**Materials and Methods**

The objective of this study was to define HS endotypes, not only based on the patients’ morphologic profiles of the disease, but also on the main available biomarkers that have been related to it. The study protocol was accepted by the ethics committee of our hospital (CEIm code 2015520). Written informed consent was obtained from all study participants. We included 103 adult Caucasic patients from the Metropolitan conurbation of Barcelona (Spain) with HS fulfilling the Dessau criteria and prospectively recruited in our HS monographic clinic from May to December 2015. Blood collection was programmed in every patient before the initiation of therapy, incorporating plasma, serum, and blood cells in a sample collection.

The following variables were studied:

– Age at the first visit

– Sex

– Medical conditions such as history of pilonidal sinus, inflammatory bowel disease, diabetes, thyroidal alterations, psoriasis, Down syndrome, Dowling-Degos syndrome, hypertension, obesity, dyslipidemia

– Onset of HS. The age at which the subject first developed lesions. It is considered early if the subject presented the lesions at ≤20 years of age.

– Family history of HS and family history of acne in first-related familiars

– Alcohol and tobacco use

- Body mass index

– Type of lesions:

• Abscess

• Nodule

• Tunnel

– Location of the lesions in anterior or posterior sites of the body: it refers to the anatomical areas where the dermatologist can see lesions

• Anterior sites include face, thorax/chest, submammary area, pubis, axillae, inguinal region, other locations

• Posterior sites include scalp, nape, back, gluteal region

– Severity of the lesions determined by the following:

• Hurley stage. Ranges from 1 to 3. Stage 1 is considered as the mildest form, which is considered when there are one or more abscesses or nodules without tunnel formation. Stage 2 happens when more lesions appear, such as tunnels, but they are not multiple. Stage 3 can be identified in those patients who have multiple lesions with more extensive tunnel formation and scarring.

• Sartorius scale. This scale was introduced to include other types of lesions such as nodules, scarring, pustules, and folliculitis. It also counts the number of anatomical areas involved. It is a dynamic scale. However, in advanced stages, when scarring and tunnels coalesce, they are difficult to count. The lower the punctuation, the milder the stage.

• Physician’s global assessment. It is an assessment that ranges from 0 to 5, depending on the number of abscesses, draining fistulas, and inflammatory nodules.

• International HS severity score system (IHS4). This scale classifies the disease into mild (<4 points), moderate (4–10 points), or severe (>10 points). The lesions (nodules, abscesses, or fistulas) are multiplied by a coefficient: nodules × 1, abscesses × 2, and fistulas × 4. The punctuation of each lesion is added up to obtain the total punctuation.

– C-reactive protein measured with standardized ELISA technique.

– Serum concentrations of IL-1, IL-6, IL-17, and IL-10, all measured with standardized ELISA technique.

– Mutations in gamma-secretase subunits. Mutations in the following subunits were assessed from blood samples of the patients using next-generation sequencing: APH1A, APH1B, MEFV, NCSTN, PSEN1, PSEN2, PSENEN, and PSTPIP1.

We used a two-step cluster analysis, which consists on an exploratory analysis of the data set which tries to identify structures within it. More specifically, it tries to identify homogenous groups of cases if the grouping is not previously known [31]. Two-step cluster analysis identifies groupings by running preclustering first and then by running hierarchical methods. Input of scale and ordinal data is possible in this statistic model, and the number of clusters can be determined automatically, or they can be predefined by the researcher. The model output automatically gives an estimation of goodness, statistical power, and importance of the cluster predictors. Predictors that were less relevant for clustering were excluded. Calculations were performed with the SPSS 22 software (IBM Corp., USA).

The final model included body mass index, C-reactive protein, and serum concentrations of IL-1, IL-6, IL-17, and IL-10 (measured with standardized ELISA technique) as continuous variables, and sex, later/early onset (≤20 years), anterior/posterior lesion sites, presence/absence of sinus tracts, nodules and abscesses, positive/negative history of pilonidal sinus, and presence/absence of mutations in gamma-secretase subunits (APH1A, APH1B, MEFV, NCSTN, PSEN1, PSEN2, PSENEN, and PSTPIP1) as categorical variables. Targeted gene panel sequencing was performed by screening candidate next-generation sequencing methods in an Illumina© platform, and potential pathogenic variants were confirmed by means of the Sanger method of DNA sequencing.