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# A new pigment from mesenchymal stem cell's secretome for segmental vitiligo: A case report

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**Abstract**
Vitiligo is a chronic skin disorder characterized by white macules due to melanocyte destruction in the skin and mucosa. The disease not only has a negative impact on aesthetics, but also self-confidence and psycho-social well-being. While there are several treatment options to stop depigmentation and stimulate repigmentation, there is no specific or gold standard treatment that is highly satisfactory. This case report presents a 19-year-old male who came to the dermatology clinic with milky white patches on the right side of his face, cheeks and nose since one month prior. Initially, the patches were small, then expanded and multiplied. On dermatologic examination, multiple depigmented macula-plaques, with firm borders, irregular edges, unilateral distribution, and varying in shape and size were found. The patient was diagnosed as Segmental Vitiligo with VETF 7, 6. The patient was treated with dermapen (microneedling therapy) every 2 weeks for 9 months by applying 0.3 cc of 5% CM-WJMSCs (Conditioned Medium-Wharton's jelly-Mesenchymal Stem Cells) serum to the entire lesion area. The serum was also applied 2 times a day daily at home. At follow-up, it was found that the lesions slowly started to repigment with VETF 5.6. Secretome has many functions especially immunomodulatory which could modify the immune system of vilitigo. In this patient, the therapy produced good results without hyperpigmentation in the lesions. Thus, secretome might be a good treatment choice for vitiligo.

**Keywords:** Vitiligo, depigmentation, secretome, conditioned medium, case report

## Introduction
Vitiligo is a chronic autoimmune skin disease characterized by patches of depigmentation due to loss of melanocytes [1, 2]. This dermatological condition affects the skin and hair and is characterized by the presence of white patches (Macules-plaques) of varying shapes such as oval, round, linear or irregular, well demarcated with normal skin, can be segmental or generalized, with sizes ranging from millimeters to centimeters, and when affecting haired locations, the hair can turn white. Vitiligo has no gender predilection but the disease usually starts at thirty years of age, although manifestations before this age are also found. Currently, vitiligo cases in the world account for 2% of the total population. Geographically, vitiligo prevalence varies considerably. Higher prevalence rates are reported in areas with dark-skinned populations. This is because these people are more concerned and therefore have a higher willingness to seek health care. Conversely, under-reporting of vitiligo cases may occur because some health services ignore vitiligo and consider it an aesthetic problem rather than an autoimmune disease [3, 4].

This disease not only negatively affects aesthetics, but also self-confidence and psycho-social well-being. Seventy-five percent of vitiligo patients have psychological disorders and decreased confidence in social life. Until now, the pathogenesis of vitiligo is still unknown, but autoimmune, oxidative stress, and genetics are suspected [2]. The main principle of vitiligo therapy aims to minimize disease progression by stabilizing and repigmentation. Vitiligo treatment is influenced by several factors such as patient preference (cost and accessibility) and patient's response to treatment. Vitiligo can be treated with various modalities such as phototherapy, surgery, topical treatments such as corticosteroids, immunosuppressive agents, calcineurin inhibitors and vitamin D, but up to now, there is no optimal treatment because the effectiveness of therapy in each patient is different and none has proven consistent in the process of skin repigmentation [2, 4].

Conditioned medium (CM) is rich in biological and growth factors, has many benefits including immunomodulation, regeneration, and anti-inflammation. The role of CM particularly in immunomodulation, can modify the immune system, whose main target is CD8+T cells, which are important in the pathogenesis of vitiligo, so CM is a good therapeutic option for vitiligo [5, 7]. Therefore, the purpose of this case report is to report clinical improvement in vitiligo patients with CM administration.

## Case Report

A 19-year-old male with complaints of milky white patches on the right side of his face, cheeks and nose since one month prior. Initially the patches were small, then expanded, became whiter and more numerous. The spots were painless, not itchy and not preceded by injury or inflammation (Figure 1A). There were no systemic symptoms and other complaints found in the patient. The patient had no previous history of other diseases and had not received any treatment. Family history of vitiligo and other autoimmune diseases were denied by the patient. Physical examination revealed a good general condition with normal vital signs. On dermatologic examination, depigmented macules, multiple, firm borders, irregular edges, unilateral distribution, varying in shape and size from lenticular to plaques were found. Wood lamp examination revealed milky white color in the lesions. The patient was diagnosed with Segmental Vitiligo with VETF 7.6. The patient was treated with dermapen (microneedling therapy) every 2 weeks by applying 0.3 cc of 5% CM-WJMSCs gel to the entire lesion area at the clinic and applying it twice a day daily at home. After 6 months of therapy, the patient's VETF was 6.6, depigmentation was reduced and repigmentation began and no new lesions were found (Figure 2A). After 9 months of therapy, the results improved even more, with a VETF of 5.6, reduced depigmentation, skin repigmentation, and no new lesion formation (Figure 3A).

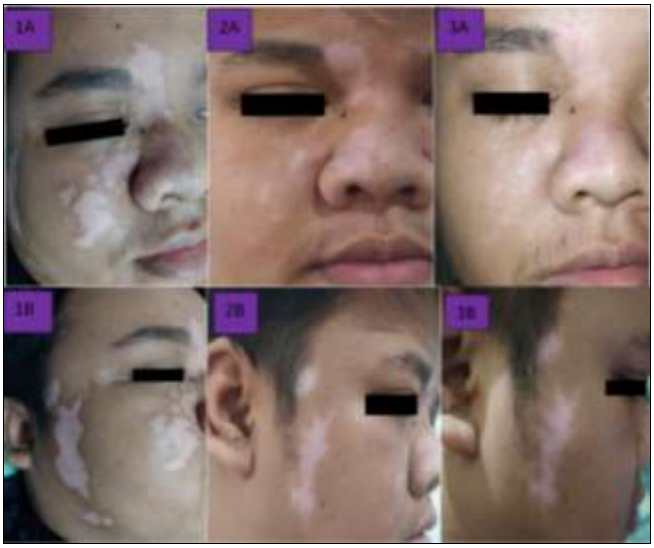

**Fig 1A, 1B:** The clinical features when first came to the clinic with a VETF of 7.6

**Fig 2A, 2B:** Clinical features after 6 months of therapy with VETF 6.6

**Fig 3A, 3B:** Clinical features after 9 months of therapy with VETF 5.6

## Discussion

Vitiligo is an autoimmune chronic skin disease where CD8+ T cells cause the destruction of melanocytes resulting in depigmentation of the skin, hair or mucosa [1, 2, 6, 7]. The dermatological condition is characterized by the presence of white patches (Macules-plaques) with varying shapes such as oval, round, linear or irregular with clear boundaries with normal skin, which can be segmental or generalized, with sizes ranging from millimeters to centimeters. Vitiligo is most common among dark-skinned thirty-year-olds with no gender predilection [1, 4]. Until now, there is no satisfactory specific therapy or gold standard for vitiligo because the effectiveness of therapy in each patient is different and none has been proven consistent in the process of skin repigmentation, so it is a challenge for doctors to choose the appropriate therapy. The existing therapies include phototherapy, surgery, topical treatments such as corticosteroids, immunosuppressive agents, calcineurin inhibitors and vitamin D. The main principle of vitiligo therapy aims to reduce disease progression by stabilizing and repigmentation which is influenced by several factors such as patient preference (Cost and accessibility) and patient's response to treatment [2, 4].

Conditioned medium (CM) is known as secretome secreted by Mesenchymal Stem Cells (MSCs) which is rich in biological and growth factors and can be used for various therapies especially in dermatology [5]. MSCs can be isolated from several sources such as bone marrow, umbilical cord and placenta, amniotic fluid, gums, and fat tissue. Currently, CMs are attracting attention because they provide more advantages than MSCs. Based on research, MSCs that derived from fetal tissues are reported to be superior to MSCs from adult tissues. CM can be produced in large quantities, packaged and stored for long periods of time, making it easier to transport [8, 10]. The secretome contains a variety of growth factors, cytokines, chemokines, angiogenic factors, and extrassacellular vesicles. These elements exhibit regenerating, anti-inflammatory, and immunomodulating effects, thus potentially providing advantages for various types of skin disorders. In addition, because it is a number of acellular molecules, the secretome is safer than cells which is thought to address safety concerns including tumorigenicity, infection transmission, and immune incompatibilities [5, 9].

Conditioned Medium-Wharton's jelly-Mesenchymal Stem Cells (CM-WJMSCs) isolated from umbilical cord tissue have high effect and durability, low immunogenicity, and are less affected by environmental factors and genetic changes. The therapeutic effects of secretomes are due to their paracrine properties, which are divided into soluble factors (Growth factors, cytokines, chemokines, and enzymes) and extracellular vesicles (Exosomes and microvesicles/ectosomes). Exosomes and microvesicles have a role in intracellular communication. Exosomes also play a role in cellular defense and induce immune responses by being antigen-presenting vesicles. Albumin and alpha-2-macroglobulin are the most expressed proteins in CM-WJMSCs that contribute to wound healing. They are rich in interleukin 1-alpha (IL-1α), IL-1β, IL-6, IL-8, and granulocyte-macrophage colony-stimulating factor (GM-CSF), showing pro- and anti-tumorigenic effects [3, 4]. Other factors such as IL-2, IL-7, IL-12, IL-15, monocyte chemoattractant protein-1 (MCP-1), macrophage inflammatory protein-1beta (MIP-1β) play a role in cell

proliferation and tissue repair. There are also chemoattractants (MCP1, MIP-1β, RANTES, hepatocyte growth factor (HGF), fibroblast growth factor-2 (FGF-2), PDGF-AA) that facilitate the mobilization of immune cells. Four hundred and thirty-six genes were found to be expressed in CM-WJMSCs which play a role in immunomodulation, angiogenesis, wound healing, apoptosis, antitumor, and chemotaxis, making CM-WJMSCs superior to MSCs derived from bone marrow.[10–12] CM's ability to immunomodulate modifies the immune system, inhibiting the proliferation of CD8+ T cells and increasing the proportion of Treg cells (regulatory T cells). CD8+ T cells themselves are key in the pathogenesis of vitiligo, where they destroy melanocyte cells resulting in depigmentation. Extracellular vesicles are believed to be a new signaling medium for intracellular communication between melanocytes and keratinocytes through exosomes, stimulating skin pigment [5, 7, 10, 12]. Dermapen therapy (microneedling therapy) with standardized doses and protocols in the clinic[13] was performed on patients before the application of 0.3 cc 5% CM-WJMSCs gel serum, with the aim of repairing cell damage (through skin regeneration properties) after skin layer injury and as a facilitator of drug penetration. Serum application, also has cell repair benefits so that it can have a better effect when combined with dermapen which aims to repair damaged pigment in vitiligo. [6, 13]

The challenge in this case is the need for cooperation between doctors and patients, because the selection of therapy and patient compliance in treatment and control may also affect the results of therapy. In this case, the patient complied with treatment and control to the clinic as recommended by the doctor, so the results of therapy were satisfactory, there was skin repigmentation in the patient, and there were no side effects, but further therapy and further research are still needed in vitiligo cases.

## Conclusions

Vitiligo is a chronic skin disease resulting from the destruction of melanocytes in the skin and mucosa. This dermatological condition affects the skin and hair and is characterized by milky white patches (macules-plaques) that can be segmental, localized in one area of the body or generalized. CM has functions as an immunomodulator, anti-inflammatory and cell regenerator. This principle can be applied to treat vitiligo especially in modifying the immune system. The results of CM intervention on vitiligo are quite satisfactory, without any side effects and patient is satisfied with the results.

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