IADVL

SIG Pigmentary Diseases (IADVL Academy) Newsletter

Issue 3, February 2018

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Message from Dr. Nilendu Sarma, Coordinator SIG-pigmentary disorders (2014–2016)

Dear all,

Wish you all a happy new year.

During my tenure as coordinator of IADVL SIG-pigmentary disorders 2014–2016, SIG conducted many scientific activities and has achieved some important milestones.

The "Melasma guideline" project required almost 2 years of continuous and coordinated work among the SIG members as well as other senior IADVL members. Review and treatment recommendation was done following the protocol of Oxford Centre for Evidence-Based Medicine (OCEBM). This large exhaustive scientific project was published as "Evidence-based Review, Grade of Recommendation, and Suggested Treatment Recommendations for Melasma."

The pan Indian Vitiligo study was another ambitious project begun during my tenure and completed in 2017. This study has collected possibly the largest data on vitiligo the world has ever generated. This extensive data is under process of evaluation.

I wish the present SIGpigmentary disorders all the success in future.

Regards

Dr. Nilendu Sarma

Message from Dr. Shital Poojary, Coordinator, SIG-pigmentary disorders

A happy new year to all. SIG-pigmentary disorders has had an eventful 2017 with two workshops/CME being conducted: Vitiligo Surgery at Pune and Vitiligo update at Mumbai. The MEDEC-V Study (A multicentric clinico-epidemiological study of vitiligo) started during Dr. Nilendu's tenure was completed. Most important of all, evidence-based guidelines for treatment of melasma were completed and published in IDOJ. A heartfelt appreciation of the 2 years' worth of efforts by Dr. Nilendu and thanks to the IADVL Academy for guiding us through the process.

This newsletter under the able editorship of Dr. Nirmal is an effort to bring to you the latest in the field of vitiligo as well as snippets about other hypopigmentary disorders

FROM THE EDITOR'S DESK

Dear colleagues and friends,

It gives me immense pleasure to edit the second newsletter of SIG-pigmentary disorders. The theme this time is "hypopigmentary disorders" with specific emphasis on vitiligo. We have tried to address the questions on stability of vitiligo and provided excerpts from recently published literature. The newsletter also has quiz and interesting trivia on hypopigmentary disorders.

I thank Dr. Imran Majid, Dr. Deepti Ghia, and Dr. Sayantani Chakraborty for their valuable contributions to this newsletter. I am grateful for the support of both the past coordinator Dr. Nilendu Sarma and the present coordinator Dr. Shital Amin Poojary.

Hope you enjoy reading this issue of the newsletter compiled by us. Do look out for the next issue. More to come.

Photos of SIG meeting this year with event details

1. **Vitiligo Surgery Workshop at Pune:** SIG-pigmentary disorders in association with IADVL Maharashtra branch and Smt. Kashibai Navale Medical College conducted a live vitiligo surgery workshop on April 23, 2017 in Pune. Convenor of the work shop was Dr. Vinay Saraf who delivered a lucid and insightful lecture about social stigma attached to vitiligo and various surgical modalities of treatment. The agenda of the workshop was to perform live vitiligo surgeries and interactive discussion sessions to update the knowledge of students and delegates.

All surgical modalities were described and demonstrated in detail by well-known faculties Dr. Manas Chatterji, Dr. Girish Shah, Dr Yuvraj More, and Dr. Nitin Bendsure. Chief Panellists were Dr. Neeta Gokhale, (Head of Department of Dermatology SKNMC & GH and Organizing Chair), Dr. Swapna Khatu, and Dr. Pradeepkumari. Around 120 delegates were benefited by this excellent academic event.

2. **CME: Vitiligo Update** was held on June 25, 2017 (Vitiligo Day) in association with IADVL Maharashtra Branch at KEM Hospital, Mumbai. The CME focussed on recent advances in pathogenesis as well as management of Vitiligo. Dr. Nitin Nadkarni elaborated on recent advances in pathogenesis of vitiligo and their practical relevance. Dr. Binod Khaitan shared his vast experience on segmental vitiligo. Other esteemed faculty included Dr. Uday Khopkar, Dr. Ramesh Bhat, Dr. Vinay Saraf, Dr. Manas Chatterjee, Dr. Sharmila Patil, and Dr. Meghana Phiske.
3. **SIG-pigmentary disorders session at CUTICON Maharashtra** December 2017:
   i. Immunosuppressants in vitiligo: With a focus on
   Are we justified in using them?
   Which immunosuppressant to use?
   How long do we use?
   Moderator Dr. Swagata Tambe conducted the session adroitly with the esteemed panellists: Dr. Manas Chatterjee, Dr. Sushil Pande, Dr. Lalit Gupta, and Dr. Narsimha Rao
   ii. Facial melanosis: Achieving the best possible outcome: A case series: Expert opinion.: Panel Discussion conducted by DRSharmila Patil with panellists DR Priti Shenai, DR Manjyot Gautam, DR Prashant Jadhav and DR Vijay Zawar

Stability in vitiligo: how unstable is the concept?

Dr. Imran Majid

Stability in vitiligo can be defined in the most simplistic terms as "vitiligo where no new lesions are occurring and the lesions already present are not increasing in size over sufficient period of time." However, the concept of stability in vitiligo is not so simple when it comes to practical aspects.

WHY IS "STABILITY" IMPORTANT FOR US?

For a treating dermatologist, stability of the disease process in vitiligo has two main practical implications. First, in an unstable disease, the priority for the treating physician is to control the progression of disease.

Second and more important practical significance of "stability" is in deciding about the feasibility of surgical intervention or grafting in vitiligo. There is a possibility of depigmentation of the grafts as well as koebnerization at the donor site if any surgical intervention is performed in a patient with unstable vitiligo.

WHAT ARE THE CLINICAL PARAMETERS OF VITILIGO STABILITY

The most important clinical parameters for labeling vitiligo as "stable" include the following:

1. No history of fresh lesions
2. No extension or progression of existing lesions
3. Absence of Koebner's phenomenon

In addition to these three main parameters, there are some other concepts that have been described in the context of vitiligo stability. These are

VIDA score

This score grades the level of activity of the disease process in vitiligo. The activity of vitiligo is graded from −1 to +4 indicating increasing levels of disease activity.

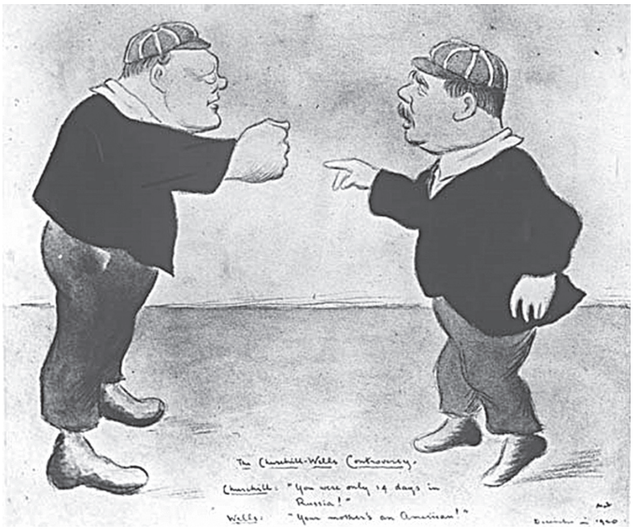
Score −1: Indicates disease with spontaneous repigmentation
Score 0: Disease stable for last 1 year
Score 1: Disease stable for 6 months but history of progression in last 1 year
Score 2: Disease stable for 3 months only
Score 3: Disease stability for the previous 1 month only
Score 4: Actively spreading vitiligo

Minigrafting test

In this test, some test punch grafts are transplanted into the center of a vitiligo lesion with postprocedure sun exposure for 15 minutes daily. The response is assessed after 3 months and if repigmentation is observed beyond 1 mm of the implanted grafts, the test is considered to be positive.

WHAT ARE THE CONTROVERSIES AND LIMITATIONS OF TESTING VITILIGO STABILITY

Stability in vitiligo is riddled with controversies. We still don't know the answers to many questions in the context of vitiligo stability. These questions can be summarized as follows.



IS STABILITY PATIENT SPECIFIC OR LESION SPECIFIC?

In many vitiligo patients the disease is progressing at one site while there is spontaneous repigmentation at other sites simultaneously. Even after a grafting procedure, one can see donor site depigmentation with simultaneous repigmentation at recipient site in many patients. The reverse is also sometimes seen when the grafts depigment totally while there is normal repigmentation at the donor site. All these phenomena point towards lesion-specific stability.

What should be the minimum duration of nonprogression be before we can label the disease as stable?

Interestingly, there is no consensus among the world authorities on the minimum duration of stability before vitiligo can be safely taken up for grafting or transplantation. While some authors suggest a minimum period of 6 months (Boersma BR, 1992), others recommend a waiting period of 3 years (Falabella, 1992).

Can the minigraft test predict stability of disease in all cases?

There are many fallacies of the minigraft test and doubts have been expressed about the suitability of this test in predicting response to vitiligo grafting. In many cases, a positive response to grafting has been observed in minigraft-negative cases. On the contrary, even in patients with a positive minigraft test, no favorable response to grafting has been observed.

Should the issue of stability be determined by clinical parameters or by cellular methods?

As the clinical parameters described above have failed to provide a foolproof method of determining stability, many researchers have proposed to use cellular and biochemical methods for determining vitiligo stability. A lot of advances have been made in this realm.

CONTROVERSIES REGARDING STABILITY IN VITILIGO

- Simultaneously, vitiligo can be progressive at one site and stable or regressive at other site.
- Graft depigmentation and donor repigmentation, and conversely, graft repigmentation and donor depigmentation can be observed after vitiligo grafting.
- No consensus on the minimum duration of stability for surgical intervention in vitiligo.
- No consensus on whether the disease stability or the lesional stability is relevant to surgical intervention.
- Assessment of stability by cellular or immunological methods is not clear as of now.

MICROSCOPIC PARAMETERS TO ASSESS STABILITY

Vacuolar changes in basal epidermal cells and dermal lymphocytic infiltrate along with melanophages are more prominently seen in active vitiligo in the perilesional area. Ultrastructurally, melanocytes in active vitiligo have been shown to demonstrate larger perinuclear zone and small dendrites with clubbed ends and also less adhesion to collagen type IV. Immunohistochemical staining reveals increased expression of epidermal ICAM-1 and CD3, CD4, and CD8 T-lymphocytes in the perilesional skin of active vitiligo cases. On the contrary, CCL22 expression is decreased in these patients.

BIOCHEMICAL PARAMETERS FOR ASSESSING STABILITY

Among the biochemical parameters, both plasma and urinary levels of catecholamines have been correlated with the disease activity in vitiligo. Urinary excretion of catecholamine metablites like homovanillic acid (HVA) and vinylmandelic acid (VMA) are increased in active vitiligo patients in comparison with those having stable disease. Similarly, plasma levels of catecholamines and their

metabolites viz. norepinephrine, metanephrine (MN), dopamine (DA), and 5-hydroxy indole acetic acid (5-HIAA) have been reported to be increased in patients with active vitiligo. Serum and RBC oxidant status has also been correlated with activity of vitiligo, demonstrating higher levels of superoxide dismutase and lower levels of glutathione peroxidase. Similarly, plasma levels of neuropeptide Y (NPY) have been found to be higher in progressive vitiligo than in stable disease or in controls.

LESIONAL VERSUS DISEASE STABILITY

There are no studies available on the relative importance of lesional stability versus disease stability in vitiligo. There is still no consensus on the operability of a lesion that has been stable for many years in a patient with a clinically stable disease of a few months only. Only one clinical study has looked at this aspect and the study concluded that lesional stability is as important and as relevant as disease stability in surgical management of vitiligo.

CONCLUSIONS

Vitiligo is a disease whose exact pathogenesis is not known with utmost clarity. And as of now, there are no foolproof methods to categorize vitiligo as "stable" or "unstable." However, for a practicing dermatologist, a patient who does not demonstrate any enlargement of pre-existing lesions or appearance of new lesions, will be designated as having a "clinically stable disease." Such a clinically stable disease will not need any immunosuppressive therapy and will be amenable for surgical intervention.

EXCERPTS FROM RECENT LITERATURE

Dr. Nirmal B.

New discoveries in the pathogenesis and classification of vitiligo.

Rodrigues M, Ezzedine K, Hamzavi I, Pandya AG, Harris JE. Vitiligo Working Group. *J Am Acad Dermatol*. 2017;77:1–13.

International consensus report (2012) recommended that the umbrella term "vitiligo" be used for all forms of vitiligo except the segmental variant of the disorder as it has distinctive progression and treatment response.

Interferon (IFN)-gamma production pathway and IFN-gamma induced gene expression are predominantly observed in vitiligo and the cytokine is required to recruit melanocyte-specific, autoreactive CD8 T cells to the skin through chemokine CXCL10 and its receptor CXCR3. Hence, interfering with this pathway might be a new treatment strategy in vitiligo.

Current and emerging treatments for vitiligo.

Rodrigues M, Ezzedine K, Hamzavi I, Pandya AG, Harris JE. Vitiligo Working Group. *J Am Acad Dermatol*. 2017;77:17–29.

Afamelanotide is a potent synthetic analogue of alpha-melanocyte-stimulating hormone. It enhances the efficacy of NB-UVB in patients with vitiligo and was an effective adjunct to NB-UVB in a double blind, multicenter study. Side effects included hyperpigmentation, pruritus, and nausea.

Targeted immunotherapy targeting the interferon (IFN)-gamma–CXCL10 chemokine axis appears to be an important target for the development of new treatments for vitiligo. Tofacitinib and ruxolitinib inhibit IFN-gamma signalling. Both drugs are found to be efficacious but repigmentation regressed when ruxolitinib was discontinued, suggesting that continuous treatment is necessary. Serum CXCL10 level was reduced during treatment with ruxolitinib, suggesting that it may serve as a biomarker for disease activity and treatment response.

The first transepidermal transplantation of non-cultured epidermal suspension using a dermarolling system in vitiligo: A sequential histological and clinical study.

Benzekri L, Gauthier Y. *Pigment Cell Melanoma Res*. 2017;30:493–7.

The technique used in this short communication involves preparation of a trypsinized keratinocyte/melanocyte suspension from a nonlesional area over the patient's scalp skin and transepidermal delivery of the suspension using a 0.2 mm needle dermaroller. The technique causes epidermal microinjuries without inflammation. Five patients with stable vitiligo lesions over the face underwent the treatment with mild repigmentation in two cases and excellent repigmentation in three cases after 6 months. The advantage of dermarolling for intraepidermal melanocyte delivery is that it is simple, minimally invasive, and has a better control over melanocyte distribution in recipient area.

Combined epidermal and follicular cell suspension as a novel surgical approach for acral vitiligo.

Razmi T M, Parsad D, Kumaran SM. *J Am Acad Dermatol*. 2017;76:564–7.

In this study, epidermal cell suspension (ECS) was mixed with follicular cell suspension (FCS) in a 1:5 ratio and the combined suspension was transplanted to the recipient area without any additional treatment. The superior repigmentation obtained in combined ECS and FCS was postulated to be due to keratinocyte growth factors like stem cell factor or basic fibroblast growth factor from ECS facilitating stem cells in FCS. Treatment resistance in acral vitiligo is mainly due to stem cell defect and hence, this new approach may be a good therapeutic option in acral vitiligo.

QUIZ

Dr. Sayantani Chakraborty

1. Gene mutation responsible for APECED syndrome- ----------

2. Hermansky-Pudlak Syndrome is an autosomal recessive condition associated with oculocutaneous albinism (OCA), ceroid deposit in the reticuloendothelial (RE) system, and haemorrhagic diathesis. Haemorrhagic diathesis is due to absence of -------- bodies in platelets.

3. Giant platelets and giant melanocytes are found in -------.

4. This syndrome is associated with retinitis, unilateral vitiligo, unilateral poliosis.

5. This micronutrient deficiency leads to hypopigmentation of skin and hair.

6. Trisomy 13 leads to --------- hypopigmentation.

7. Eye manifestation observed in Vogt–Koyanagi–Harada syndrome (VKHS)- ----------

8. OCA1B is also known as ---------- mutant albinism.

9. Tyrosinase positive OCA is also known as ---------- OCA

10. These occur as earliest manifestation of tuberous sclerosis- ----------.

PHOTO QUIZ

Dr. Deepti Ghia

Identify the disease condition

Upcoming pigmentary meetings

UPCOMING PIGMENTARY CONFERENCES

- ASPCR conference 2018
  9th Asian Society for Pigment Cell Research (ASPCR) conference, August 15–18, 2018, Colombo, Sri Lanka

ANSWER TO PHOTOQUIZ

Congenital Hetrochromia Iridis

Heterochromia iridis is a condition in which the iris in one eye has a different color than the iris of the other eye. Heterochromia iridis is to be differentiated from heterochromia (difference in color) iridum (within the iris of one eye).

Brown eyes have large amounts of melanin pigment deposits, and blue eyes have a lack of melanin. Although eye color is inherited, the inheritance pattern is complex, with interaction of more than one gene. These genes interact to provide the full constellation of colors.

The incidence of congenital heterochromia iridis is approximately six out of a 1,000, although in most of these cases, it is hardly noticeable and unassociated with any other abnormality.

Congenital syndromes which may be characterized by heterochromia iridis include Waardenburg syndrome, piebaldism, Sturge–Weber syndrome, neurofibromatosis type 1, tuberous sclerosis, Incontinentia pigmenti, Parry-Romberg syndrome.

ANSWERS TO WORD QUIZ

1. AIRE
2. Dense
3. Chediak-higashi syndrome
4. Allezandrani
5. Copper
6. Phylloid
7. Uveitis
8. Yellow
9. Brown
10. Ashleaf macules

IMAGE TRIVIA IN HYPOPIGMENTARY DISORDERS

Dr. Deepti Ghia

Albino animals with their normo-pigmented counter parts

http://motswariblog.blogspot.in/2011/02/breaking-news-10th-february-white-lions.html

http://uncyclopedia.wikia.com/wiki/File:Albino_and_regular_chimpanzee.PNG

Vitiligo in birds

http://boredomtherapy.com/animal-color-mutations/

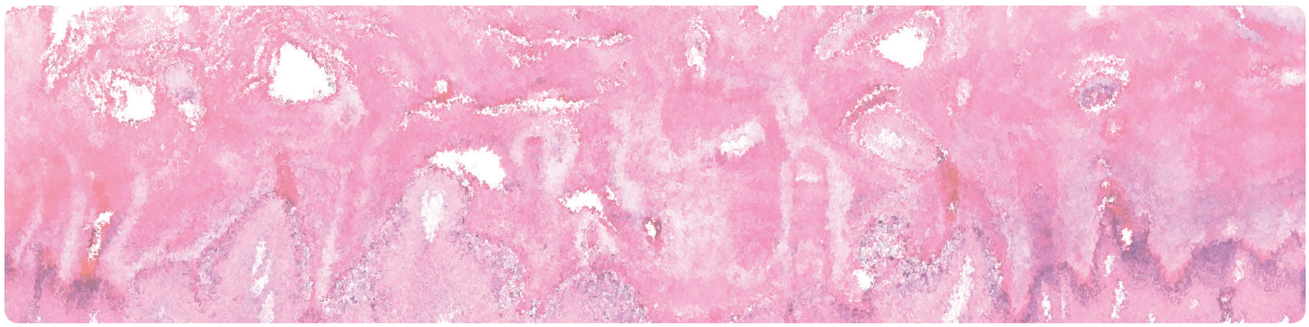
Dr Deepti Ghia

Squamous cell carcinoma in an albino "Pink" Dolphin

https://dolphinproject.com/blog/
dolphin-project-vet-pink-dolphins-skin-cancer-very-advanced/

Vitiligo in elephants

https://www.pinterest.co.uk/pin/
375276581422471617/



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