SUPPLEMENTARY METHODS

Participants

Of the 207 cases initially identified, 114 were excluded (70 cases had features not consistent with Sweet Syndrome (SS), 18 cases had insufficient clinical data to be correctly classified, and 26 cases had a revised diagnosis after evaluation (6 cases of infection, 5 cases of vasculitis, 12 cases of pyoderma gangrenosum and 3 cases of erythema nodosum). Finally, 93 patients satisfied the Su and Liu diagnostic criteria.

Data collection

We obtained demographic data, comorbidities, clinical symptoms and signs, laboratory and histopathologic findings, and treatment from patients' medical records. Treatment response was classified as no response, partial response and complete response based on physician-reported examination at follow-up. Where patients had associated malignancies, we determined type of malignancy (solid or hematologic, and subtype), disease status at diagnosis, and molecular information (drive mutations, karyotype, and next-generation sequencing (NGS) panels of somatic mutations involved in hematologic malignancies). Long-term follow-up through the medical system of our institution and shared medical history in the Catalonian health system was performed to determine the development of malignancies or inflammatory diseases following SS diagnosis.

Patient classifications

Patients were classified into four groups according to their clinical presentation: Malignancy-associated (MA-SS), Reactive-SS(11), Inflammatory/Autoimmune-associated (A-SS) and idiopathic-SS. Classically, SS patients were classified as idiopathic, MA-SS and drug-associated(2,14,20). However, this latter approach included idiopathic-SS patients with previous infections, autoimmune or autoinflammatory conditions and patients without a known trigger factor. Thus, we preferred to divide patients into these four groups and separate those without an unknown factor (idiopathic-SS) from others.

Histopathological subtypes were classified into four different groups: classic, subcutaneous, histiocytoid and others. The written pathological report of 80 patients could be reviewed and included in the specific analysis of pathological variants. However, in 13 patients we had the pathological diagnosis of SS without descriptions or specifications of the infiltrate. Thus, these latter patients were not included in the analysis.

Classic Sweet syndrome histology is characterized by a dense infiltrate of mature neutrophils[1,2,3] and marked edema in the reticular dermis, without primary vasculitis. Histiocytoid Sweet syndrome presents as histologically similar to classic SS, although with the inflammatory infiltrate composed of mononuclear cells mimicking histiocytes but of myeloid lineage (positive myeloperoxidase)[9]. The diagnostic criteria of subcutaneous Sweet syndrome was initially defined by Sutra-Loubet et.al.[3,11,12,14] and requires exclusion of other etiologies of neutrophilic panniculitis. Histologically, it is characterized by subcutaneous neutrophilic infiltrates of lobular or, less frequently, septal patterns, with minimal dermal involvement. Leukocytoclasia, fat necrosis, and mild reticular dermal edema can occasionally be present.