Clinical and genealogical assessment of patients with incontinentia pigmenti in the Ural region (Russia) between 1976 and 2012.

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Summary
This paper presents the results of the follow up of 33 patients diagnosed with incontinentia pigmenti between 1976 and 2012. Cutaneous manifestations of the disease were diagnosed in 12 girls within the first year of life, including 4 in the neonatal period, and three boys. Three family trees in 4 generations are presented, including 14 female patients having various manifestations of the disease affecting the skin, teeth, eyes, etc. The prognosis depends in part on the extracutaneous associated malformations, which may range from minor to severe.

Key words
Incontinentia pigmenti, family tree.

Incontinentia pigmenti is a genetically determined systemic disease characterized by distinctive skin changes with ectodermal or mesodermal abnormalities (i.e. pathology of the central nervous system, teeth, eyes, hair, nails, or musculoskeletal defects). The first patient with incontinentia pigmenti was demonstrated by Garrod in 1906. Clinical signs of the disease were described by Bloch in 1925, while Sulzberger studied the disease in detail in 1928 (4, 10). The pathogenesis of skin and systemic changes remain unclear (5). In Russia there are publications about clinical manifestations of incontinentia pigmenti in one or two children (7,8,12). Our review of the follow up of 21 patients with incontinentia pigmenti was first presented at the V Russian scientific-practical conference in Saint-Petersburg in 2011 (11).

Case reports
For the first time we diagnosed incontinentia pigmenti in 1976 and 1979 in two girls. One of them has been followed up to date. We have analyzed clinical manifestations of incontinentia pigmenti in 33 patients. Along with the skin changes (erythematous, bullous, verrucous and hyperpigmented) we noted dental defects: complete absence of primary teeth in one patient and permanent teeth in the second patient, the lack of 2 to 9 permanent teeth (7 patients, including one man). Diastema of the upper teeth was found in 7 patients, teeth degeneration (needle-shaped teeth) in 2 patients.

Ocular defects and vision impairment, i.e. astigmatism, myopia, lack of the visual acuity of the right eye due to hypoplasia of the optic nerve were observed in 5 patients.

Severe hair dystrophy with total absence of eyelashes was observed in 4 patients. Severe local hypertrichosis occurred in 2 children and nail dystrophy in two patients.

Neurological pathology occurred as muscular tonic syndrome and encephalopathy.

"Cleft lip" and "cleft palate" were diagnosed in a girl with incontinentia pigmenti followed up since the age of 1 year and 3 months.
Endocrine pathology accompanied by obesity was observed in one patient at 10 years of age.

Here we report the family trees of three family groups who were followed up for 3-4 generations.

Family tree 1. In 1979 a woman (family tree 1, III5) came for a consultation with a three-month-old daughter (IV8) with disseminated bullous, papular and hyperkeratotic lesions on the legs, buttocks and hands. The girl's general condition was satisfactory. Local symptomatic therapy was prescribed. The above lesions regressed by the age of 7-8 months. Hyperpigmentation areas soon appeared on her body skin, and depigmentation and atrophic areas, linearly distributed, developed by the age of 3 to 4 years. In 2006 by the age of 26 years the patient's pregnancy from her first marriage resulted in abortion (fetal sex unknown). The daughter from her second marriage was born in 2009, with severe manifestations of incontinentia pigmenti (family tree 1, V4) with pronounced manifestations in the third stage, namely hyperpigmentation lesions in the form of swirls on the limbs and trunk. The maternal grandmother (III5) and great grandmother (H3) had absent dentition since birth, nail dystrophy, and atrophic and hypopigmented skin lesions.

Family tree 2. A 21-year-old woman (family tree 2, III7) with a one-month-old baby (IV, 4) was referred to the authors in 2001. The baby girl presented with severe skin lesions (bullous, urticarial rash), and neurological disorders. The baby was hospitalized in the pediatric clinic, where the death occurred due to massive brain hemorrhage. The woman had on the limbs linearly arranged atrophic streaks and areas of hyperpigmentation in the inguinal folds. She was unaware of her incontinentia pigmenti. All her family members have been examined and followed up since 2001 to date.
The patient (III7) in her second marriage with a 23 years older man gave birth to a girl (IV5), who developed multiple depigmentation lesions reminiscent of hypomelanosis of Ito, diastema and dental dystrophy at the age of 8 years; the baby girl received the final diagnosis of incontinentia pigmenti.

The younger sister of the patient (III4) had skin lesions in the form of atrophic and hyper-pigmented elements, damaged optic nerve of the right eye and absence of 6 permanent teeth. Her daughter (IV1) from the first marriage had manifestations of incontinentia pigmenti, hair dystrophy, diastema, and incomplete dentition. Her second pregnancy (IV2) resulted in abortion (fetal sex unknown). Her son (IV3) from her second marriage was born without any symptoms of incontinentia pigmenti.

The mother of these two sisters (I115) had pronounced atrophic and hypopigmented streaks on the skin of the shins and thighs. The patient’s grandmother (I12) showed marked manifestations of incontinentia pigmenti.

Family tree 3. The follow-up of family 3 began with the visit of a patient (III8), 19 years of age with a 6.5-months-old baby girl (IV1) from her first marriage, presenting severe and profuse verrucous and bullous eruptions on the legs and armpits and at the same time hyperpigmentation on both sides of the trunk. Later on the girl (IV, 1) presented with incomplete lower and upper dentition and diastema. Her mother (III, 8) presented with pronounced hypopigmented and atrophic streaks on the legs. She had three pregnancies from her second marriage: the first two resulted in miscarriage, while the third pregnancy (male fetus) regressed at 13.5 weeks. The mother of patient III8 (II, 2) had incontinentia pigmenti with hypopigmented streaks located linearly on the legs; she had no teeth since birth. Her obstetric history revealed six miscarriages before the birth of our patient. Finally, the grandmother (I, 2) of patient III8 had no permanent teeth after her primary teeth loss.

Discussion

Our follow-up of patients with incontinentia pigmenti has shown that the onset of pigmentation is not associated with previous eruptions. This confirms the findings by Elkin et Al. (7) that pigmentation in 40% of patients with incontinentia pigmenti was not associated with previous eruptions.

Physicians should remember (9) that dental abnormalities as well as depigmented reticulated lesions could be the only manifestations of incontinentia pigmenti. Careful examination of the patients’ family members and their personal and family history analysis is necessary to confirm the diagnosis of incontinentia pigmenti and make the disease prognosis for the following generations.

Extradermal disorders included ocular disturbances, nail dystrophy and dental defects. Death occurred in a 1-month-old little girl (family tree 2) with severe skin lesions (bullous-papular eruptions) and brain hemorrhage.

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