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  - A photographic essay that includes both clinical and pathological photographs in color. The diagnosis and legends for the photographs should be listed after the references in the article. The article should be no more than 2-3 pages in length.

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  - Letters to the editor and short notes. Contributions should not exceed 600 words, two figures, and 10 references.

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  - An article relating to the surgical aspects of treatment. Article types may include Review, Report or Case Report Format.

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  - An original article including, whenever possible, an Introduction, Materials and Methods, Results, Comment and References. A Structured Abstract of not more than 240 words must be included. It should consist of four paragraphs, labelled Background, Methods, Results, and Conclusions. It should describe the problem studies, how the study was performed, the main results, and what the author(s) concluded from the results.

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  - By invitation only. A major didactic article that clarifies and summarizes the existing knowledge in a particular field. It should not be an exhaustive review of the literature, and references should not exceed 100 in number. Tables, diagrams, and selected figures are often helpful. The length is left to the judgment of the author, although it generally should not exceed 5000 words. Topics may include updates in clinically relevant basic science and cutaneous biology.

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For example:

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For example:

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Send illustrations as tiff or jpeg files. In the case of photomicrographs, the stain type and original magnification should be stated. Each figure should bear a reference number corresponding to a similar number in the text.

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*No abstract required
Malaysian Journal of Dermatology

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ANOUNCEMENT

CPD
56 39th Annual General Meeting and Dermatology Conference 2014

57 73RD American Academy of Dermatology Annual Meeting San Francisco 2015

58 23RD World Congress of Dermatology Vancouver 2015
Malaysian Clinical Practice Guidelines for the Management of Psoriasis Vulgaris 2013: Summary of recommendations

Choon Siew Eng FRCP, on behalf of the Guideline Development group

Malaysia Health Technology Assessment Section, Medical Development Division, Ministry of Health Malaysia


Introduction
Psoriasis is a genetically determined, systemic immune-mediated chronic inflammatory disease that affects primarily the skin and joints. It has been estimated to affect 1 - 3% of the general population worldwide. There is no population-based prevalence study on psoriasis in Malaysia. However, new cases of psoriasis accounted for 2 to 6% of all new dermatology clinic attendees in Malaysia1,2. There are several distinctive clinical sub-types of psoriasis. Psoriasis vulgaris (Figure 1), the most common type, is seen in 85% of the 4,445 patients registered in the Malaysian Psoriasis Registry3. Psoriatic arthritis (PsA) is present in 16%.

Psoriasis can be as physically and mentally disabling as other major medical diseases such as cancer, heart disease, diabetes, hypertension, arthritis and depression4,5. Patients not only have to deal with their highly visible skin disease, they also endure physical discomfort such as skin tightness, pain, bleeding and itch. When tested with SF36, patients with psoriasis only score better than patients with congestive heart failure in terms of physical health and they are only better off than patients with depression and chronic lung disease in terms of mental health5. Psoriasis is a systemic chronic inflammatory disease with significant increased risk of cardiovascular morbidity and mortality. Numerous studies demonstrated that patients with psoriasis are

Figure 1 Well demarcated erythematous plaques with silvery scales.
more prone to metabolic syndrome or the individual component of metabolic syndromes namely obesity, diabetes mellitus, dyslipidemia, and hypertension\textsuperscript{6-10}. Co-morbidities are also common in Malaysian patients with psoriasis. Among 4445 Malaysians with psoriasis, 36.8% were overweight, 34.2% obese, 24.6% had hypertension, 17.4% had diabetes mellitus, 15.9% had dyslipidemia, and 5.6% had ischaemic heart disease. Young adults with severe psoriasis have a 3-fold increased risk of developing MI and a reduction of 3 - 4 years in life expectancy\textsuperscript{7,8,11}. There is also increasing evidence that controlling chronic inflammation of psoriasis with systemic agents or biologics reduces cardiovascular co-morbidity\textsuperscript{8,11-14}.

Effective treatments are available. Unfortunately, surveys showed that patients frequently received suboptimal care or were on ineffective treatment for longer than necessary\textsuperscript{15-16}. To improve care of patients living with psoriasis, the Malaysia Health and Technology Assessment Section of the Ministry of Health (MaHTAS) recently published a clinical practice guidelines(CPG) for the Management of Psoriasis Vulgaris in adults\textsuperscript{17}. This article summarises recommendations from this evidence-based CPG. Evidence levels for the recommendations are indicated in brackets.

**Table 1** Grades of recommendations.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At least one meta-analysis, systematic review, or RCT, or evidence rated as good and directly applicable to the target population</td>
</tr>
<tr>
<td>B</td>
<td>Evidence from well conducted clinical trials, directly applicable to the target population, and demonstrating overall consistency of results; or evidence extrapolated from meta analysis, systematic review, or RCT</td>
</tr>
<tr>
<td>C</td>
<td>Evidence from expert committee reports, or opinions and/or clinical experiences of respected authorities; indicates absence of directly applicable clinical studies of good quality</td>
</tr>
</tbody>
</table>

Principles of care

- Management should start with patient education.
- Treatment of psoriasis should be a combined decision between patients and their healthcare providers.
- Treatment goal and minimal target set should be based on disease severity and patient preferences.
- Treatment goals achieved should be monitored regularly to detect loss of response which may necessitate modification of therapy (Table 2)

Assessment of disease severity (Grade C)

- Assess severity and impact of psoriasis on patient’s quality of life
  - At first presentation
  - Before referral for dermatologist advice and at each referral point in the treatment pathway (Algorithm 1)
  - To evaluate effectiveness of interventions at specific time points (Table 2)

- Use percentage of body surface area involved (BSA) or psoriasis area and severity Index (PASI) score to measure physical severity of psoriasis
- Use DLQI to measure impact of psoriasis on patient’s quality of life
- Classify severity into mild, moderate or severe psoriasis (Algorithm 1 & 2)

Recommendations

MaHTAS recommendations are based on systematic reviews of the best available evidence. When evidence is insufficient, recommendations are based on the Guideline Development Group’s experience and opinion of what constitutes good practice in Malaysia. The evidence used in these guidelines were graded using the US/Canadian Preventive Services Task Force Level of Evidence (2001), while the grading of recommendation was modified from grades of recommendation of the Scottish Intercollegiate Guidelines Network (Table 1). These clinical practice guidelines (CPG) are meant to be guides for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not necessarily guarantee the best outcome in every case. Every healthcare provider is responsible for the management of his/her unique patient based on the clinical picture presented by the patient and the management options available locally.
Identification of PsA and other comorbidities (Grade C)

- Assess joint involvement at first presentation and then regularly (at least annually) by looking for relevant signs and symptoms
  - Joint swelling
  - Dactylitis
  - Significant early morning stiffness >1/2 hour
- Assessment of patient with psoriasis should include psychosocial measure and patients should be referred to mental health services if necessary.
- Psoriasis patients should be regularly screened for metabolic syndrome and risk factors of atherosclerosis-related diseases
- Patient with psoriasis or PsA should be encouraged to adopt a healthy lifestyle
  - Regular exercise
  - Maintain healthy body weight (Body Mass Index 18.5 - 24.9)
  - Stop smoking
  - Avoid alcohol or drink in moderation

Indications for referral

- Dermatology referral
  - Diagnostic uncertainty.
  - Erythodermic (Figure 2) or generalised pustular psoriasis (Figure 3) should be referred urgently for specialist assessment and treatment.
  - Patients who have failed adequate trial of topical therapy for 6 -12 weeks.
  - Psoriasis that requires phototherapy or systemic therapy.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Time to evaluate initial response (weeks)</th>
<th>Minimal targets</th>
<th>Time to evaluate maintenance of response (months)</th>
</tr>
</thead>
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<tr>
<td>Topical agents</td>
<td>6</td>
<td>↓ BSA ≥ 50% or PASI ≥ 50 or DLQI ≤ 5</td>
<td>6-12</td>
</tr>
<tr>
<td>Phototherapy</td>
<td>6</td>
<td>↓ BSA ≥ 75% or PASI ≥ 75 or DLQI ≤ 5</td>
<td>6</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclosporin</td>
<td>16</td>
<td></td>
<td></td>
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<tr>
<td>Acitretin</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infliximab</td>
<td>10</td>
<td>PASI ≥ 75 or</td>
<td>6</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>16</td>
<td>PASI 50 to &lt; 75 plus DLQI ≤ 5</td>
<td></td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etanercept</td>
<td>24</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

↓ BSA ≥ 50% - at least a 50% reduction in body surface area involved (BSA)
PASI ≥ 50 - at least a 50% reduction psoriasis area and severity index (PASI) score
DLQI – Dermatology Life Quality Index; DLQI ≤ 5 means disease has little or no effect on patient’s quality of life

Figure 2 Erythrodermic psoriasis: generalised redness with thick scales on back.

Figure 3 Generalised pustular psoriasis showing superficial pustules and lakes of pus.
• Rheumatology referral
  - Diagnostic evaluation of patients with suspected arthritis.
  - Formulate management plan for PsA.

Topical therapy
• Patients with mild or moderate psoriasis with minimal impairment in quality of life (DLQI < 5) should be treated with topical agents. (Grade C)
• Emollient should be used regularly. (Grade C)
• Tar-based preparations may be used as a first-line topical therapy. (Grade A)
• Short-term use of potent and very potent topical corticosteroid may be used to clear limited plaques. (Grade A)
  - Avoid use on the face, genitalia and body folds. (Grade C)
  - Limit use of super potent corticosteroid to less than 30gm/week. (Grade C)
  - Limit use of potent corticosteroid to less than 60gm/week. (Grade C)
  - Continuous use of potent corticosteroid should not exceed four weeks. (Grade C)
  - Continuous use of super potent corticosteroid should not exceed two weeks. (Grade C)
• Mild potency corticosteroid may be used for face, genitalia and body folds. (Grade C)
• Vitamin D analogue may be used may be used for short-term treatment. (Grade A)
  - Limit use to less than 100g/week
• Fixed dose combination of vitamin D analogue and corticosteroid may be used for short-term treatment. (Grade A)
• Review patient 6 weeks after starting a new topical agent
  - Evaluate tolerability and initial response to treatment.
  - Reinforce the importance of adherence when appropriate.
  - Reinforce the importance of not using potent or very potent corticosteroids long term.
  - If there is little or no improvement at this review.
• Discuss next treatment options (refer dermatologist or change to another topical agents).

Phototherapy
• Phototherapy should be offered to patients who failed topical therapy before starting them on systemic agents. (Grade C)
• Phototherapy 2-3 sessions per week may be offered to patients with moderate to severe psoriasis. (Grade A)
• Life time exposure to PUVA and UVB should not exceed 200 and 350 sessions respectively. (Grade C)
• Review patient 6 weeks after starting phototherapy
  - Evaluate tolerability and initial response to treatment.
  - Reinforce the importance of adherence when appropriate.
  - If there is little or no improvement at this review, consider conventional systemic therapy.

Conventional systemic therapy
• Conventional systemic therapy should be offered to patients with moderate to severe psoriasis who failed or have contraindications to phototherapy or when phototherapy is not available. (Grade C)
• Pre-treatment assessment (Box 1) and regular monitoring for toxicity should be done. (Grade C)
• Offer methotrexate as the first choice of systemic agent except when contraindicated because of safety concerns. (Box 2) (Grade A)
  - Neutropenia and hepatotoxicity should be closely monitored. (Box 3 & Algorithm 3) (Grade C)
• Cyclosporine may be offered as short-term treatment for rapid disease clearance in moderate to severe psoriasis. (Grade A)
• Cyclosporine may be offered as second-line systemic agent to patients who failed, are intolerant or have contraindications to methotrexate. (Grade A)
  - Cyclosporine should NOT be used for more than 2 years. (Grade B)
  - Cyclosporine should be avoided in patient with previous PUVA exposure. (Grade B)
  - Blood pressure, renal function, lipid profile should be monitored closely in psoriasis patient on cyclosporine (Box 4). (Grade C)
• Acitretin may be offered for the treatment of moderate to severe plaque psoriasis. (Grade A)
  - Acitretin should be avoided in women of childbearing age without reliable contraception and in those who are planning pregnancy. (Grade C)
  - However; it is safe for men who are planning to have a child. (Grade C)
  - Lipid profile and LFT should be monitored regularly (Box 5). (Grade C)
Biologics
- Biologic should be offered by a dermatologist to patients with moderate to severe plaque psoriasis who failed, have intolerance or contraindications to conventional systemic treatment and phototherapy. (Grade A)
- Careful evaluation for contraindication should be done prior to initiation of biologics for psoriasis patients (Box 6). (Grade A)
- Safety issues should be monitored during and after treatment of biologics (Box 7). (Grade A)
- All patients on biologics should be registered in National Psoriasis Registry. (Grade C)
- Psoriasis patients with latent tuberculosis should be referred to respiratory physician for treatment before biologics initiation. (Grade A)

Box 1: Baseline assessment before starting conventional systemic/biologics therapy.

History and examination to exclude the following:
- Current and previous history of TB infection
- Current and previous history of malignancy
- Active infection
- HIV infection
- Hepatitis B/C
- Congestive heart failure
- Demyelinating disease
- Pregnancy
- Intention to get pregnant
- Breast-feeding

Investigations
- FBC (Full blood count)
- ESR (Erythrocyte sedimentation rate)
- CRP (C-reactive protein)
- UFEME (Urine analysis)
- LFT (Liver function test)
- FLP (Fasting lipid profile)
- FBS (Fasting blood sugar)
- RP (Renal profile)
- HBsAg - If positive refer Gastroenterologist/General Physician
- Hepatitis B core antigen - If positive refer Gastroenterologist/General Physician
- HCV Ab - If positive refer Gastroenterologist/General Physician
- HIV
- ANA - If positive to refer Rheumatologist/General Physician
- CXR
- Mantoux test
- Interferon gamma release assay if indicated (extra pulmonary tuberculosis)
- Urine pregnancy test (UPT)

Box 2: Risk factors for methotrexate toxicity.

Risk factors for methotrexate induced hematologic toxicity
- Renal insufficiency
- Advanced age
- Lack of folate supplementation
- Medication errors
- Drug interactions
- Hypoalbuminemia
- Excess alcohol intake
- Multiple concurrent medications

Risk factors for methotrexate induced hepatotoxicity
- Diabetes mellitus
- Obesity
- History of or current alcohol consumption
- Persistent abnormal liver chemistry studies
- History of liver disease, including chronic hepatitis B or C
- Family history of inheritable liver disease
- History of significant exposure to hepatotoxic drugs or chemicals
- Lack of folate supplementation
- Hyperlipidemia
Box 3: Treatment regime and monitoring of methotrexate in patients with psoriasis.

Before initiation of therapy
- Ensure normal baseline assessment. (Box 1)
- Discuss benefit and risk of treatment with patients.

Initial therapy
- Start with oral test dose of 5.0 - 7.5 mg/week.
- Supplement with Folic acid 5mg od (except the day of methotrexate) or 5mg once a week (the day after methotrexate).
- Repeat Full Blood Count (FBC), Liver Function Test (LFT) and Renal Profile (RP) within 2 weeks.

Maintenance therapy
- Escalate dose from 7.5 mg/week till clinical response (maximum 20 mg/week) [administered as a single dose or divided into 3 doses and administered at 12-h intervals over 2 consecutive days].
- Monitor FBC/LFT/RP monthly for the first 3 months and then after every 1 to 3 monthly.
- More frequent monitoring is needed with dose escalation.
- Do blood test 5 - 7 days after last dose of methotrexate.
- Monitor total cumulative dose of methotrexate
- Consider Procollagen III aminopeptide/Fibroscan/Fibrotest or Liver biopsy when total cumulative dose reach 3.5 to 4.0g in patients without risk factors for hepatotoxicity or 1.0 to 1.5g for those with risk factors for hepatotoxicity.

Box 4: Treatment regime and monitoring of cyclosporine in patients with psoriasis.

Before initiation of therapy
- Ensure normal baseline assessment (Box 1).
- Discuss benefit and risk of treatment with patients.

Initial therapy
- Start with 2.5 mg/kg body weight/day, divided in 2 doses.
- Escalate dose every 4 to 6 weeks till clinical response (maximum 5 mg/kg/day).

Maintenance therapy
- Treatment for more than 2 years is not recommended.
- Monitoring while on therapy:
  - Blood pressure, renal function, uric acid, potassium, lipids, liver enzymes, serum bilirubin, and magnesium should be monitored monthly.

Box 5: Treatment regime and monitoring of acitretin in patients with psoriasis.

Before initiation of therapy
- Ensure normal baseline assessment (Box 1).
- Discuss benefit and risk of treatment with patients.

Initial therapy
- Start with dose of 0.5 - 1 mg/kg/day for 2 - 4 weeks.

Maintenance therapy
- Adjust according to response, usually within range of 25 - 50 mg daily (max 75 mg daily).
- Repeat lipid profile and LFTs every 4 - 8 weeks until stable, then every 6-12 weeks.
Box 6: Indications and contraindications for initiation of biologics therapy.

**Indications**
Patients with psoriasis vulgaris may be considered for biologics intervention if they have severe disease as defined in Criteria A and fulfill at least one of the clinical categories in Criteria B.

**Criteria A**
Severe Disease
1. PASI ≥20 OR
2. BSA ≥30 OR
3. DLQI ≥20

**Criteria B**
Clinical Categories
1. Contraindications to phototherapy and standard systemic therapies AND/OR
2. Intolerance/inaccessibility to phototherapy and standard systemic therapies AND/OR
3. Failed phototherapy and standard systemic therapies.

**Absolute contraindications**
- Active infection including current tuberculosis.
- Current history of malignancy.
- Congestive cardiac failure class 3 or 4.
- Demyelinating diseases.

**Relative contraindications**
- Previous history of tuberculosis
- HIV infection
- Hepatitis B/C
- Current and/or previous history of malignancy
- Congestive cardiac failure
- Pregnancy or breast-feeding
- Intention to get pregnant
- Patient who have had prior PUVA (>200 sessions) and UVB (>350 sessions)

Box 7: Treatment regime and monitoring of biologics therapy in patients with psoriasis vulgaris.

**Before initiation of therapy**
- Ensure normal baseline assessment (Box 1).
- Discuss benefit and risk of treatment with patients.

**Dosing regime**
- **Infliximab**
  - Intravenous, 5mg/kg bodyweight at week 0, 2, 6 and then 8 weekly.
- **Ustekinumab**
  - Subcutaneous, 45mg (90mg for bodyweight >100kg) at week 0, 4 and then 12 weekly.
- **Adalimumab**
  - Subcutaneous, 80mg at week 0 and then every other week.
- **Etanercept**
  - Subcutaneous 25mg biweekly or 50mg weekly or 50mg biweekly.

**Monitor for adverse events**
- 6 monthly FBC, ESR, CRP, LFT, RP, HbsAg, HCV Ab, HIV, ANA.
- Repeat lipid profile and LFT’s every 4 - 8 weeks until stable, then every 6-12 weeks.
- Yearly screening for latent tuberculosis (CXR, Mantoux test).
ALGORITHM 1:
MANAGEMENT OF PSORIASIS VULGARIS IN PRIMARY CARE

PSORIASIS PATIENT PRESENTING TO PRIMARY CARE

1. Assess
   - Severity
   - Arthritis (PsA)
   - co-morbidities
2. Educate patient

Presence of co-morbidities such as obesity, hypertension, diabetes, depression etc.

SEVERITY

YES

REFER DERMATOLOGIST

SEVERITY

Mild
(BSA ≤10% or PASI ≤ 10)

Moderate
(BSA >10% to 30% or PASI 10 to 20)

Severe
(BSA >30% or PASI >20)
Erythrodermic or generalised pustular psoriasis: urgent referral is indicated)

YES

MILD

TOPICAL THERAPY

RE-ASSESS IN 6 WEEKS

YES

RESINICER

RE ASSESS IN 6 WEEKS

TOPICAL THERAPY

RE-ASSESS IN 6 WEEKS

TOPICAL THERAPY

YES

RESPONDER

Regaular follow-up as indicated
Annual assessment:—
• Document severity
• Assess co-morbidities and articular symptoms
• Optimise topical treatment

NO

TOPICAL THERAPY

RE-ASSESS IN 6 WEEKS

TOPICAL THERAPY

NO

RESPONDER

(BSA - Body Surface Area
PASI - Psoriasis area and severity index
DLQI - Dermatology Life Quality Index
Responder - BSA ≥50% reduction or PASI ≥50 achieved
ALGORITHM 2: TREATMENT OF PSORIASIS VULGARIS

**PSORIASIS VULGARIS**

- **Mild**
  - BSA ≤10%
  - or
  - PASI ≤10
  - **Topical Therapy**
    - Tar
      - (Preferred therapy suitable for extensive disease)
    - Dithranol
      - (Large plaque)
    - Corticosteroids
      - (Short-term therapy)
    - Vitamin D analogues
      - <100g/week
    - Calcineurin inhibitors
      - (Face & Flexures)

- **Assess DLQI**
  - DLQI ≤10
  - Topical Therapy

- **Moderate**
  - BSA >10% to 30%
  - or
  - PASI >10 to 20
  - **Topical Therapy**
    - Assess DLQI
    - DLQI ≤10
    - Topical Therapy
    - DLQI >10
    - Phototherapy

- **Severe**
  - BSA >30%
  - or
  - PASI >20
  - Phototherapy
  - **Assess DLQI**
    - DLQI ≤10
    - Topical Therapy
    - DLQI >10
    - Phototherapy
    - Fail / contraindicated / not available
    - Systemic Therapy
      - Mothotrexate
        - (first-line)
      - Cyclosporine
        - (short- term therapy)
      - Acitretin
    - Fail / contraindication / intolerance with BSA >30 or PASI >20 or DLQI >20
    - Biologics
      - Ustekinumab
      - Adalimumab
      - Etanercept
      - Infliximab

**Assess DLQI**

- DLQI ≤10
  - Topical Therapy
- DLQI >10
  - Phototherapy
  - Fail / contraindicated / not available
  - Systemic Therapy
ALGORITHM 3: MONITORING HEMATOXICITY AND HEPATOTOXICITY OF METHOTREXATE

Initiation of Methotrexate by Dermatologist

- Ensure normal baseline screening (refer appendix 7) prior to Methotrexate (MTX)
- Assess risk factor for hematotoxicity & hepatotoxicity
- Discuss benefit & risk of MTX with patient (provide Patient Information Leaflet)

Neutropenia / Thrombocytopenia / Anaemia

Stop MTX and change to other treatment

Raised liver enzymes

Repeat Hep B / C screening

Positive

Refer gastroenterologist / hepatologist

Negative

Assess other risk factors for hepatotoxicity

Presence of risk factors

YES

Persistent elevation of ALT / AST (> 2 fold for 2 to 3 months)

NO

Elevation of ALT / AST (>3 fold upper limit)

Stop MTX and change to alternative drug

Moderate elevation of ALT / AST (>2 but <3 fold upper limit)

Review ALT / AST in 2 to 4 weeks Decrease dose as needed

Persistent elevation in 5 out of 9 ALT / AST in a year

Consider:
- Procollagen III aminopeptide / Fibroscan / Fibrotest / Liver biopsy
- Consider alternative drug

Presence of risk factors

YES

Persistent elevation of ALT / AST (> 2 fold for 2 to 3 months)

NO

Elevation of ALT / AST (>3 fold upper limit)

Stop MTX and change to alternative drug

Moderate elevation of ALT / AST (>2 but <3 fold upper limit)

Review ALT / AST in 2 to 4 weeks Decrease dose as needed

Persistent elevation in 5 out of 9 ALT / AST in a year

Consider:
- Procollagen III aminopeptide / Fibroscan / Fibrotest / Liver biopsy
- Consider alternative drug
References


Abstract

Background: The standard allergen series used in patch testing contains only the top three metals causing allergic contact dermatitis.

Aim: To study the pattern of metal allergy among patients who underwent patch test in Selayang Hospital from March 2012 until March 2013.

Methods: This is a retrospective prevalence study of all patients who underwent patch test in Selayang Hospital from March 2012 to March 2013. Only patients suspected to have metal allergy were tested with European Baseline Series plus additional metal series. Patch test readings were recorded according to the International Contact Dermatitis Research Group recommendation. The data of all patients with metal allergy detected were analysed using SPSS Version 12.0.

Results: 254 (1.94%) of new patients (13,081) were patch tested. 18 patients were suspected to have metal allergy. Of 212 (83.4%) patients who had positive patch test, 136 patients were tested positive to metal (64.1%). 15 patients (7.1%) were suspected to have metal allergy. Among the 15 patients who were suspected to have metal allergy, 3 patients (20%) were tested positive to both standard and metal series, 11 patients (73%) were positive to metal series but negative to standard series and one patient (7%) were positive to standard series but negative to metal series. The top metal allergens were nickel sulphate (77.7%), cobalt chloride (34.7%), potassium dichromate (17.4%), copper oxide (4.4%), gold sodium thiosulphate (3.7%) and palladium chloride (2.9%). The clinical distribution of the dermatitis were upper limb only (31.6 %), face (19.9%), lower limbs only (19.1 %), all limbs (15.4%), trunk (5.9%), lips (4.4%) and whole body (3.7%).

Conclusion: This study highlighted metal allergies that would have been missed without patch testing for additional metal series sensitizers. Under-diagnosis of metal allergy can be overcome by learning to recognise clinical signs of metal allergy and by including metal series sensitizers for patch testing.

Keywords: nickel, cobalt, potassium dichromate, copper oxide, gold, palladium, dermatitis

Introduction

Metal and metal salts are among the most common agents causing allergic contact dermatitis. The standard allergen series used in patch testing worldwide contains only the three most common metals causing allergic contact dermatitis, namely nickel chromium and cobalt.

There has been documentation of patients developing allergic reactions to other metals like aluminum, beryllium, copper, gold and palladium. Palladium is one of the noble metals that are chemically similar to platinum and it is used in jewellery, dental fillings and in the electronics industry.
Aim
This study analysed the pattern of the various metal allergies in patients with positive patch test to metal series in Selayang Hospital.

Material and methods
This is a retrospective analysis of all patients who underwent patch test in Selayang Hospital from 1st March 2012 until 31st March 2013. All patients who underwent patch testing for suggested allergic contact dermatitis from the time period were identified from medical records. Consent was obtained from patients prior to the patch test being done. Patch test was conducted using allergens from the European Baseline Series (SE) and those who were suspected of having metal allergy were patch tested with an additional metal series (MS) from Chemotechnique Diagnostics.

The allergens were prepared by using the IQ Chambers and occluded at the back for 2 days. Readings were done on day 3 and day 5 in accordance to recommendation of the International Contact Dermatitis Research Group. The medical records of the patients patch tested to metal sensitizers were analyzed. Site of dermatitis were grouped as lip, face, upper limbs, lower limbs, all limbs, trunk and whole body. Patients were grouped into 2 groups; less than 35 years old and equal or more than 35 years old.

Data obtained were analyzed using SPSS Version 21. Association between categorical variables was analyzed using the chi square test. Statistical significance was set at p<0.05.

Results
A total of 254 (1.94%) new patients (13,081) who attended dermatology clinic during this study period were patch tested. Of these, 212 (83.4%) patients had positive patch test. Among those tested positive, 136 (64.1%) patients were positive to metal sensitizers. Of these, only 15 patients (7.1%) were suspected to have metal allergy according to the medical records. The majority were only diagnosed of metal allergy from the positive patch test to metal sensitizers.

Table 1 Frequency of positive patch test to metal sensitizers in patients with suspected metal allergy.

<table>
<thead>
<tr>
<th>Suspected Metal Allergy</th>
<th>N=15</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive MS, positive SE</td>
<td>3</td>
<td>20.0</td>
</tr>
<tr>
<td>Positive MS, negative SE</td>
<td>11</td>
<td>73.3</td>
</tr>
<tr>
<td>Negative MS, positive SE</td>
<td>1</td>
<td>6.7</td>
</tr>
</tbody>
</table>

Table 2 Demographic characteristic of the patients with metal allergy.

<table>
<thead>
<tr>
<th></th>
<th>Metal allergy suspected N=15</th>
<th>Metal allergy not suspected N=121</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>11</td>
<td>37</td>
<td>35.3%</td>
</tr>
<tr>
<td>Male</td>
<td>4</td>
<td>84</td>
<td>64.7%</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>7</td>
<td>67</td>
<td>54.4%</td>
</tr>
<tr>
<td>Malay</td>
<td>5</td>
<td>44</td>
<td>36.0%</td>
</tr>
<tr>
<td>Chinese</td>
<td>3</td>
<td>9</td>
<td>8.1%</td>
</tr>
<tr>
<td>India</td>
<td>0</td>
<td>1</td>
<td>1.5%</td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
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<td>8</td>
<td>69</td>
</tr>
<tr>
<td>&gt;35 years &amp; above</td>
<td>7</td>
<td>52</td>
<td>28.7%</td>
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<tr>
<td>Atopy</td>
<td>2</td>
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<td>4.4%</td>
</tr>
<tr>
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<td>0</td>
<td>6</td>
<td>19.9%</td>
</tr>
<tr>
<td>Lips</td>
<td>2</td>
<td>25</td>
<td>31.6%</td>
</tr>
<tr>
<td>Face</td>
<td>7</td>
<td>36</td>
<td>19.1%</td>
</tr>
<tr>
<td>Upper limbs</td>
<td>3</td>
<td>18</td>
<td>15.4%</td>
</tr>
<tr>
<td>Lower limbs</td>
<td>0</td>
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<td>5.9%</td>
</tr>
<tr>
<td>All limbs</td>
<td>0</td>
<td>5</td>
<td>3.7%</td>
</tr>
<tr>
<td>Trunk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whole body</td>
<td></td>
<td></td>
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</table>
Table 3 Clinical and demographic characteristics related to positive patch test to the top 4 metal allergens.

<table>
<thead>
<tr>
<th></th>
<th>Positive Patch test</th>
<th>Negative Patch test</th>
<th>P value</th>
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<tr>
<td><strong>NICKEL SULPHATE</strong></td>
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</tr>
<tr>
<td>Gender</td>
<td></td>
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<td></td>
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<td>15</td>
<td>33</td>
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<td>Female</td>
<td>50</td>
<td>38</td>
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<tr>
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</tr>
<tr>
<td>Malay</td>
<td>37</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>Non Malay</td>
<td>28</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
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<tr>
<td>&lt;35 years</td>
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<td>40</td>
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<td>31</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Lips</td>
<td>5</td>
<td>1</td>
<td>0.172</td>
</tr>
<tr>
<td>Face</td>
<td>16</td>
<td>11</td>
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<tr>
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<td>14</td>
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</tr>
<tr>
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<td>82</td>
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<tr>
<td>&lt;35 years</td>
<td>7</td>
<td>70</td>
<td>0.832</td>
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<td>&gt;35 years &amp; above</td>
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<td>53</td>
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<tr>
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<tr>
<td><strong>POTASSIUM CHROMATE</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
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<tr>
<td>Male</td>
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<td>41</td>
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<td></td>
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<tr>
<td>Race</td>
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<td>8</td>
<td>66</td>
<td>0.587</td>
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<tr>
<td>Non Malay</td>
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<td>57</td>
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<tr>
<td>&gt;35 years &amp; above</td>
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<td></td>
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<tr>
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<td></td>
<td></td>
</tr>
<tr>
<td>Lips</td>
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<td>6</td>
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</tr>
<tr>
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<td>Female</td>
<td>P value</td>
</tr>
<tr>
<td>--------</td>
<td>------</td>
<td>--------</td>
<td>---------</td>
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<td>Non Malay</td>
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</tr>
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<td>&gt;35 years &amp; above</td>
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</tr>
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<td>Lips</td>
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<td>Face</td>
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<tr>
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<td>Lower limb</td>
<td>1</td>
<td>24</td>
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<tr>
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<tr>
<td></td>
<td>Trunk</td>
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<td>8</td>
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<tr>
<td></td>
<td>Whole body</td>
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<td>4</td>
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</tbody>
</table>

Table 4 Relationship between occupation and common metal allergens.

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Nickel sulphate N=65</th>
<th>Potassium dichromate N=13</th>
<th>Cobalt chloride N=13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office workers</td>
<td>24</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Student</td>
<td>20</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Metal and mechanical workers</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Cashier</td>
<td>3</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Housewife</td>
<td>12</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Retired</td>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

**Discussion**

Allergic contact dermatitis (ACD) to metals is expressed in a wide range of cutaneous reactions following dermal and systemic exposure to products such as cosmetics, tattoos, detergents, jewellery and piercing, leather tanning, articular prostheses and dental implants. Apart from the well known significance of nickel in causing ACD, other metals such as aluminium, beryllium, chromium, cobalt, copper, gold, iridium, mercury, palladium, platinum, rhodium and titanium represented emerging causes of skin hypersensitivity.

Allergy patch-test reactions to metals may be more prevalent than previously suspected. The less common sensitizing metals are not included in the standard series. Metal series is a useful adjunct to the standard allergen series for the detection of metal allergies. The metal series has evolved over time to include multiple metals in different salts and concentrations. Patients may react to one concentration of a metal and not to another; similarly patients may react to one preparation of a metal and not to another.

As only selected patients were patch tested with metal series, the frequency of sensitization of different metal sensitizers are not directly comparable. In Standard European series, there are only 3 metal allergens tested: nickel sulphate, potassium dichromate and cobalt chloride. The results of our study showed that nickel sulphate is the most frequently positive metal allergen and its
allergy is significantly more common in women. This concurs with findings in other studies where woman is 10 times at risk compared to men. Other studies also associated nickel allergy with upper and lower limb dermatitis. Sources of nickel sensitization include jewellery, belt buckles, metal fasteners, spectacles frames and ear rings. The epidemiology of metal allergy has recently changed in Europe as the prevalence of nickel allergy among ear-pierced Danish women has decreased following regulatory intervention on nickel release from consumer products. In the United States, the prevalence of nickel allergy is still increasing, which may be explained by the absence of regulation.

Although nickel sensitivity is more common than cobalt sensitivity, the two are frequently linked. Rystedt and Fischer reported that a quarter of nickel-sensitive patients developed a cobalt allergy and patients with simultaneous nickel and cobalt allergies have more severe dyshidrotic eczema. Cobalt is a metal found naturally in soil, dust and seawater and it is usually found in association with nickel allergy. In this study, cobalt sensitization is the second most common metal allergy among our study population. There is increased in cobalt sensitization with upper limb dermatitis in younger males ≤ 35 years old) as compared with previous study. Thyssen et al. in a retrospective study of 10,335 Danish women between 1985 and 2007 noted that nickel allergy diminished in younger women and increased in older ones, whereas cobalt sensitization remained relatively unchanged.

Potassium dichromate is a chromium salt and it is a common metal making up a significant part of the earth’s crust. Chromium allergic contact dermatitis mainly affects male patients and often results from occupational skin contact with hexavalent chromium in cement. Most people relate chrome to the bright, shiny and durable finish of some metal products. However, contact with chrome plated objects is

![Figure 1 Clinical presentations in relation to the common metal allergens.](image-url)
an unlikely cause for chromium allergy. Exposure to this sensitizer is at workplace where chromium salts are used as an ingredient in the manufacture of products such as cement, mortar, leather and paints. In this study, chrome allergy is significantly associated with limb dermatitis. The prevalence of chromium allergy is increasing in the United States, Singapore, and Denmark among dermatitis patients. This increase is significantly associated with leather exposure in Denmark.

The other common metal allergens are copper oxide, gold sodium thiosulphate and palladium chloride. There is an increase in prevalence of contact allergy to gold and palladium recently. Gold causes dermatitis mainly on the face and eyelids. Bjorkner et al reported that among their patients, gold was the second most common allergen following nickel. In our study, gold allergy is commoner in men with limbs dermatitis. However there is no statistical significance difference in both sexes and sites of allergy.

The role of nickel as an occupational allergen is still unclear. According to some authors, up to 12% of the total estimated cases of occupational contact dermatitis are thought to be due, at least partially, to nickel. In this study, nickel sensitization was found to be more common in office workers and students. Cobalt sensitization is believed to be involved in the onset of allergic contact dermatitis in several occupations: hairdressing, building, hygiene and cleaning works. Francesca et al found that in the female group, nickel sensitization was significantly associated with metal and mechanical work, chromate sensitization was significantly associated with construction work in both sexes and cobalt sensitization was significantly associated with textile and leather work.

Management of patient with metal allergy includes avoidance of the allergen, no-touch technique at any possible time and avoiding foods containing nickel. Patients are advice to avoid or minimize contact with silver coins, keys, artificial jewellery (necklaces, earrings, bracelets, rings, and watchbands), buckles, zippers, buttons, bra hooks, suspender clips, pens, hair clasps, electrical shavers, paperclips, and power tools that contain metal. Patients can purchase alternative products that are not made of metal. For instance, patients can safely use coloured paper clips that are coated with plastic. Patients can wear hypoallergenic, stainless steel, solid gold, sterling silver, or plastic jewellery. Patients should look for clothing with plastic-coated or painted metal zippers, buttons, or clasps.

Metal allergy has also been associated with device failures following the insertion of intracoronary stents, hip and knee prostheses, and other implants. Gao et al reported a case of contact dermatitis most likely caused by exposure to chromium after a total knee arthroplasty, although this complication is very rare. The majority of total joint prostheses are now made of cobalt-chromium alloys with a nickel content of less than 1%. The occurrence of ACD is particularly uncommon following total knee arthroplasty because there is a polyethylene insert between the femoral and tibial components and no metal-on-metal contact exists.

This study also showed that 73% of patients who were suspected to have metal allergy would have been missed if they were not tested with additional metal series. In addition, 57% of patients suspected of contact dermatitis were not suspected to have metal allergy.

From our study, we find that under-diagnosis of metal allergy can be overcome if clinicians are able to recognize signs of metal allergy clinically and add metal series sensitizers beside standard baseline series in patch test. A more extensive multicentre study is required to substantiate the findings of this study.

Acknowledgement
The authors would like to thank the Director General of Health, Malaysia for permission to publish this paper.

References
Dyskeratosis congenita (DC) is classically characterised by a mucocutaneous triad of reticulated poikiloderma, nail dystrophy and mucosal leukoplakia together with bone marrow failure and increased risk of malignancy. Due to its rarity and clinical heterogeneity it is not easily recognised and patients are often treated for other entities. We report a case of dyskeratosis congenita who presented to us with the classical triad in his late twenties after years of being treated as lichen planus.

Case report
A 29 year-old Malay man presented with 20-nail dystrophy, reticulate pigmentation on the sun-exposed areas of the skin and whitish adherent plaques on his tongue. He also suffered from painless, reddish watery eyes. The changes had been gradually appearing starting with the nail since aged 13, followed by the other features two years later which were progressive in nature.

Born of consanguineous parents who were first cousins, all five of his siblings except one had short stature. None of them shared his physical abnormalities. Earlier in 1998 in another hospital, he had oral biopsies in which the buccal mucosa showed mild epithelial dysplasia while the tongue revealed atrophic glossitis. An ophthalmologist diagnosed bilateral lacrimal duct stenosis causing epiphora and corrective surgery was advised, which he declined. No skin biopsy was performed and he was treated as lichen planus with topical corticosteroids, with very little effect.

Physical examination revealed multisystem abnormalities. He had diffuse, poikilodermatous skin over photo distributed areas (Figure 1). Nail examination revealed pterygium with total nail loss in all 20 digits (Figure 2). All fingers showed shiny, tight skin with loss of dermal ridges at the fingertips and there was palmar hyperhidrosis. Leukoplakia was present on the tongue (Figure 3).

Dental caries were most severe on the lower molars. A triangular patch of leukotrichia was present in the frontal hairline. His eyes were reddish and congested. Apart from small build and short stature (height 144 cm, weight 45 kg), other systems including the genitals and secondary sexual characteristics were unremarkable.

Skin biopsy from the forearm showed epidermal atrophy with focal basal cell vacuolation, pigmentary incontinence as well as sparse lymphoplasmacytic infiltrates in the dermis, consistent with poikiloderma. The direct immunofluorescence study was negative. His full blood counts and peripheral blood film were normal and antinuclear antibody (ANA) was non-reactive. Serum IgM was low (0.28 g/L). Mutational analysis study by direct DNA sequence analysis and restriction enzyme digestion (Centre for Paediatrics, Institute of Cell and Molecular Science, Barts and the London School of Medicine and Dentistry) demonstrated that the patient was hemizygous for DKC1 mutation (Ala353Val), the commonest missense mutation in classical X-linked DC.
Figure 1  Shows diffuse, reticulated hyperpigmentation on the nape of the neck.

Figure 2  Shows eschewed and almost absent nails in all fingers.

Figure 3  Shows extensive white adherent plaques on the tongue.
Discussion

First described by Zinsser in 1910, DC is now recognized with three patterns of inheritance: X-linked recessive, autosomal dominant and autosomal recessive\textsuperscript{1-4,5}. In the last 15 years, eight DC genes (DKC1, TERC, TERT, NOP10, NHP2, TIN2, C16orf57, and TCAB1) have been characterized. Seven of these are involved in telomere function, mutations of which lead to stem cell depletion and premature aging\textsuperscript{3-6}. DKC1 gene mutation in X-linked DC is the commonest, which encodes dyskerin, an essential component of small nucleolar RNAs involved in ribosomal RNA processing and the telomerase complex\textsuperscript{2,4}. DC is therefore viewed as a disease of defective telomere maintenance, and has been linked to several other ‘telomereopathies’ such as the severe multisystem disorders Hoyeraal-Hreidarsson and Revesz syndromes\textsuperscript{2-5}.

In classic DC, the mucocutaneous features usually appear first, below the age of 10 years\textsuperscript{1-4}. Bone marrow failure develops later with up to 80% of patients showing signs of bone marrow failure by the third decade\textsuperscript{1-7}. In addition to reticulated hyperpigmentation, other skin changes include atrophy, hyperhidrosis of palms and soles, telangiectasia and loss of dermal ridges\textsuperscript{7}. There is a predisposition to hematological malignancy and carcinomas\textsuperscript{1,2,7}. Bone marrow dysfunction results in peripheral cytopenias and biopsy shows hypocellular marrow with predisposition to myelodysplastic syndrome and acute myeloid leukaemia\textsuperscript{2,4}. The main causes of mortality are bone marrow failure/immunodeficiency (60-70%), pulmonary complications (10-15%) and malignancy\textsuperscript{3,5,8} (10%). A wide spectrum of abnormalities have been described involving the eye, neurological, pulmonary, skeletal, dental and gastrointestinal systems, hair loss or graying and the genitourinary tract\textsuperscript{1-5,7}.

The diagnosis of DC is often challenging due to heterogeneous clinical presentations which have variable age of onset and degree of severity. Diagnosis is often made later, when the findings become more obvious with age\textsuperscript{1-3,7,8}. It is also not uncommon for bone marrow failure or an abnormality in another system to precede the more classical features\textsuperscript{1,3,5,8}. Even when the classical features are present, the rarity of this disorder may not alert the physician to the diagnosis.

Skin biopsy is not diagnostic as the histological differential diagnosis could include burnt out lichen planus, drug eruption, lupus and graft-versus-host disease (GVHD). The minimal clinical criteria for diagnosis of DC include the presence of at least 2 of the 4 major features (abnormal skin pigmentation, nail dystrophy, leukoplakia, and BM failure) and 2 or more of the other somatic features known to occur in DC. Genetic studies are often necessary to confirm the diagnosis; however in 50% of patients the genetic mutation has not been identified\textsuperscript{8}.

Summary

A diagnosis of DC should be suspected when a patient present with the classical features or symptoms and signs of bone marrow failure. Missing the diagnosis could have fatal implications as majority of patients tend to develop bone marrow failure.

References

GENERAL DERMATOLOGY - Short Case

GENERALISED SWEET SYNDROME LESIONS ASSOCIATED WITH BEHCET’S DISEASE

Ling Hee Ninh1, Julian Matius Tagal2, Pubalan Muniandy1

Keywords: plaques, oral genital ulceration, arthritis, lacunar infarct

Introduction
Sweet’s syndrome (SS) or acute febrile neutrophilic dermatosis is characterized by painful erythematous papules, nodules and plaques in which mature neutrophilic infiltration of the upper dermis is seen histo-pathologically. SS can be divided into 5 subtypes based on aetiology, namely Classical (Idiopathic), Paraneoplastic, Drug-induced, Pregnancy related & associated with inflammatory and autoimmune disorders.

Behcet’s disease is a clinical diagnosis and the International Study Group (ISG) for Behcet’s Disease is the best accepted criteria for diagnosis. Generalized Sweet syndrome lesions are typically associated with malignancies. SS lesions if present in patients with Behcet’s disease are usually few in number. Herein, we describe a rare case of generalized Sweet syndrome lesions associated with Behcet’s disease.

Case report
A 44 year-old woman presented with sudden eruption of painful, raised erythematous plaques with fever, spreading from face, arms to her whole body over 3 days. She had recurrent painful oral ulcers and arthritis in the preceding 2 months. Old records (7 years earlier), showed she previously had recurrent painful oral and genital ulceration, bouts of cellulitis (left leg, both hands) and multiple lacunar infarcts. Her symptoms responded well to Prednisolone 30mg daily. Unfortunately she defaulted treatment then.

Correspondence
Ling Hee Ninh
Department of Dermatology,
Sarawak General Hospital, Kuching, Malaysia
Email: heeninh@yahoo.com.sg

Figure 1 Juicy Erythematous Plaques.

Figure 2 Multiple oral aphthous ulcerations.
Figure 3  Diffuse dermal neutrophilic infiltrates 4x H&E.

Figure 4  Dermal spongiosis & diffuse dermal neutrophilic infiltrates 20x.
Investigations showed elevated inflammatory markers with ESR of 101mm/hour, CRP of 96mg/L with leukocytosis 11,900cells/mm3 & Neutrophilia (73%). Pathergy test was positive. Renal and liver function tests were normal. The hepatitis B surface antigen, anti hepatitis C antibody, HIV, and antinuclear antibody were negative. Eye examination was unremarkable. Malignancy screen uncovered a solitary right thyroid nodule that proved to be benign post hemi-thyroidectomy.

Histopathological examination of an excised erythematous nodule showed marked edema of papillary dermis and diffuse infiltrate of inflammatory cells, predominantly neutrophils with some eosinophils. No subepidermal bullae. Skin appendages were surrounded by inflammatory cells (lymphocytes, polymorphs and some eosinophils). Adjacent dermis showed a perivascular infiltrate of similar cells.

Thus, a diagnosis of Sweet syndrome with underlying Behcet’s disease was made. Both skin lesions and the mucosal ulcers resolved rapidly with steroids. Frequent recurrences of ulcers, both cutaneous and mucosal were observed on tapering the oral steroids. She was then commenced on azathioprine and colchicine in addition to oral steroids. She is currently being closely monitored for possible underlying malignancy & complications of immunosuppresion.

Discussion
This patient has longstanding BD that was poorly controlled and presented with SS lesions 7 years later. Differentiation between SS associated with BD versus SS lesions seen in BD is difficult.

One of the main distinguishing features is that HLA B51 is more common in BD, whereas HLA B54 is predominantly positive in SS. We were unable to perform HLA typing. Another feature for differential diagnosis is the lack of fibrinoid necrosis on vessel walls in SS. In the histopathologic examination of this patient’s skin biopsy, no fibrinoid necrosis was observed. The pathogenesis of both SS and BD is unknown. It has been proposed that HSV may have triggered an immune-regulatory defect in a genetically predisposed patient and thus caused SS and BD to occur simultaneously.

Conclusion
More studies are needed to establish whether a common etiology (immunology, environmental or genetic) exists between BD and SS.

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References