Annular granuloma (Lat. *granuloma annulare* – GA) is a mild chronic inflammatory dermatosis, classified as a granulomatous skin disease. It is estimated that in the European population, its incidence is 0.1–0.4% [1]. The disease occurs mainly in young adults and children. However, it can appear at any age [1, 2]. Women suffer twice as often, especially in the 5th–6th decade of life [3]. Etiology of the disease has not been fully understood yet. The prevailing view today is that a delayed type immune response plays a key role in the pathogenesis of GA. Local damage to the dermis is believed to activate CD4+ T lymphocytes, secreting pro-inflammatory factors, e.g., interferon-γ (INF-γ), interleukin-2 (IL-2), tumor necrosis factor (TNF), which stimulate macrophages to produce extracellular matrix metalloproteases, which in turn results in the degradation of collagen fibers and the formation of granulomas visible in the histopathological picture [4, 5].

Typical clinical manifestation of GA involves hard, slightly raised lumps and nodules, with a smooth surface, flesh-colored or pale red in color, with a tendency to form ring-shaped foci that widen peripherally. Skin lesions are most often located on dorsal surfaces of hands and feet, but they can also occur in other locations. Usually they are not accompanied by subjective symptoms. However, itching of varying intensity may be present.

There are few publications in the dermatological literature on the methods of treating GA. Most of them are case studies. The choice of the appropriate therapy depends primarily on the clinical form of GA.

The most common type is the localized granuloma annulare (LGA), which occurs in about 75% of pa-
patients, more often in children and young adults [1]. In most LGA patients, skin lesions resolve spontaneously, usually within 2 years [1], therefore in some cases, especially in pediatric patients, a wait-and-see attitude may be considered [6]. In other cases, topical treatment with glucocorticosteroids, 0.1% tacrolimus or 5% imiquimod [7], and according to recent reports also 2% tofacitinib proves effective [8]. Another LGA therapeutic method involves intralesional injections of glucocorticosteroids or INF-γ [9]. Good effects of cryotherapy [10], photodynamic therapy [11] and laser treatments [12] have also been reported.

The second most common type is generalized granuloma annulare (GGA), also referred to as disseminated granuloma annulare (DGA). It is found in approximately 15% of GA patients, mainly in adults [13]. Skin lesions in GGA are more often accompanied by varying degrees of itching. Moreover, it is characterized by a more chronic course and a worse response to treatment compared to the localized form. In addition, in patients with GGA the disease more likely coexists with systemic diseases, which may further complicate selection of an effective therapeutic method. The most common diseases coexisting with GA include: diabetes mellitus, dyslipidemia, thyroid disease, HBV, HCV and HIV infections, and malignant neoplasms (mainly lymphomas) [14]. Local therapy for GGA is seldom sufficient, therefore systemic treatment is indicated.

We present difficulties in selecting an effective therapeutic method in a 58-year-old patient with GGA. Skin lesions in the form of itchy erythematous, annular papules, showing a tendency to cluster in a reticulated pattern, located around the trunk and limbs, appeared about a year before admission to the Dermatology Ward, without any detectable triggering factor (figs. 1, 2). Previous outpatient treatment has generally used anti-histamines and topical anti-inflammatory preparations – with no satisfactory improvement. In addition, the patient had a history of hypertension, type 2 diabetes, hypothyroidism and lipid metabolism disorders. No significant deviations were found in the laboratory and imaging diagnostics performed during hospitalization (X-ray of the chest and ultrasound of the abdomen). In the microscopic image of a biopsy specimen from the follicular lesion, foci of collagen necrosis with peri-annularly arranged epithelial cells of the granulomatous nature were visible. Based on the clinical presentation and result of the histopathological examination, the diagnosis of GGA was made. According to literature data, the basic therapeutic method in the case of GGA involves the use of various forms of phototherapy, including NB-UVB (311 nm), UVA1 and PUVA [15]. Therefore, in the presented patient, irradiation with NB-UVB was started, which the patient continued further on an outpatient basis. After the treatment, only 75% of patients, sometimes in children and young adults. In most LGA patients, skin lesions resolve spontaneously, usually within 2 years [1], therefore in some cases, especially in pediatric patients, a wait-and-see attitude may be considered [6]. In other cases, topical treatment with glucocorticosteroids, 0.1% tacrolimus or 5% imiquimod [7], and according to recent reports also 2% tofacitinib proves effective [8]. Another LGA therapeutic method involves intralesional injections of glucocorticosteroids or INF-γ [9]. Good effects of cryotherapy [10], photodynamic therapy [11] and laser treatments [12] have also been reported.

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a slight flattening of skin lesions was observed, and the skin itching persisted. Therefore, a switch to PUVA therapy was planned. This method seems to be particularly useful in the treatment of GGA not only due to the immunosuppressive effect on CD4 T cells, and consequently limiting the destruction of the extracellular matrix, but also due to the direct cytotoxic effect on histiocytes, fibroblasts and other inflammatory cells. However, caution should be exercised due to the possibility of provoking new skin lesions or exacerbation of the present ones as a result of exposure to light [16]. In order to exclude any contraindications to this therapeutic method, the patient was consulted ophthalmologically – inflammatory changes in the cornea, diabetic retinopathy, and the initial stage of cataract were diagnosed, and glaucoma was suspected. Due to ophthalmic reasons, PUVA-therapy was abandoned [17]. Moreover, antimalarial treatment was abandoned due to the negative influence of these drugs on the retina (the so-called chloroquine retinopathy) [18]. According to the literature data, chloroquine and hydroxychloroquine are effective in the treatment of GGA. They exhibit anti-inflammatory and immunosuppressive effects. Probably the efficacy in the treatment of GA results from inhibition of TNF production, and consequently from limited degradation of the extracellular matrix. Moreover, antimalarial drugs have lipid-lower-

Figure 1. The papular skin lesions with a characteristic ring pattern on the back
Rycina 1. Zmiany skórne grudkowe o charakterystycznym ukladzie obrączkowatym na plecach

Figure 2. The papular skin lesions with a tendency to focus on the arm
Rycina 2. Zmiany skórne grudkowe z tendencją do skupiania się na ramieniu

poczęto nasięwiania NB-UVB, które mężczyzna kontynuował w trybie ambulatoryjnym. Po zastosowanym leczeniu obserwowano tylko nieznaczne spłaszczenie zmian skórních, nadal utrzymywały się świąd skóry. Zaplanowano zmianę terapii na PUVA. Metoda ta wydaje się szczególnie przydatna w leczeniu GGA nie tylko z uwagi na immunosupresyjny wpływ na limfocyty T CD4, a w konsekwencji ograniczenie destrukcji macierzy pozakomórkowej, lecz także na bezpośredni cytotoksyczny wpływ na histiocyty, fibroblasty i inne komórki nacieku zapalnego. Należy jednak zachować ostrożność ze względu na możliwość sprowokowania nowych zmian skórných lub zaostrzenia obecnie występujących pod wpływem ekspozycji na światło [16]. W celu wykluczenia ewentualnych przeciwwskazań do powyższej metody terapeutycznej pacjenta skonsultowano okulistycznie – rozpoznano zmiany zapalne w obrębie rogówki, retinopatię cukrzycową, początkowe stadium zaćmy oraz wysośnie podjęto podejrzenie jaskry. Z przyczyn okulistycznych odstąpiono od włączenia PUVA-terapii [17]. Poza tym zrezygnowano z terapii lekami przeciwmalarycznymi z powodu negatywnego wpływu tych preparatów na siatkówki (tzw. retinopatię chlorochinową) [18]. Według danych z piśmiennictwa chlorochina i hydroksychlorochina są skuteczne w leczeniu GGA. Mają one działanie przeciwzapalne i immunosupresyjne. Prawdopodobnie skuteczność w terapii GA wynika z hamowania produkcji TNF, a także ograniczania degradacji macierzy zewnętrznokomórkowej. Poza tym leki antymalaryczne
Generalized annular granuloma/Uogólniony ziarniniak obrączkowaty

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KONFLIKT INTERESÓW

Autorzy nie zgłaszają konfliktu interesów.
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