Six cases of chloracne in Italy: the success of combined therapy

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Six cases of chloracne in Italy: the success of combined therapy

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Running head: Chloracne and management

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Dear Editor,

Chloracne is a rare disfiguring disease related to dioxin exposure. A paucity of literature exists on the clinical manifestations of this disease and how best to treat it[1].

Dioxin acts in humans through an intracellular receptor, the aryl hydrocarbon receptor (AhR), which causes gene encoding of the enzyme cytochrome P450 1A1(CYP1A1). The expression of CYP1A1 in human skin is a diagnostic biomarker in acne-like lesions known as chloracne or "metabolizing acquired dioxin-induced skin hamartomas'(MADISH)[2,3].

In April 2014 six Pakistani patients (3 males and 3 females) with suspected chloracne were enrolled in this study at Dermatology Unit in Bologna (Italy) (Table 1).

The eruption had occurred suddenly and simultaneously (1 week before the consultation) in all the family members. Clinical examination revealed numerous small comedone-like lesions (open comedones and skin pits), and some inflammatory lesions such as cysts and folliculitis. In addition, the skin appeared rough and wizened, with a grayish pigmentation (Figure 1a-d).

Histological examination was consistent with chloracne (Figure 1 e). CYP1A1 immunohistochemical analysis proved strongly positive in patients No 1 and 2 (Figure 1f).

The chloracne/MADISH score proposed by Fabbrocini et al. was used to assess the diagnosis[2] which is likely when the score is ≥ 6[2].

In our sample the chloracne/MADISH score, laboratory analyses and abdominal ultrasound were assessed (Table 1).

Toxicological exams were performed in all patients in serum of the six patients. High values of 2,3,4,6,7,8-(HxCDF), 1,2,3,4,6,7,8,9-(OCDD) and PCB 105, 118 and 157, were detected especially in two adult male patients (No 1 and 2). All foods recently assumed were analysed but resulted negative for dioxins. The culprit for the dioxin poisoning was not detected.

All patients included in the study were put on a diet with a reduced intake of saturated fatty acids and simple sugar, and an increase in the consumption of fruit, vegetables and whole foods. Regular fibre consumption was prescribed, together with daily physical activity, aimed at weight loss, bowel transit and mobilisation, and excretion of dioxins from adipose tissue storage.

In the 3 adults a pharmacological therapy with a fenofibrate 145 mg once a day plus lipidium colonfit twice a day was also performed, combined with a mechanical dermabrasion and multiple micro punch extraction under local anaesthesia. The 3 children were treated with topical adapalene 0.1% gel or topical tretinoin 0.05% cream producing exfoliation until complete healing of the skin in two years.

The combined metabolic and dermatologic therapy lasted 16 months leading to a normalization of triglyceride and cholesterol blood levels, and complete resolution of acneiform lesions with the persistence of pit scars (Figure 1 g-i). Abdominal ultrasound also showed a marked improvement in steatosis. Over the following 3 years laboratory and ultrasound exams were monitored resulting normal.

The sudden onset of a large number of comedones on the face and neck in the same household should lead the clinician to consider chloracne[5]. Histopathological findings and the increased expression of CYP1A1 in the skin at immunohistochemistry are the key markers for differential diagnosis[6,7]. Familial comedones syndrome was excluded[2].

In our sample more severe manifestations in patients 1 and 2 were probably related to the high serum level of PCB that promoted an overstimulation of AhR favouring the expression of its signalling pathway[7].

The therapeutic approach for chloracne patients is still an open topic. However, interference with the absorption of dietary organochlorines (OCs) by nutritional intervention and administration of drugs such as fenofibrate and Lipidium colonfit is a possible strategy to reduce systemic accumulation of OCs and increases the faecal excretion of DDT and DDE[8-10]. Finally, mechanical dermabrasion is as a useful therapy in clearing chloracne cutaneous lesions[3].

In conclusion, this Italian case series has shown that PCBs could promote an overstimulation of AhR in the skin, favouring the consequent acneic eruption. A combined dermatologic and metabolic therapy can lead to a complete healing of chloracne.

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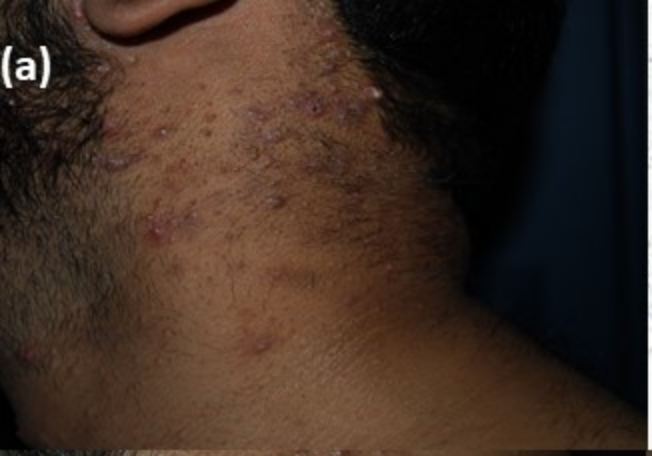
Figure 1: **(a,b)** In patient No 1 numerous small open comedones and skin pits, and some inflammatory lesions such as cysts and folliculitis involved the face, especially the forehead, the temporal, periauricular and mandibular area in the adult patient. A grayish skin pigmentation was evident on the periorbital site. **(c,d)** In patients Nos 4 and 5 small open comedones areas on grayish skin background involved mainly the forehead, malar, mandibular areas and the neck. **(e)** The epidermis showed follicular hyperkeratosis with fairly marked hair follicle cystic infundibulum and disappearance of sebaceous glands, as well as moderate-dense mixed, granulomatous infiltrate around the follicular infundibulum, which was plugged by orthokeratotic cells. **(f)** CYP1A1 immunohistochemical analysis with the use of an immunoperoxidase technique showed a strong uniform homogeneous positivity (100 μm). **(g-i)** Patients No 1, 4, 5 after three years of follow-up. Complete healing of cysts and folliculitis of the face after combined dermatologic and metabolic therapy.

Table 1: Histological, CYP1A1 immunohistochemical, laboratory analyses and abdominal ultrasound in our case series. Chloracne/MADISH score was calculated for each patient.

PATIENT No	AGE	SEX	LABORATORY FINDINGS	ABDOMEN ULTRASOUND	MADISH/CHLORACNE SCORE
1 (father)	39	M	triglycerides 2120 mg/dl total cholesterol 419 mg/dl γ-GT 69 U/L	Steatosis	-Number of sebaceous glands: 2 -Cystic lesions: 2 -Mantle-like epithelial projections: 2 -CYP1A1 immunohistochemistry, Distribution: 2 -CYP1A1 immunohistochemistry, Intensity: 2 **TOTAL: 10**
2 (father's brother)	38	M	triglycerides 1005 mg/dl total cholesterol 239 mg/dl	Steatosis	Number of sebaceous glands: 2 -Cystic lesions: 2 -Mantle-like epithelial projections: 2 -CYP1A1 immunohistochemistry, Distribution: 2 -CYP1A1 immunohistochemistry, Intensity: 2 **TOTAL: 10**
3 (mother)	39	F	triglycerides 822 mg/dl total cholesterol 310 mg/dl	Normal	Number of sebaceous glands: 2 -Cystic lesions: 2 -Mantle-like epithelial projections: 2 -CYP1A1 immunohistochemistry, Distribution: 0 -CYP1A1 immunohistochemistry, Intensity: 0 **TOTAL: 6**
4 (son)	5	M	triglycerides 213 mg/dl total cholesterol 221 mg/dl amylases 113 U/L LDL 189 mg/dl	Hepatomegaly longitudinal diameter > 12 cm	Number of sebaceous glands: 2 -Cystic lesions: 2 -Mantle-like epithelial projections: 2 -CYP1A1 immunohistochemistry, Distribution: 0 -CYP1A1 immunohistochemistry, Intensity: 0 **TOTAL: 6**
5 (son)	4	M	triglycerides 190 mg/dl total cholesterol 189 mg/dl	Hepatomegaly longitudinal diameter > 8 cm	Number of sebaceous glands: 2 -Cystic lesions: 2 -Mantle-like epithelial projections: 2 -CYP1A1 immunohistochemistry, Distribution: 0 -CYP1A1 immunohistochemistry, Intensity: 0

					TOTAL: 6
6 (daughter)	7	F	triglycerides 185 mg/dl total cholesterol 201 mg/dl	Normal	Number of sebaceous glands: 2 -Cystic lesions: 2 -Mantle-like epithelial projections: 2 -CYP1A1 immunohistochemistry, Distribution: 0 -CYP1A1 immunohistochemistry, Intensity: 0 **TOTAL: 6**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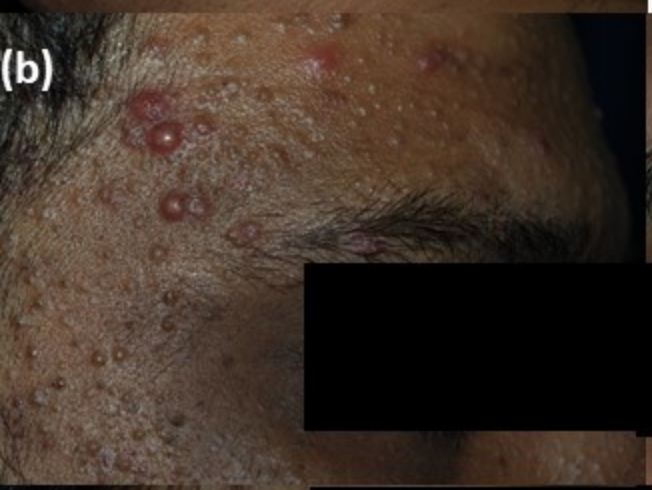
(f)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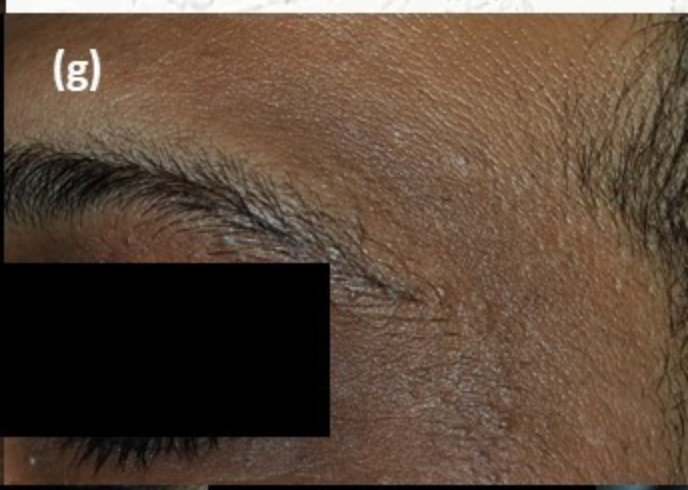
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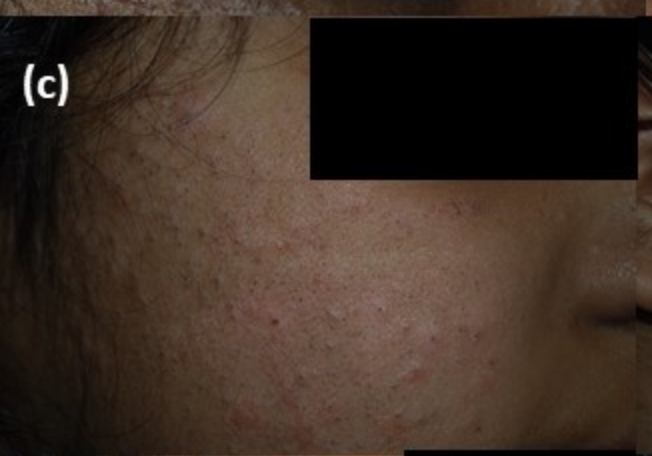
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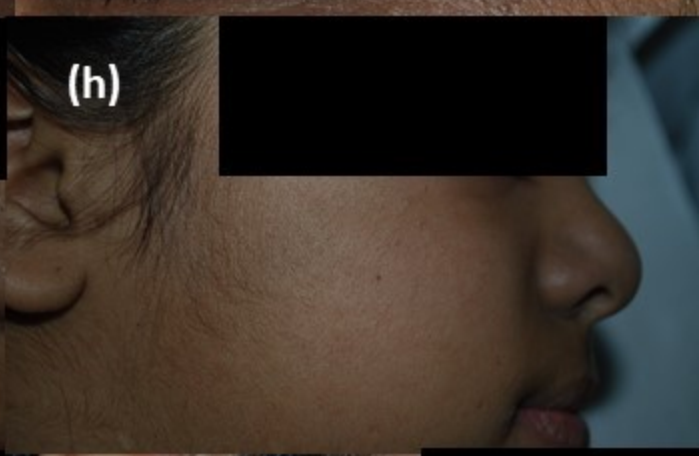
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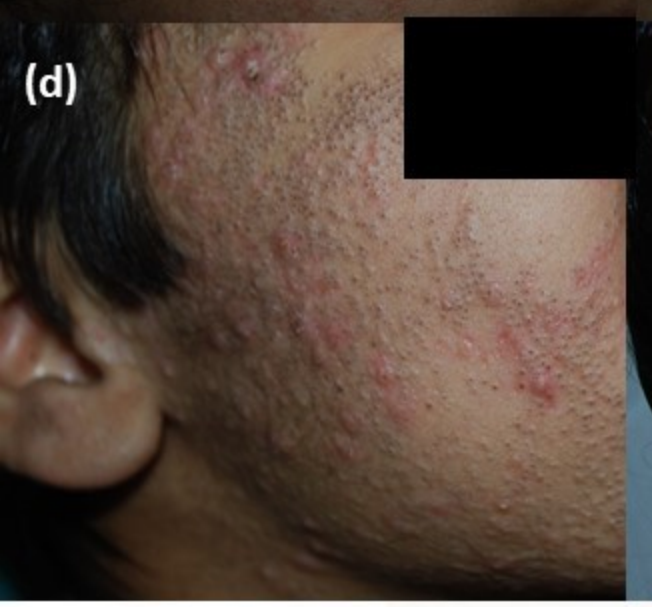
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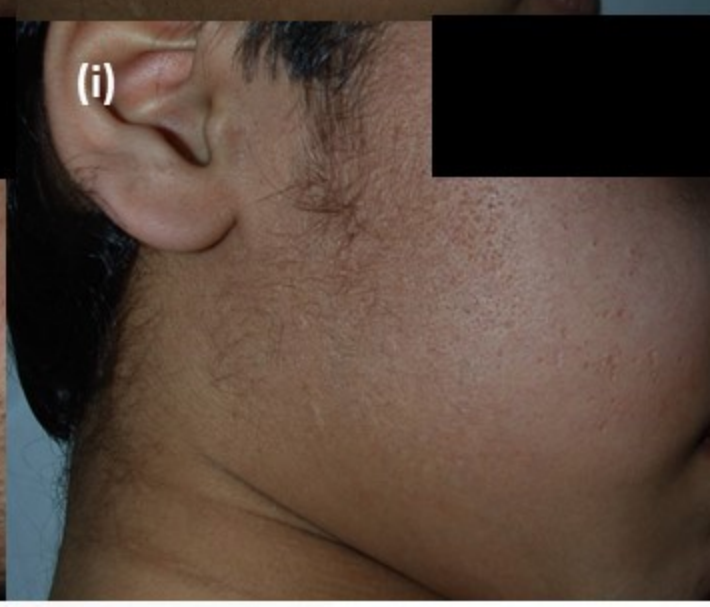
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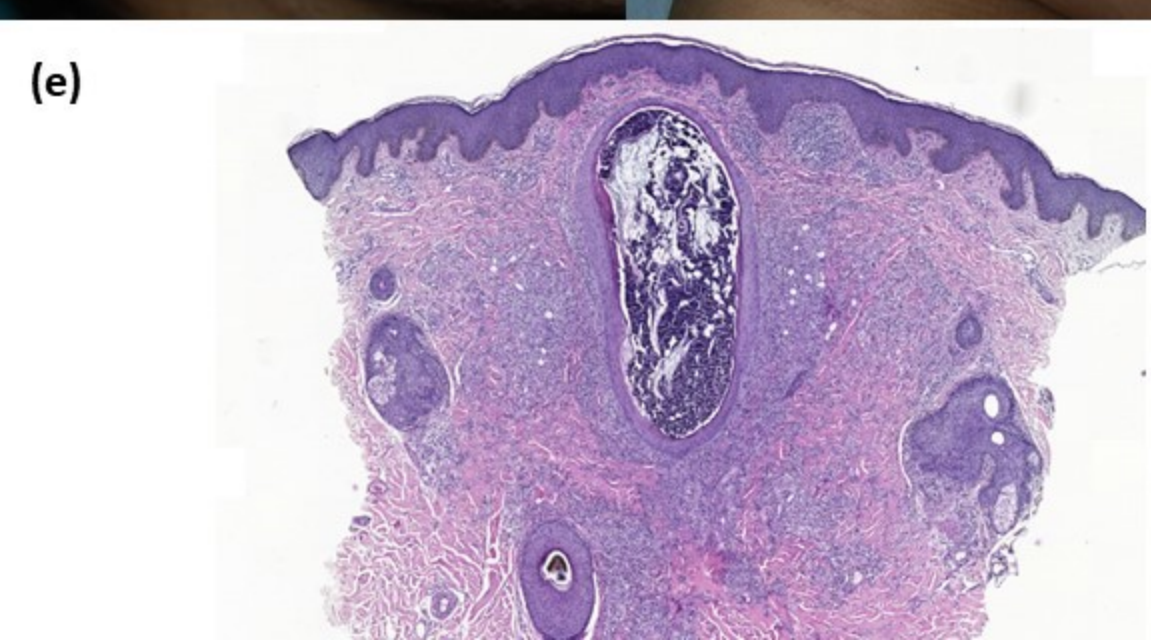
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