delineated the clinical, laboratory and genetic features. Four families carried the p.Thr309Lys mutation in *F12* gene. Haplotyping confirmed the hypothesis of a common founder. Six families were affected by U-HAE and 13 patients by sporadic InH-AAE. C4 levels were significantly lower in FXII-HAE than in InH-AAE. In the FXII-HAE group, none had attacks exclusively in high estrogenic states; acute attacks were treated with icatibant. Prophylaxis with tranexamic acid reduced the attack frequency in most patients. Our study provides new data on the diagnosis, clinical features and treatment of non-histaminergic angioedema, underlying the role of the screening for *F12* mutations.

Abbreviations: C1-INH, C1 inhibitor; HAE, hereditary angioedema; FXII-HAE, hereditary angioedema with factor XII mutation; U-HAE, hereditary angioedema with unknown genetic mutation; InH-AAE, idiopathic non-histaminergic acquired angioedema; SERPING1, serpin peptidase inhibitor, clade G, member 1.

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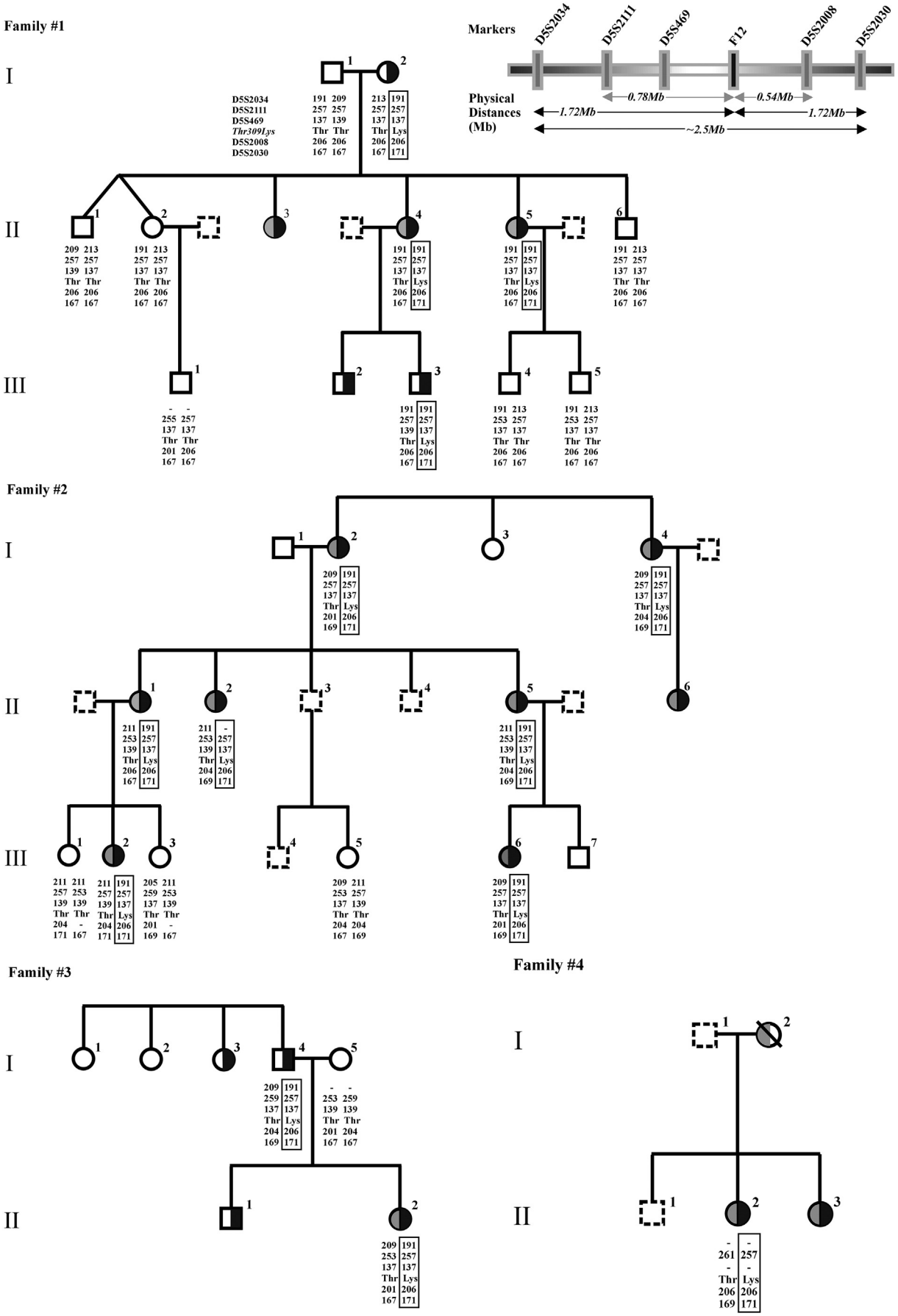
http://dx.doi.org/10.1016/j.clim.2015.02.013
1521-6616/



Please cite this article as: D. Firinu, et al., Characterization of patients with angioedema without wheals: The importance of *F12* gene screening, Clin. Immunol. (2015), http://dx.doi.org/10.1016/j.clim.2015.02.013