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Vitiligo with familial aggregation, associated with autoimmune diseases

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SUMMARY

It is still a subject of debate whether the nonsegmental vitiligo is an autoimmune disease or not, although doubtless the presence of this disease increases the susceptibility for autoimmunity. We report a case of a 69 year-old woman suffering from vitiligo universalis associated with Hashimoto disease and rheumatoid arthritis, in whose onset and evolution the environmental factors, as emotional stress, infections, sun exposure, mechanical trauma, could interfere in a certain measure. The patient belongs to a family with several members affected by vitiligo, associated with at least one autoimmune disorder. This case sustains the plurifactorial etiopathology of the disease as well as the hypothesis the predisposition to autoimmunity is genetically conditioned.

It is currently believed that vitiligo is a multisystemic acquired disorder in which the association between skin depigmentation and oculary, as well as auditory abnormalities is not uncommon (1). There are several theories trying to explain the etiopathogenesis of the disease, focusing on immune, neural and impaired redox status evidence (2-5). Clinical experience suggests that various factors, including particulary, localized trauma, stress, sun exposure, infections, as well as autoimmune predisposition, may be involved in triggering and perpetuating melanocytic loss (6-8).

THE CASE PRESENTATION

It is presented the case of a 69 year-old woman with complete skin depigmentation, living in a rural region, whose personal history includes atopic dermatitis from the age of 5, which preceded the appearance of depigmentation, as well as, repeated episodes of recurrent and persistent infections of the upper respiratory tract. From the patient's family history we emphasize:

- father, deceased at present: suffered from vitiligo from the age of 46 and from Hashimoto thyroiditis from the age of 54.
- a brother: insulin-dependent diabetes mellitus from the age of 15.

The patient's depimentation started at the age of 10, on a postoperatory scar for a posterior cervical hemangioma. The evolution was progressive until the age of 40, when the depigmentation was complete; it was worsened by repeated sun burns, taking into account hat the main occupation was agriculture. Emotional stress was persent in her life starting from childhood. It was caused mainly by family conflicts and difficulties (the patient has a large family with eight children).

The examination of the skin surface showed complete depigmentation associated with leukotrichia and with complete greying of the hair of her scalp, axillary and pubic regions, as well as of some depigmented patches on the genital and buccal mucous membranes. There were symmetric erythemato-squamous patches with lichenification and excoriations on the posterior aspect of the forearms and hands *(Fig 1.)*. There were also present a bulky thyroid and hands tumefaction on the proximal metacarpophalangeal joints associated with painful limitation of the movements.

Laboratory analysis:

Routine tests: ESR elevated (33/58 mm), normochromic normocytic anemia (hemoglobin 110 g/l, hematocrit 34,7%, MCV 82,1 mm^3, MCH 26 g/cell) with normal iron level (13 µmol/L), leucocytes: $6,8x10^3/mm^3$ with discreet eosinophilia (differential: neutrophils: 60%, lymphocytes 25%, monocytes 7%, eosinophils 7%, basophiles 1%); serum glucose and lipids, renal and liver functions tests and VDRL were normal. Thyroid hormones: TSH elevated: 5,9 microIUML^{-1}, (ELISA assay, normal values = 0,44-3,45 microUml^{-1}); free T4 low: 8,8 pmolL^{-1}, (ELISA assay, normal values = 10,3-25,7 pmolL^{-1}).

Immunological parameters: antithyroid peroxidase antibodies (ATPO) positives at 600 Uml^{-1} (immunochemiluminescence, normal value <34 Uml^{-1}), rheumatoid factor (RF) positive at 160 Ul (nephelometric assay, normal value <20 UI), antinuclear antibodies (ANA) positives at 1/180, with speckled pattern – indirect immunofluorescence, normal value <1/20, antistreptolisine antibodies positives in titer of 1200 UI (nephelometric assay, normal value <200 UI); serum immunoglobulins were normal.

Thyroid sonography: bulky thyroid with "chess table" aspect. The comparative radiography of the hands: marginal erosions of metacarpophalangeal and interphalangeal proximal joints and juxtaarticular osteoporosis. The fundoscopy and biomicroscopy: retinal and choroidal depigmentation.

Based on anamnesis, clinical and laboratory examinations, we established the diagnosis of universalis vitiligo associated with atopic dermatitis, Hashimoto thyroiditis and rheumatoid arthritis (in conformity to ARA criteria) (9).

There were examined the patient's first degree relatives and the patients' mother (89 years), as well as a brother (65 years) and a sister (51 years) were diagnosed as suffering from vitiligo. For them, the same laboratory analysis are performed and the following abnormalities of interest were found:

- mother: ESR elevated 35/72, RF positive (71 UI), ATPO positive: 163,7 UIml^{-1}).

the sister: ESR elevated 30/56, RF positive (76 UI), ATPO positive (>600). Both mother and sister showed clinical and radiographic aspects characteristic for rheumatoid arthritis (ARA criteria). TSH and free T4 were normal as well as the thyroid sonography.

- the brother: ESR elevated (34/60 mm), serum glucose: 126 mg%, hypercholesterolemia (300 mg%). He presents diabetes

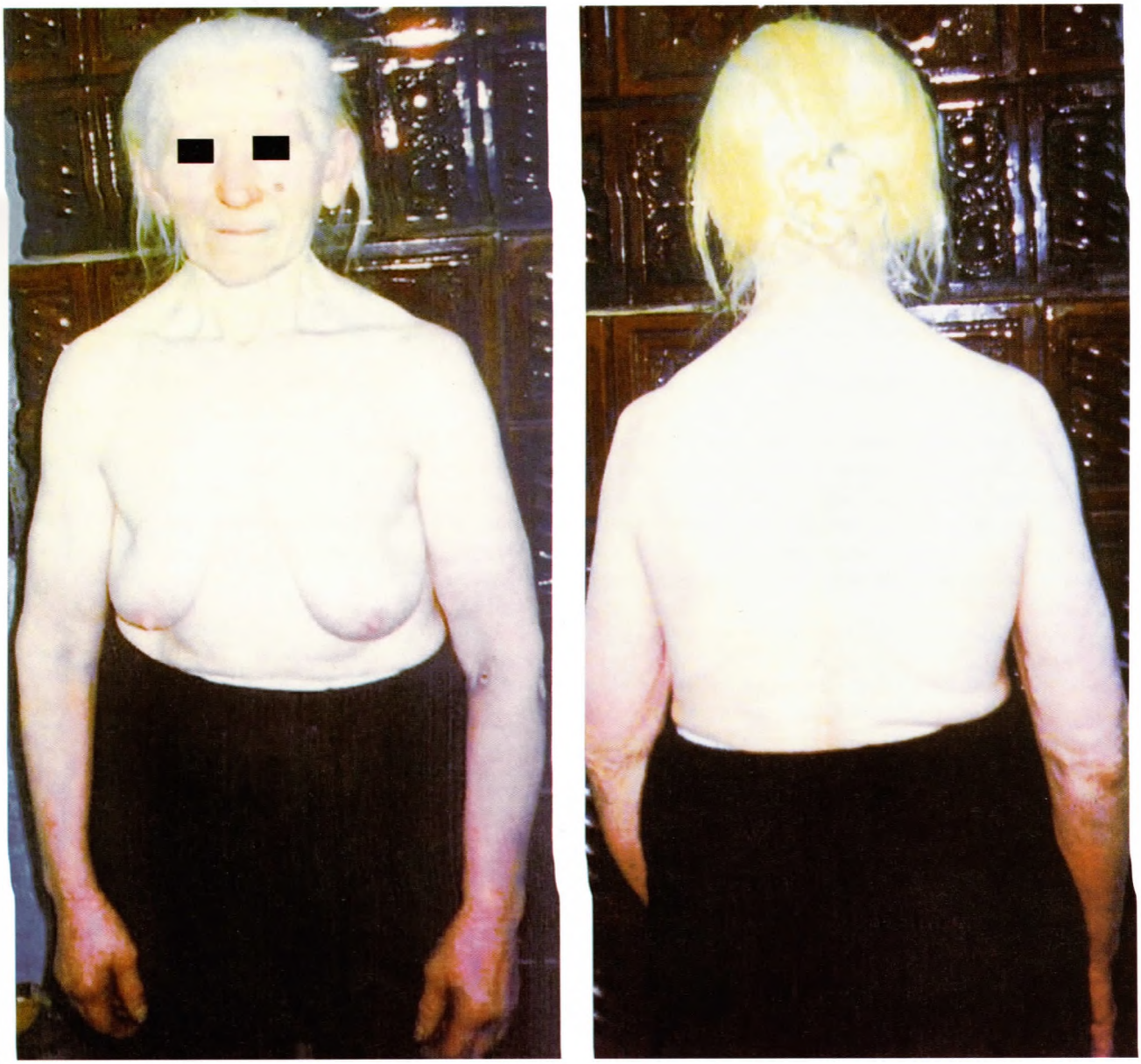

Fig. 1
Complete cutaneous depigmentation with the complete greying of the scalp hair; erythemato-squamous patches on the forearms and hands with lichenification

mellitus type 1 and is currently treated for chronic hepatitis. The patient's mother and sister were diagnosed with vitiligo associated with rheumatoid arthritis and subclinical autoimmune thyroidopathy *(Fig 2.)*.

DISCUSSIONS

An eloquent proof of autoimmune vitiligo theory is the frequent association of depigmentation with autoimmune disorders like Hashimoto thyroiditis, diabetes mellitus type 1, pernicious anemia, Addison disease, systemic lupus erythematosus, etc. (10, 11). Moreover, some clinical observations note the association of vitiligo with rheumatoid arthritis (9, 12, 13). The importance of the genetic factors in vitiligo was suggested by the significant family aggregation (in 6-38%, of the cases) (14, 15). The severity of this case was "announced" from childhood by early onset, rapid evolution of depigmentation and the association with atopic dermatitis. It is well known that the atopy is a poor prognostic factor for vitiligo, as well as Koebner phenomenon (the appearance of depigmentation on sun burn and postoperatory scar areas), the family history, the type and the long duration of vitiligo, the presence of leukotrichia and mucous membranes involvement (16, 17). The rapid and early extension of depigmentation was for certain encouraged by the occupational exposure to UV radiation. Also, we suppose that, the presence of the persistent and recurrent infections of upper respiratory tract as well as the emotional stress are factors which have perpetuated the depigmentation and

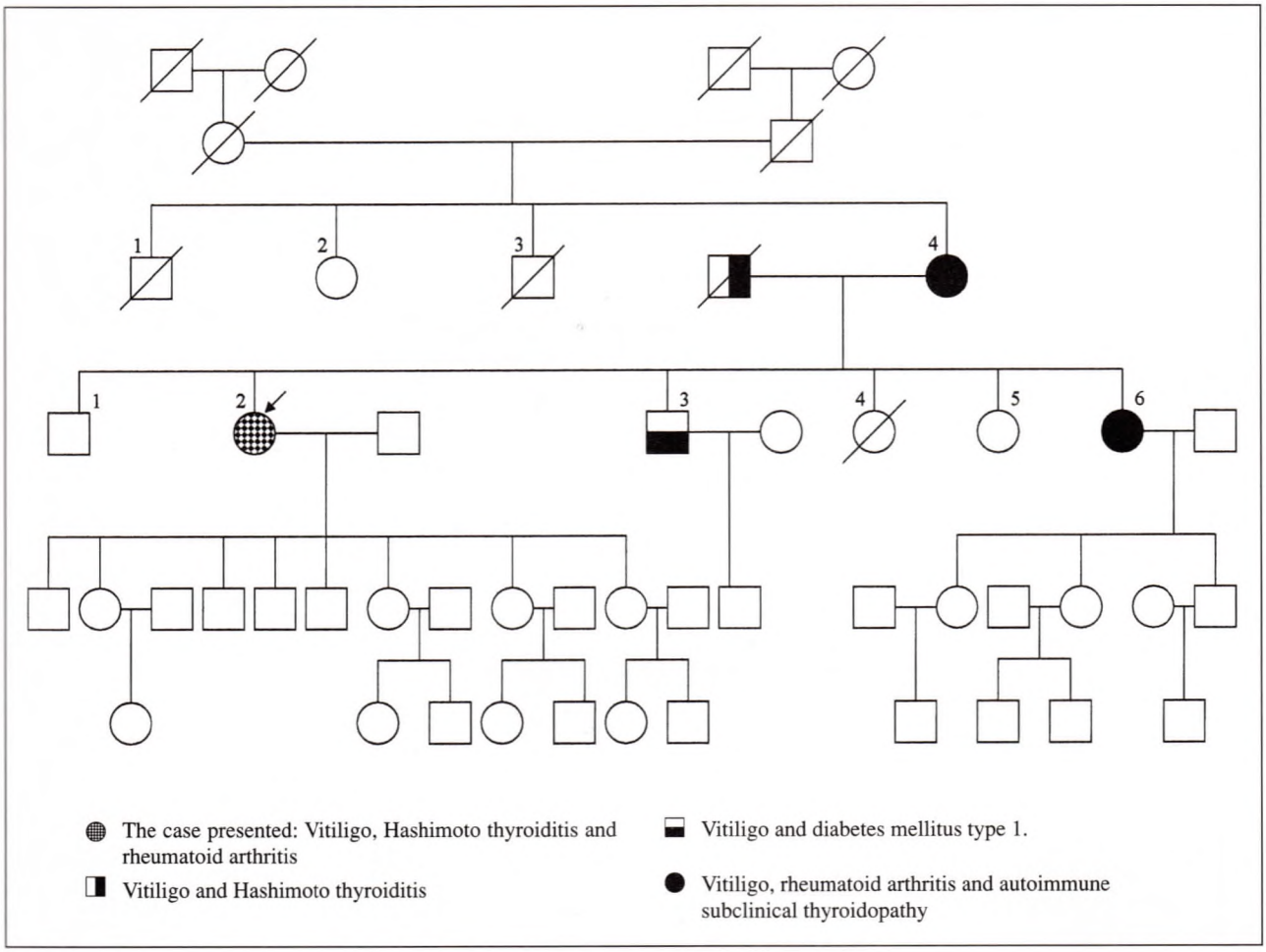

Fig. 2
The pedigree of the patient and the distribution of the autoimmune diseases in vitiligo subjects

have negatively influenced its evolution. The association of autoimmune diseases in vitiligo affected members of this family supports the hypothesis of a genetic predisposition in the development of autoimmunity (14). In this regard, additional data can be brought by exploring the autoimmunity on unaffected family members *(Fig. 2.)* and by genetic studies of linkage and mapping. The complexity of this case is also determined by the association between skin and ocular depigmentation, suggesting that the mechanism of melanocyte destruction unfurls on two levels (ocular and skin), as previously has been reported (18, 19). In the absence of cutaneous / systemic manifestations of lupus we interpret at the moment the presence of ANA with speckled pattern at a fairly low titer, as part of an inflammatory syndrome (like rheumatoid arthritis or streptococcal infection).

Conclusion: The phenotypical expression of the disease and its evolution in this case is probably influenced and conditioned by the presence of some susceptibility genes for vitiligo and autoimmune diseaes as mentioned before, in association with triggering factors (stress, infections, sun exposure, mechanical trauma); this idea brings new proofs on the support of plurifactorial etipathology of the disease.

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Hazai Hírek

A Magyar Dermatológiai Társulat Kontakt Dermatitis Munkacsoportja 2004. november 2-án a Semmelweis Egyetem Bőr-, Nemikórtani és Bőronkológiai Klinika tárgyalótermében ez évi ülését megtartotta.

A munkacsoport ülésén az alábbi előadások hangzottak el:

„Foglalkozási bőrbetegségek bejelentésével kapcsolatos tapasztalatok és problémák" *(Kohánka V.).*

„Kontakt szenzibilizáció diagnosztikája – metodikai kérdések" (ESCD 2004 ülés – Koppenhága – konszenzus alapján *(Temesvári E.).*

„Helyi érzéstelenítők tesztelési lehetőségei" *(Baló J. M.).*

A munkacsoport a fenti program szerint áttekintette a foglalkozási bőrbetegségek hazai bejelentési kötelezettségét előíró jogszabályt, az Európai Közösség államainak e témához kapcsolódó előírásait és az ettől eltérő hazai adatok indokait.

Az ülésen ismertetésre került a munkacsoport hazai multicentrikus felmérésében vizsgált helyi corticosteroid kontakt szenzibilizáció eredményeit és konzekvenciáit tartalmazó munka.

A munkacsoport áttekintette a „Magyar sor" kontakt allergenjeit, továbbá – a nemzetközi tapasztalatokból várható – további bővítések lehetőségeit (pl. localis steroidok, konzerválószerek, és az ún. „experimental panel"). A jelenlévők a kontakt szenzibilizációt kiváltó új allergének és új tesztelési lehetőségek ismertetése során az új „foto patch" sor kontakt allergénjeinek hazai tesztelhetőségét is megbeszélték. A munkacsoport a 2004 év ESCD kongresszus epicutan bőrtesztekre vonatkozó konszenzusainak ismertetése és megvitatása kapcsán az epicutan tesztelések kritériumait, kontraindikációit, értékelési előírásait és az expozíciós idők (20 perc, 24 és 72 óra) kritériumait is elfogadta, valamint áttekintette a kontakt szenzibilizáció expoziciós lehetőségeit, valamint az ún. „saját anyag" tesztelésére vonatkozó előírásokat is.

Az ülésen ismertetésre és megvitatásra kerültek a helyi érzéstelenítők in vivo tesztelésének új elfogadott metodikái.

Budapest, 2004. november 2.

Temesvári Erzsébet dr.
Kontakt Dermatitis Munkacsoport elnöke