ACNE, ROSACEA, AND RELATED DISORDERS (INCLUDING HIDRADENITIS SUPPURATIVA)

A NOVEL PATHOGENIC NCSTN VARIANT IN A LARGE AUSTRALIAN PEDIGREE AFFECTED WITH HIDRADENITIS SUPPURATIVA

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Background: Hidradenitis Suppurativa (HS) is a chronic inflammatory follicular occlusion disorder characterized by recurrent painful abscesses and sinuses with estimated prevalence of 0.2% – 4%. Over one-third of HS patients have a positive family history, showing an autosomal dominant inheritance pattern. The gamma secretase complex [consisting of four protein subunits: PSEN1 (presenilin-1), nicastrin (NCSTN), APH-1 (anterior pharynx-defective 1), and PEN-2 (presenilin enhancer 2)] has been implicated in pathogenesis underlying familial HS, with the disease mechanism suggesting downstream Notch signalling pathway suppression and phosphoinositide 3-kinase/AKT signalling pathway induction.

Observation: We report the case of a 41 year old male patient with simultaneous HS and acne conglobata, who had a strong autoinflammatory disease family history. A poor clinical response was noted to various medical therapies including systemic antibiotics, retinoid therapy, and biologic agents Infliximab, Adalimumab, and Anakinra. The most notable therapeutic response was to surgical therapy. Initial genetic sequencing revealed he was a heterozygous carrier for the microsatellite (CCTG) polymorphism of the Proline-Serine-Threonine Phosphatase Interacting Protein 1 (PSTPIP1) gene. Whole exome sequencing was performed of the patient and extended family, with a novel variant identified in the NCSTN gene (NCSTN c.1485C>T) segregating with disease.

Key message: We have identified a novel pathogenic variant within the NCSTN gene associated with HS.