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# Response letter to “Latent class analysis of 216 patients with adult-onset Still’s disease” by Sugiyama et al.

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## Abstract

Sugiyama et al. recently described in “Latent class analysis of 216 patients with adult-onset Still’s disease,” baseline characteristics, laboratory tests, treatment, relapse, and death of adult-onset Still’s disease (AOSD) patients from a Japanese hospital. They identified two subgroups: Class 1 ( $n=155$ ) with a younger age and typical symptoms of AOSD and Class 2 ( $n=61$ ) with older patients and fewer typical symptoms of AOSD. In 2022, VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome, an established X-linked disease associated with a somatic mutation in *UBA1*, is considered as a differential diagnosis for AOSD particularly in elderly. These patients from Class 2 could benefit from more explorations for mild myelodysplasia and VEXAS.

**Keywords:** Adult-onset Still’s disease, Myelodysplastic syndrome, VEXAS

Dear Editor,

With great interest, we read the recent article entitled “Latent class analysis of 216 patients with adult-onset Still’s disease,” published online in your journal. In this paper, Sugiyama et al. performed a retrospective latent class analysis about baseline characteristics, laboratory tests, treatment, relapse, and death of 216 adult-onset Still’s disease (AOSD) patients in nine Japanese hospitals. They were able to identify two subgroups: Class 1 ( $n=155$ ) with a younger age and typical symptoms of AOSD and Class 2 ( $n=61$ ) with older patients with a median age of 66.8 vs 41.5 years old in Class 1 and fewer typical symptoms of AOSD.

Recently, Beck et al. [1] described a newly established X-linked disease associated with a somatic mutation

in *UBA1*, a gene encoding ubiquitin-like modifier activating enzyme 1 and named VEXAS for vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic syndrome. It is characterized by fever, skin lesions, lung infiltrates, but also arthralgia, lymph node enlargement, and macrocytic anemia, mostly among elderly men [2]. In 2022, VEXAS is considered as a differential diagnosis for AOSD particularly in elderly [3] as illustrated in a recent retrospective Dutch case series of 12 patients with adult-onset auto-inflammation caused by somatic mutations in *UBA1*, two were initially suspected with AOSD [4]. Interestingly, Class 2 patients of Sugiyama et al.’s work seem to present deeper anemia (10.6 vs 11.2g/dl) according to supplementary table 1, it could be inflammatory anemia but also partly macrocytic anemia so it would be useful to know the mean corpuscular volume of each group. In the same way, patients of Class 2 experienced less typical skin rash but did they have other cutaneous features or other atypical symptoms?

Therefore, we think that it would be very interesting to have patients from Class 2 group screened for myeloid neoplasm at least and for *UBA1* mutation in Sanger

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technique in order to know if this identified group could be patients with autoinflammation linked to *UBA1* mutation or another somatic mutation not identified yet.

Patients in the Class 2 group may not all be VEXAS syndrome, considering the female predominance, but their age and, for example, the presence of two cases of interstitial pneumonia in a small group of 61 should encourage for more explorations including VEXAS and mild myelodysplasia [5, 6].

#### Abbreviations

AOSD: Adult-onset Still's disease; UBA1: Ubiquitin-like modifier activating enzyme 1; VEXAS: Vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic syndrome.

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#### Availability of data and materials

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#### Declarations

##### Ethics approval and consent to participate

Not applicable.

##### Consent for publication

Not applicable.

##### Competing interests

The authors declare that they have no competing interests.

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#### References

1. Beck DB, Ferrada MA, Sikora KA, Ombrello AK, Collins JC, Pei W, et al. Somatic mutations in UBA1 and severe adult-onset autoinflammatory disease. *N Engl J Med*. 2020;383(27):2628–38.
2. Georjin-Lavialle S, Terrier B, Guedon AF, Heiblig M, Comont T, Lazaro E, et al. Further characterization of clinical and laboratory features occurring in VEXAS syndrome in a large-scale analysis of multicenter case-series of 116 French patients. *Br J Dermatol*. 2022;186(3):564–74.
3. Delplanque M, Aouba A, Hirsch P, Fenaux P, Graveleau J, Malard F, et al. USAID associated with myeloid neoplasm and VEXAS syndrome: two differential diagnoses of suspected adult onset Still's disease in elderly patients. *J Clin Med*. 2021;10(23):5586.
4. van der Made CI, Potjewijd J, Hoogstins A, Willems HPJ, Kwakernaak AJ, de Sevaux RGL, et al. Adult-onset autoinflammation caused by somatic

mutations in UBA1: a Dutch case series of patients with VEXAS. *J Allergy Clin Immunol*. 2021;S0091-6749(21):00819–8.

5. Mitrovic S, Fautrel B. Complications of adult-onset Still's disease and their management. *Expert Rev Clin Immunol*. 2018;14(5):351–65.
6. Fauter M, Gerfaud-Valentin M, Delplanque M, Georjin-Lavialle S, Sève P, Jamilloux Y. Adult-onset Still's disease complications. *Rev Med Interne*. 2020;41(3):168–79.

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