Aloe vera induced oral mucositis: a case report
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Citation

Abstract
Aim: To report a probable case of Aloe vera induced oral mucositis in a two year old child.
Case summary: A two years old female child brought to our emergency department with a severe form of oral mucositis. History from her mother revealed that the child had chewed the fleshy stalk of an Aloe vera plant leaf that grows in her garden. On the following day the child developed a severe form of oral mucositis and dermatitis of the peri-oral skin without much of constitutional symptoms. The child improved with symptomatic treatment.
Discussion: The probability of etiological association is analyzed with the help of Naranjo Probability Scale which showed Aloe vera to be the "Probable" cause of mucositis in this child.
Conclusion: Aloe vera, although has many healing properties, serious adverse reactions are also possible and has to borne in mind.

A two years old previously normal female child was brought to our pediatric department with severe stomatitis (figure 1). She developed the lesion overnight without much systemic manifestations. Fig. 2 & 3 shows the course of recovery of the child in one week.

Figure 1
Figure 1: Presentation on day 1: Shows severe mucositis of oral mucosa and dermatitis of the peri-oral skin.

Figure 2
Figure 2: Presentation on day 3: Shows improvement with conservative management.
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Figure 3
Figure 3: Presentation on day 5: The lesion healed with a post inflammatory hypopigmented area.

CLINICAL EXAMINATION
On general examination, she was moderately built, afebrile and conjunctival mucosa appeared slightly pale. No evidence of jaundice or generalized lymphadenopathy. Vital parameters were within normal limits. Systemic examination was normal.

LOCAL EXAMINATION OF THE ORAL CAVITY
Oral cavity showed severe mucositis involving the lips and buccal mucosa. The lesion appeared boggy and erythematous with few areas of pin point hemorrhages. The skin of the peri-oral area which came in contact with the aloe vera juice also showed dermatitis. No significant regional lymphadenitis noted.

INVESTIGATIONS
Complete Blood count and peripheral blood smear showed microcytic, hypochromic anemia and a normal leukocyte count. Renal, Liver function test and serum proteins estimations were within normal limits. A cytological smear from the mucosal lesion showed normal squamous epithelial cells and a few leucocytes in a dirty background. Swab taken from the lesion on culture showed Streptococcus viridians and negative in fungal studies.

OUTCOME
The child was managed symptomatically with proper oral hygiene, topical emollients and analgesics. The lesions healed in one week leaving a post inflammatory hypopigmented area. The etiological association of aloe vera with the clinical presentation is analyzed with Naranjo's probability scale(1) in table 1.

DISCUSSION
ALOE VERA INDUCED IRRITANT CONTACT MUCOSITIS
History from the mother revealed that on the previous evening she found her child chewing the fleshy leaf of an Aloe vera plant growing in her garden. She immediately removed it from her mouth and made a thorough rinsing with water. The child did not have any immediate local manifestations. On the following morning the child developed a severe form of oral mucositis and dermatitis of the peri-oral skin. The child had no systemic manifestations.

History were negative for any infection in the recent past or any drug in-take prior to onset of the event. The child was on her regular food habits.
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Figure 5

Table 1: Naranjo's Algorithm Legends: AR = Adverse Reaction; ADR = Adverse Drug Reaction

<table>
<thead>
<tr>
<th>No.</th>
<th>Criteria</th>
<th>Yes</th>
<th>No</th>
<th>Don't know</th>
<th>Score in this patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Are there previous conclusion reports on this reaction?</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>Did the suspected event appear after the offending agent was administered?</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>Did the AR improve when the offending agent was discontinued or a specific antagonist was administered?</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>Did the AR reappear when the offending agent was unknowingly re-administered?</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>Are there alternate cases that could equally have caused the AR?</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>Did the AR reappear when a placebo was given?</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>Was the agent detected in blood/serum or body fluid to be toxic?</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>Was the reaction more severe when the dose was increased or less when the dose was decreased?</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>Did the same patient have similar reaction to cause or similar drug in any previous exposure?</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>10</td>
<td>Was the AR confirmed by objective evidence?</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Naranjo et al. 2000

Score of Naranjo’s Algorithm:

> 9 = Definite ADR
5-8 = Probable ADR
1-4 = Possible ADR
< 1 = Doubtful ADR

According to the results from Naranjo's probability scale, a conclusion of “Probable” Aloe vera induced irritant contact mucositis was made.

IRRITANT CONTACT MUCOSITIS:

It is the result of inflammation arising from the release of pro-inflammatory cytokines from epithelial cells, usually in response to noxious stimuli. The three main pathophysiological changes are Skin barrier disruption, Epithelial cellular changes, and Cytokine release.

Irritant contact mucositis falls into three categories—Simple Acute irritant mucositis which occurs within minutes after exposure or Acute delayed, occurring 8-12 hours and Cumulative irritant mucositis which may be delayed by weeks after exposure.

Irritant contact mucositis is a clinical diagnosis. History of contact with an offending agent and subsequent development of lesions in the exposed areas suggests the diagnosis. Treatment is symptomatic and preventing further exposures.

Aloe vera: A perennial plant, belonging to the family Liliaceae. The aloe leaf is the source of two herbal preparations: Aloe gel and latex. Aloe gel is the clear mucilaginous substance produced by parenchymal cells, composed mainly of water (99%) and monosaccharides (mainly mannose-6-phosphate) and polysaccharides (gluco-mannans). Recently, a glycoprotein with antiallergic properties, called Alprogen and a novel anti-inflammatory compound, C-glucosyl chromone, has been isolated. Pericyclic tubular cells produce a bitter yellow irritant substance, the Aloe latex. It is used as laxative(_2_).

The role of Aloe vera in medicine is well appreciated since the days of ancient civilizations. In modern days the extracts of the plant are used in skin care, cosmetics and as nutraceuticals. Table 2 shows a few medicinal uses of Aloe vera based on scientific evidences(_3_).

Figure 6

Table 2

<table>
<thead>
<tr>
<th>Uses based on scientific evidences</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>As a laxative</td>
<td>B</td>
</tr>
<tr>
<td>Genital Herpes</td>
<td>B</td>
</tr>
<tr>
<td>Psoriasis vulgaris</td>
<td>B</td>
</tr>
<tr>
<td>Seborrheic dermatitis</td>
<td>C</td>
</tr>
<tr>
<td>Cancer prevention</td>
<td>C</td>
</tr>
<tr>
<td>Canker sores</td>
<td>C</td>
</tr>
<tr>
<td>Diabetes (type 2)</td>
<td>C</td>
</tr>
<tr>
<td>Dry skin</td>
<td>C</td>
</tr>
<tr>
<td>HIV infection</td>
<td>C</td>
</tr>
<tr>
<td>Lichen plans</td>
<td>C</td>
</tr>
<tr>
<td>Skin burns</td>
<td>C</td>
</tr>
<tr>
<td>Skin ulcers</td>
<td>C</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>C</td>
</tr>
<tr>
<td>Wound healing</td>
<td>C</td>
</tr>
<tr>
<td>Mucositis</td>
<td>D</td>
</tr>
<tr>
<td>Pressure sores</td>
<td>D</td>
</tr>
<tr>
<td>Radiation dermatitis / mucositis</td>
<td>D</td>
</tr>
</tbody>
</table>

Key to grades

A Strong scientific evidence for this use
B Good scientific evidence for this use
C Unclear scientific evidence for this use
D Fair scientific evidence against this use (it may not work)
F Strong scientific evidence against this use (it likely does not work)

Aloe vera is generally regarded as a safer herb. Few adverse effects occur because the process of separation of gel from the sap is not always complete(_4_). They includes irritations, hives, mild itching on topical application and cramping, diarrhea and electrolyte imbalance on internal use. Rare incidences of serious toxicities like severe hepatitis(_5_), renal failure(_6_), radiation-aloe vera induced dermatitis(_7_).
death on parenteral injections\(^{(3)}\) have been reported. Aloe vera shows significant drug interactions with digoxin (Lanoxin), diuretics, oral hypoglycemics, steroids and sevoflurane\(^{(8)}\). The internal use of Aloe vera is not recommended in pregnancy and in breast feeding mothers\(^{(3)}\).

**CONCLUSION**

Clinicians must remember that the growing popularity on the use of Aloe products may stimulate its use 'as is' by the patients. Since because our patient gave a very clear history of Aloe vera intake prior to the onset of the event, we could get the cause and manage successfully. It would have been more cumbersome when such clear history is lacking or missed. Furthermore, it is important to specifically ask patients about the use of these products, because they consider it as innocuous and thus would not spontaneously provide such information. In the lights of increasing evidences for adverse effects associated with the use of Aloe vera, more strict regulations should be imposed on the manufacturing standards and its 'over-the-counter sale'.

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7. Erkan topkan, et al, Acute radiation-Aloe vera induced dermatitis in a malignant eccrine tumor of left gluteal region, Turkish journal of Cancer, 2006, Volume 36, Number 3, Page(s) 138-141
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