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VEXAS Syndrome: A Comprehensive Review of Clinical Mimickers and Differential Diagnosis at the Rheumatology–Haematology Interface

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Abstract

VEXAS syndrome is a newly described autoimmune disorder in adults caused by a somatic mutation in the UBA1 gene located on the X chromosome, occurring almost exclusively in older men. The disease combines features of severe chronic inflammation with hematopoietic disorders, resulting in a heterogeneous and multi-organ clinical picture and frequent diagnostic difficulties. The aim of this study is to present the characteristics of VEXAS syndrome and discuss the most important diseases mimicking its course, with particular emphasis on differential diagnosis. The clinical picture of the syndrome includes recurrent fever, neutrophilic skin lesions, chondritis, vasculitis, lung involvement, and an increased tendency to thrombosis. Haematological abnormalities, primarily macrocytic anaemia and thrombocytopenia, often coexisting with myelodysplastic syndromes, are an integral part of the disease. A characteristic, though not pathognomonic, finding is the presence of cytoplasmic vacuoles in myeloid and erythroid precursors in the bone marrow. VEXAS syndrome can mimic many rheumatological, autoinflammatory, and haematological diseases, such as recurrent chondritis, Sweet's syndrome, or systemic vasculitis, and its course is often characterized by resistance to standard immunosuppressive treatment. Including VEXAS syndrome in the differential diagnosis of older men with unexplained inflammation and macrocytosis is crucial for shortening the time to diagnosis and implementing appropriate treatment.

The aim of the work. The aim of this review was to summarize current knowledge on VEXAS syndrome and to present its clinical and haematological characteristics in comparison with other autoinflammatory and myelodysplastic disorders, highlighting key aspects of differential diagnosis.

Materials and Methods. This article presents a comprehensive narrative review of the current scientific literature on VEXAS syndrome, with a focus on its clinical presentation, differential diagnosis, and relationship to autoinflammatory and myelodysplastic disorders. Relevant publications were identified through systematic searches conducted in the PubMed, Google

Scholar, and Web of Science databases. Additionally, the reference lists of selected articles were reviewed to identify further studies not captured in the primary search. The search strategy included the following key terms and their combinations: “VEXAS syndrome,” “UBA1 mutation,” “autoinflammatory diseases,” “myelodysplastic syndromes,” “relapsing polychondritis,” “vasculitis,” “neutrophilic dermatoses,” and “differential diagnosis.” Inclusion criteria comprised: original research articles, case reports, systematic or narrative reviews, and clinical guidelines published after 2020 (the year of VEXAS discovery); studies describing clinical, haematological, or immunological aspects of VEXAS; publications available in English or Polish and accessible in full text. Exclusion criteria included: articles not related to VEXAS or its differential diagnosis; papers lacking clinical data or containing duplicated information; conference abstracts without peer-reviewed full-text versions.

The search and selection process was conducted in December 2025. All retrieved studies were critically analysed and synthesized to provide an updated overview of the current understanding of VEXAS syndrome and its differentiation from other disorders.

Keywords: VEXAS syndrome, UBA1 mutation, Autoinflammatory diseases, Myelodysplastic syndromes, Diagnostic challenges, Relapsing polychondritis, Vasculitis, Neutrophilic dermatoses

Introduction

The name VEXAS comes from an acronym that describes its most important features:

- Vacuoles – these organelles are found in the cytoplasm of precursor cells of the myeloid and erythroid lines of the bone marrow.
- E1 enzyme – this is the ubiquitin-activating enzyme 1 (UBA1), which is encoded by the mutated gene.
- X-linked – the UBA1 gene is located on the X chromosome.
- Autoinflammatory – the syndrome is primarily an autoinflammatory disorder causing chronic systemic inflammation.

- Somatic – the disease is caused by an acquired somatic mutation in the UBA1 gene, which is not inherited but occurs during life and is limited to haematopoietic cells (Al-Hakim et al., 2023).

This condition is a relatively new disease entity that began to be described in 2020, when Beck et al., using a genotype -first approach, sequenced the entire exome in patients with undiagnosed generalised inflammation or fever of unknown aetiology, leading to the discovery of a mutation in the UBA1 gene (Beck et al., 2020). It seems to mainly affect elderly men, as the median age of onset is 64–69 years (Al-Hakim et al., 2023). In the original 2020 study, all patients with the UBA1 mutation were male (Beck et al., 2020). Although VEXAS syndrome was initially thought to be very rare, more recent epidemiological data suggest that it is much more prevalent. In the Geisinger MyCode Community Health Initiative population study, analysis of exome data from 163,096 participants showed a prevalence of approximately 1:14,000 in the entire cohort and approximately 1:4,000 in men over 50 years of age (Beck et al., 2022). Other sources report a frequency of 1:4,269 in men over 50 (Tan et al., 2024; Kottas et al., 2025). Rare cases of VEXAS syndrome in women have also been reported, most often associated with X monosomy or somatic mosaicism (Al-Hakim et al. , 2023). VEXAS syndrome is characterised by a heterogeneous, multi-organ clinical picture resulting from a chronic and severe inflammatory process and coexisting haematological disorders (Georgin-Lavialle et al., 2021). The symptoms of the disease are often progressive, and their non-specific nature poses a significant diagnostic challenge.

One of the most common and earliest manifestations are systemic symptoms, often chronic, recurrent and resistant to treatment, requiring doses of glucocorticosteroids ≥10 mg of prednisone per day (Al-Hakim et al., 2023). The dominant symptom is recurrent non-infectious fever, observed in the majority (64-92%) of patients (Beck et al., 2020; Suszek et al., 2023; Bourbon et al., 2021). The fever is often accompanied by significant fatigue (75%), weight loss (38-62%) and muscle pain, contributing to the picture of a severe inflammatory disease (Georgin-Lavialle et al., 2021; van der Made et al., 2022).

Skin lesions occur in most patients (82–100%) and are often an early manifestation of VEXAS syndrome (Georgin-Lavialle et al., 2021). They are most commonly neutrophilic dermatoses, including Sweet's syndrome (17–46%) and leukocytoclastic vasculitis. Other forms of skin lesions, such as erythema nodosum, urticarial lesions or inflammatory periorbital oedema (8–30%), are less common (Tan et al., 2024; Sterling et al., 2023). These lesions are often recurrent and may be resistant to standard treatment.

A characteristic manifestation of the disease is also cartilage involvement in the form of recurrent chondritis, observed in 36–64% of patients (Tan et al., 2024; Georgin-Lavialle et al., 2021). The involvement mainly affects the cartilage of the auricles and nose, but may also involve the respiratory tract. Compared to the idiopathic form of relapsing polychondritis, the form associated with VEXAS syndrome is more likely to coexist with fever, skin lesions, lung involvement and myelodysplastic syndromes (Khitri et al., 2022; Sterling et al., 2023).

Respiratory manifestations are equally common and are observed in approximately 49–72% of patients. They include pulmonary infiltrates, pleural effusion, as well as interstitial pneumonia, bronchiolitis and fibrotic changes. These symptoms may be recurrent or chronic and often coexist with other features of active inflammation. (Beck et al., 2020; Kouranloo et al., 2023).

An important element of the clinical picture is an increased tendency to thrombosis; venous thromboembolism occurs in 35-44% of patients and includes unprovoked deep vein thrombosis and pulmonary embolism, often with a severe and recurrent course (van der Made et al., 2022; Groarke et al., 2021). Cases of arterial vasculitis, including polyarteritis nodosa (PAN) and giant cell arteritis (GCA), have also been reported (Beck et al., 2020).

The course of the disease is associated with persistent inflammatory activity, which is reflected in elevated inflammatory markers. Elevated CRP and ESR values are found in all patients at some point during the course of the disease (100%), with median CRP concentrations typically high at around 73–97 mg/L (Beck et al., 2020; Tan et al., 2024).

An integral and key part of the VEXAS syndrome picture are haematological symptoms, resulting from the fact that the UBA1 gene mutation is limited to haematopoietic cells (Grayson et al., 2021). The most common abnormality is macrocytic anaemia, present in almost all patients (85–100%) and constituting one of the key screening criteria in the diagnosis of VEXAS syndrome (Beck et al., 2022; Mekinian et al., 2025). Thrombocytopenia (48–91%) often coexists, as well as other cytopenias, including lymphopenia (63–80%) and monocytopenia (approximately 50%) (Beck et al., 2020; Beck et al., 2022).

Bone marrow examination reveals characteristic cytoplasmic vacuoles in myeloid and erythroid lineages, which were found in all patients who underwent bone marrow biopsy in the first described cohorts (100%) (Beck et al., 2020) . Although this change is not pathognomonic, it is an important diagnostic clue. A significant proportion of patients develop myelodysplastic syndromes (24–55%), and there is also an increased risk of other clonal haematological diseases, such as monoclonal gammopathy of undetermined significance (MGUS) or multiple myeloma (Beck et al., 2020; Beck et al., 2022; Kottas et al., 2025).

The above-mentioned broad clinical picture of the disease confirms that it is largely a syndrome of non-specific symptoms and may resemble many diseases in the field of rheumatology, adult autoinflammatory syndromes and clonal haematopoietic diseases. Due to the significant overlap of symptoms and the lack of pathognomonic clinical features, VEXAS syndrome is often confused with other disease entities, leading to diagnostic delays and suboptimal treatment. The following sections of this paper discuss the diseases that most commonly mimic the course of VEXAS syndrome and present key elements of differential diagnosis that may facilitate its correct and timely diagnosis.

Discussion

Relapsing polychondritis (RP)

Patients with recurrent chondritis constitute one of the key groups of patients in whom VEXAS syndrome has been identified, and differentiation between the idiopathic form of the disease and the form associated with the UBA1 gene mutation is of fundamental clinical and prognostic importance. Already in the original cohort in the study by Ferrada et al., which described VEXAS syndrome, as many as 60% of patients met the diagnostic criteria for relapsing polychondritis (Al-Hakim et al., 2023; Ferrada et al., 2022). Subsequent analyses of a series of French patients by Khitri M-Y et al. showed that approximately 7.6% of all patients with a clinical diagnosis of RP have a somatic UBA1 mutation, which de facto classifies them as patients with VEXA syndrome (Khitri et al., 2022) . Data from large comparative cohorts, including French and American studies, have allowed the identification of a number of features that differentiate the two forms of the disease (Ferrada et al., 2022; Khitri et al., 2022; Georgin-Lavialle et al., 2022). VEXAS syndrome with cartilage involvement affects almost exclusively older men, with a median age of onset of approximately 66 years, while idiopathic recurrent chondritis is more common in younger people and significantly more common in women. There are also differences in the location of chondritis, as the idiopathic form of the disease more often involves the cartilage of the nose and respiratory tract, while otitis externa occurs with similar frequency in both groups (Khitri et al., 2022). Significant differences are evident in systemic manifestations, which are much more severe in patients with VEXAS, who are more likely to experience non-infectious fever, neutrophilic skin lesions, pulmonary infiltrates and involvement of organs such as the heart and eyes. However, the most important diagnostic element distinguishing the two forms of the disease remains haematological disorders, as patients with VEXAS often have concomitant myelodysplastic syndromes, and laboratory tests show significantly lower concentrations of haemoglobin, platelets and neutrophils and

significantly higher values of inflammatory markers, including CRP protein (Kottas et al., 2025; Khitri et al., 2022). In this context, Ferrada's proposed screening algorithm is of particular importance, according to which the presence of macrocytosis and thrombocytopenia in a male diagnosed with RP is associated with an almost 100% probability of detecting the UBA1 mutation (Al-Hakim et al., 2023; Ferrada et al., 2022). The differences between the two forms of the disease also concern the clinical course and prognosis, as patients with VEXAS are significantly more likely to be resistant to standard immunosuppressive treatment, less likely to achieve remission and have a higher mortality rate compared to patients with idiopathic recurrent chondritis (Khitri et al., 2022). Although glucocorticosteroids and immunosuppressive drugs are used in both groups, patients with VEXAS usually require higher doses of steroids and are dependent on them, while in this subgroup, JAK inhibitors such as ruxolitinib and azacitidine treatment show some therapeutic efficacy (Heiblig et al., 2022; Comont et al., 2022).

Sweet Syndrome

As with recurrent chondritis, VEXAS syndrome often manifests in a form resembling Sweet's syndrome, making it one of the most common clinical mimics of this acute febrile neutrophilic dermatosis. In the original cohort describing VEXAS, as many as 32% of patients met the diagnostic criteria for Sweet's syndrome (Al-Hakim et al., 2023). The differentiation of VEXAS from the idiopathic form of Sweet's syndrome is based on a characteristic genetic profile and abnormalities in haematological and bone marrow tests. The p.Met41Leu variant of the UBA1 gene is closely associated with Sweet syndrome-like skin manifestations, and studies have shown that as many as 82% of patients with this variant develop neutrophilic skin infiltrates; in addition, this variant is usually associated with a milder course of the disease and a better prognosis compared to other UBA1 mutations (Tan et al., 2024; Ferrada et al., 2022). Unlike the idiopathic form of Sweet's syndrome, which can affect people of all ages and both sexes, VEXAS occurs almost exclusively in older men, with a median age of approximately 64–70 years, and is characterised by the coexistence of macrocytic anaemia (91–100%) and thrombocytopenia. Although Sweet's syndrome has long been associated with blood cancers, in VEXAS this association is due to a mutation in UBA1, which drives both skin inflammation and myelodysplasia (Grayson et al., 2021). Histopathological examination of skin lesions provides additional diagnostic clues, as infiltrates in VEXAS often have a histiocytic morphology, composed of immature myeloid cells carrying the UBA1 mutation, and show diffuse leukocytoclasia in the dermis even without overt features of necrotising vasculitis.

Stromal oedema, neutrophil tropism to sweat glands and nerve infiltration are also observed (Tan et al., 2024; Sterling et al., 2023; Ghoufi et al., 2016). Significant data are provided by a study by Gurnari et al., which analysed 19 patients diagnosed with Sweet's syndrome and concomitant haematological abnormalities requiring bone marrow biopsy; all males in whom histopathological examination revealed the presence of cytoplasmic vacuoles in myeloid precursors were found to have pathogenic UBA1 mutations. These results clearly indicate that every male diagnosed with Sweet's syndrome and cytopenia should be routinely evaluated for VEXAS syndrome (Gurnari et al., 2022). Although skin lesions in VEXAS usually respond well to glucocorticosteroids, the disease is recurrent and progressive, and patients show steroid dependence (Tan et al., 2024). In addition, neutrophilic infiltrates may coexist with or be confused with leukocytoclastic vasculitis, complicating histopathological interpretation. Furthermore, in some cases, neutrophilic (clonal) and LCV (paraclonal) infiltrates may occur in different locations in the same patient, further complicating the histological picture (Lacombe et al., 2022). In summary, in an elderly male with a clinical diagnosis of Sweet's syndrome, the presence of macrocytosis and vacuoles in myeloid precursors in the bone marrow almost unequivocally indicates VEXAS syndrome, especially if the patient shows signs of steroid dependence and recurrent skin symptoms.

Polyarteritis nodosa (PAN)

Another diagnostic and therapeutic challenge may be VEXAS syndrome under the guise of nodular polyarteritis. Nodular polyarteritis is a classic inflammation of medium-calibre vessels, whereas in VEXAS syndrome, vascular manifestations occur frequently and may involve both medium- and small-calibre vessels. The clinical symptoms of vasculitis in VEXAS can be virtually indistinguishable from idiopathic PAN and include skin lesions, hypertension and multi-organ damage, which contributes to misdiagnosis (Al-Hakim et al., 2023). The key differences between the two entities concern the demographic profile and haematological picture, as idiopathic PAN can occur in both sexes and at different ages, while the PAN-like form in VEXAS syndrome affects almost exclusively men over the age of 50 and is almost always accompanied by macrocytic anaemia, often with MCV values ≥98 fL, and thrombocytopenia [17,18]. An additional factor strongly supporting the diagnosis of VEXAS syndrome is the frequent coexistence of myelodysplastic syndromes, which do not occur in classic nodular polyarteritis [18]. The picture of vasculitis in VEXAS is heterogeneous, as in some cases medium-calibre vessels are affected, and most of these patients meet the classification criteria for PAN, but the most commonly observed form of vasculitis remains

leukocytoclastic small-calibre vasculitis, manifesting as purpura palpable to the touch (Al-Hakim et al. , 2023). Vascular changes may also take the form of reticular cyanosis and painful subcutaneous nodules (Tan et al., 2024). Analysis of available case reports and clinical series indicates that the course of VEXAS syndrome with predominant vascular manifestation is extremely severe, characterised by significant resistance to treatment, including high doses of glucocorticosteroids and standard biological therapies used in vasculitis, and is associated with high mortality. One review of the literature on vasculitis in VEXAS syndrome reported deaths in the majority of patients with medium-calibre vascular involvement, a significant proportion of whom met the criteria for PAN (Watanabe et al., 2022; Muratore et al., 2022; Diarra et al., 2022). Misdiagnosis of isolated nodular arteritis, without in-depth haematological diagnostics, often leads to a delay in the correct diagnosis of VEXAS syndrome and the implementation of adequate therapeutic strategies, such as haematopoietic clone-directed treatment or eligibility for haematopoietic stem cell transplantation (Tan et al., 2024). In any elderly male diagnosed with nodular polyarteritis who has macrocytosis, anaemia or features of myelodysplastic syndrome, VEXAS syndrome should be strongly suspected and genetic testing for the UBA1 mutation should be considered.

Giant cell vasculitis

The relatively newly discovered rheumatic disease known as VEXAS syndrome poses a considerable diagnostic problem when ruling out giant cell vasculitis. This is due to certain similarities in the course of both diseases or the possible overlap of both entities. (Watanabe et al., 2022; Midtvedt et al., 2022) Giant cell arteritis (GCA), also known as Horton's disease, is the most common type of peripheral vasculitis, most often affecting men over the age of 50. (Lyons et al., 2020; Farina et al., 2023) Typical symptoms of the disease include headache, general weakness and generalised muscle pain. Laboratory tests may reveal anaemia and elevated inflammatory markers. (Lyons et al., 2020; van der Geest et al., 2020) At least half of patients with GCA have a fever of no more than 39 °C. (Farina et al., 2023) It is noteworthy that in VEXAS syndrome, the onset of the disease usually occurs at the same age as in GCA. Beck B. et al mention a study of a group of men with VEXAS syndrome, where the median age is 64 years. In addition, an important component of this disease entity is accompanying anaemia, thrombocytopenia and elevated CRP. (Beck et al., 2020)

Patients with VEXAS syndrome may develop large vessel inflammation accompanied by giant cell vasculitis. Beck et al. describe one 60-year-old patient out of twenty-five patients with

confirmed VEXAS syndrome who had accompanying GCA, confirmed by a temporal artery biopsy. In addition to the UBA1 mutation characteristic of VEXAS, the patient also presented with symptoms such as fever, pleural effusion, macrocytic anaemia, thrombocytopenia and chondritis. (Beck et al., 2020; Watanabe et al., 2022; Midtvedt et al., 2022) Due to the rare coexistence of these two conditions and their potential to mimic each other, effective diagnosis remains a challenge. (Watanabe et al., 2022).

Myelodysplastic syndrome

Myelodysplastic syndrome (MDS) usually affects older patients, around 70 years of age (Schratz et al., 2020), and men are more commonly affected. The symptoms are usually insidious and not very characteristic, resulting from cytopenia (anaemia, thrombocytopenia, neutropenia). (Sekeres et al., 2022) Laboratory diagnosis of myelodysplastic syndrome is based on three pillars: cytopenia of unknown cause, dysplasia of morphotic elements, and evidence of clonal haematopoiesis, which, although not essential, is very useful. (Hasserjian et al., 2019) Due to the wide variety of clinical manifestations of VEXAS syndrome, it is sometimes confused with various other diseases, including haematological disorders. Furthermore, 24%–63% of patients with VEXAS syndrome also develop MDS. This should be of particular interest to clinicians, as anaemia and thrombocytopenia are pathologies characteristic of both of these diseases. What raises suspicion of VEXAS syndrome in patients with MDS is the presence of vacuoles in myeloid and erythroid precursors. (Loeza-Uribe et al., 2024)

Autoinflammatory diseases

It is worth noting the case of a patient presented by Magnol et al., who in 2010 diagnosed a 57-year-old patient with spondyloarthropathy due to persistent back pain, peripheral arthritis, sacroiliitis on magnetic resonance imaging, and the presence of HLA-27 antigen. The patient was treated with interferon alpha, resulting in rapid improvement. Over the years, despite receiving therapy, the patient developed further non-specific symptoms such as inflammation of the choroid, ear and nose cartilage, non-specific abdominal pain and weight loss. In addition, the patient's skin was affected by, among other things, neutrophilic dermatosis, painful eczema and vasculitis. C-reactive protein levels were then tested, with a result of >100 mg/l, and macrocytic anaemia was detected. This led to the conclusion that myelodysplastic syndrome was present. In 2018, Magnol et al. decided to initiate biological treatment with secukinumab,

achieving stable improvement in the patient's condition with a reduction in CRP levels to 6 mg/l. In 2020, after reading a scientific article on VEXAS syndrome, they decided to test for mutations in the UBA1 gene, confirming their suspicions. This mutation in the patient's body caused symptoms of spondyloarthropathy, an autoimmune inflammatory disease, which meant that the final, correct diagnosis was made 10 years after the first symptoms appeared. (Magnol et al., 2021)

Idiopathic Castleman's disease is another disease entity with a complex aetiology and an autoimmune basis. It is characterised by generalised inflammation, complicated by organ dysfunction and general lymphadenopathy. Although the idiopathic form of the disease is rare, it should be kept in mind when making a diagnosis, as it can clinically resemble other similar conditions, such as lupus erythematosus, Still's disease, or even VEXAS syndrome. In the case of the latter, the similarity in the histological images of these two diseases is particularly noteworthy. García et al. draw readers' attention to the fact that clinicians should pay particular attention to the possibility of overlapping symptoms and test results in order to obtain an accurate diagnosis (González García et al., 2023).

Another patient case is a 67-year-old man presenting with symptoms of arthritis lasting two years, who also reported chronic fatigue and back pain. In the past, he reported various types of skin rashes, which were consulted by a dermatologist. A biopsy of these lesions revealed neutrophilic dermatosis, leading to a suspicion of Sweet's syndrome. Jain et al. tested the patient for HLA-27 antigen, obtaining a positive result, and their MRI of the sacroiliac joints showed inflammation. As the patient met the criteria for spondyloarthropathy, it was decided to initiate appropriate treatment with anti-inflammatory drugs, sulfasalazine and methotrexate, which unfortunately did not produce satisfactory results within 3 months, so the diagnostic process started from the beginning. This time, attention was drawn to macrocytic anaemia (Hb 8.3 gm/dl, MCV 106 fl), with vitamin B12 and folic acid levels within the normal range. In addition, laboratory tests revealed elevated CRP levels of 38 mg/l. A decision was made to perform a bone marrow biopsy, which revealed vacuolisation in red blood cell precursor cells. This picture led clinicians to suspect VEXAS syndrome, which was confirmed in the patient after testing for a genetic mutation in the UBA1 gene. Treatment with prednisolone and sulfasalazine was initiated, resulting in a significant improvement in the patient's condition. Jain et al. emphasise that spondyloarthropathy symptoms are rare manifestations of VEXAS syndrome and, although establishing the correct diagnosis was quite a challenge, after a careful and thorough process, it was possible, Their conclusion is that VEXAS syndrome should be

considered, especially in men presenting with symptoms of spondyloarthropathy and concomitant macrocytic anaemia (Jain et al., 2024).

Summary

Numerous diagnostic algorithms have been proposed to distinguish VEXAS from other rheumatic diseases. First of all, this condition occurs almost exclusively in males, which is due to the location of the UBA1 gene on the X chromosome and the somatic nature of the mutation. In addition, the disease typically has a late onset, most often in the sixth or seventh decade of life, with a median age at diagnosis of approximately 64–69 years.

An important factor increasing the suspicion of VEXAS syndrome is the coexistence of macrocytosis, defined as increased red blood cell volume (MCV ≥98–100 fL), which is one of the most characteristic and early laboratory abnormalities. In addition, many patients have thrombocytopenia, usually defined as a platelet count below 200×10^9/L, which distinguishes VEXAS from classic autoinflammatory and rheumatic diseases.

Another important diagnostic clue is the presence of cytoplasmic vacuoles in neutrophil precursor cells in bone marrow examination. The presence of vacuolisation in at least 10% of neutrophil precursors, with at least one vacuole in each of these cells, is considered particularly suggestive of VEXAS. Although this feature is not pathognomonic, in the appropriate clinical context it is a strong argument for the need for molecular testing for UBA1 gene mutations.

VEXAS syndrome is a newly described, acquired autoimmune syndrome in adults, characterised by an exceptionally complex and multi-organ clinical picture. The disease lies at the intersection of rheumatology and haematology, combining features of chronic, severe inflammation with significant haematopoietic disorders. This combination of symptoms makes VEXAS syndrome very similar to many other diseases, both autoimmune and autoinflammatory, as well as clonal haematopoietic disorders.

The clinical manifestations of VEXAS syndrome, including fever of unknown origin, neutrophilic skin lesions, chondritis, vasculitis, lung involvement and concomitant cytopenias, often lead to initial diagnoses such as recurrent chondritis, systemic vasculitis, neutrophilic dermatoses or myelodysplastic syndromes. In addition, resistance to standard immunosuppressive treatment and the recurrent nature of symptoms may mask the correct diagnosis and result in a long delay in diagnosis.

Due to the relatively recent discovery of VEXAS syndrome and the lack of widely known diagnostic criteria, this disease remains a significant clinical challenge. It is particularly difficult to differentiate it from diseases with a similar inflammatory or haematological phenotype, in

which the clinical picture may partially overlap, but the pathomechanism and treatment strategy are different. In every case of VEXAS syndrome, it is crucial to ensure cooperation between specialists from various fields of medicine, i.e. rheumatologists, haematologists and geneticists.

Disclosure

Author's contribution:

Conceptualization: H.A., Z.K., J.S., K.K., K.G., M.D.; methodology: H.A., Z.K., J.S., K.K., K.G., M.D.; software: H.A., Z.K., J.S., K.K., K.G., M.D.; validation: H.A., Z.K., J.S., K.K., K.G., M.D.; formal analysis: H.A., Z.K., J.S., K.K., K.G., M.D.; investigation: H.A., Z.K., J.S., K.K., K.G., M.D.; resources: H.A., Z.K., J.S., K.K., K.G., M.D.; data curation: H.A., Z.K., J.S., K.K., K.G., M.D.; writing—original draft preparation: H.A., Z.K., J.S., K.K., K.G., M.D..; writing—review and editing: H.A., Z.K., J.S., K.K., K.G., M.D.; visualization: H.A., Z.K., J.S., K.K., K.G., M.D.; supervision: H.A., Z.K.; project administration: H.A., Z.K., J.S., K.K., K.G., M.D.

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