A case of generalized post-vaccinal complication after BCG revaccination. Skin and hypoderm tuberculosis, cicatrization stage

Summary. The article presents a case of a rare post-vaccinal complication, which appeared after BCG revaccination in the setting of insignificant catarrhal phenomena in a girl of 7 years 6 months of age. An ulcerous defect started to form on the 2nd-3rd day on the vaccine administration site. Similar ulcerous lesions started to form on facial skin on sites of cat scratches within the first week. Later, the ulceration spread on all cutaneous coverings. Multiple deep drawn-in cicatrical defects remained on the girl’s skin after long-term treatment at various inpatient hospitals. The developed generalization of the infectious process may have resulted not only from violating the vaccination technique, but also from untimely diagnostics and incorrect disease treatment tactics. The article throws light upon clinical forms and differential diagnostics of various skin tuberculosis forms and presents modern tuberculosis vaccinal prevention issues, classification and causes of post-vaccinal complications.

Keywords: skin tuberculosis, BCGitis, post-vaccinal complications, children.

INTRODUCTION

Review of modern publications dedicated to tuberculosis vaccinal prevention shows that the immunization using tuberculosis vaccine invented by Calmette and Guerin (BCG – bacillus Calmette-Guerin) remains the main method of protecting children against the most dangerous clinical forms of tuberculosis, in particular, miliary tuberculosis and tuberculous meningitis. Immunity induced by subcutaneous administration of living low-virulent mycobacteria develops ca. 6 weeks after and may remain for 10 years and more. Mechanism of post-vaccinal protection formation is based on the suppression of hematogenic spread of mycobacteria from the primary infection’s nidus; this subsequently reduces risk of disease development and process reactivation.

Tuberculosis immunization schemes are different in different countries. According to the modern recommendations of the World Health Organization (WHO) experts, most European countries and territories with unfavorable epidemiologic situation in terms of tuberculosis employ single
BCG vaccination at birth, which promotes the development of long-term immunity – up to 10 years and more.

The National preventive vaccination calendar in Russia preserves triple vaccination of children: on the 3rd-7th day of life, first revaccination at 7 years of age, the second – at 14 years of age.

Tuberculosis immunization history is accompanied by the development of a certain amount of post-vaccinal complications.

The rate of the registered post-vaccinal reactions and complications in Russia is far lower than in other European countries. Post-vaccinal complications are rare: 0.02% of cases after vaccination and 0.001% of cases after revaccination. Scientists consider that the difference is caused by the use of too high vaccinal doses in several countries (0.1-0.15mg) with a bigger number of viable bacteria in the drug [1, 2].

Post-vaccinal complications may be caused by the following factors:

- increased reactogenicity of a vaccine;
- big number of viable units per vaccination dose;
- incorrect subcutaneous vaccinal administration technique;
- wrong selection of children subject to vaccination;
- concurrent diseases;
- altered reactivity of the body.

In singular cases the disease may develop due to the vaccinated person’s contact with an infected patient shortly before vaccination [1].


I. Local manifestations (the most frequent):
   - cold abscesses (subcutaneous infiltrates, which develop 1-8 months after; may remain for 6-7 months);
   - ulcers developing 3-4 weeks after vaccination;
   - regional BCG-lymphadenitis (most often – axillary; also cervical, supra- and subclavicular): lymph node’s enlargement up to 1.5cm and more; abscess and fistula may form; resorption takes 1-2 years; calcification may sometimes take place; develops with the rate 2:10,000 (0.02%).

II. Disseminated BCG-infection (ostites, lupus etc.).

III. Generalized BCG-infection with fatal outcome. Takes its course as disseminated tuberculosis with the affection of lymph nodes and other organs and systems 1-12 months after vaccination with rate 1:1,000,000 of the primarily vaccinated people. The main factor of
pathogenesis is immunodeficiency state (chronic regional enteritis, combined immunodeficiency).

IV. Post-BCG-syndrome (keloid cicatrices of more than 10mm, erythema nodosum, allergic rashes).

**CLINICAL CASE**

The review features photographs from the patient’s family album and personal archive of Professor K.M. Yavorsky.

**Irina B., 14 years 3 months of age.** Sought consultation with complaints on cicatrical defects on skin.

*Life anamnesis.* The girl of the first, non-complicated pregnancy, of the first timely and unassisted delivery. Birth weight – 3,400g, birth length – 52cm. Discharged from the maternity hospital on the 4th day. Unremarkable early neonatal period. Breast fed until 5 months of age. Contracted acute respiratory infections 1-2 per year during infancy, had chickenpox at 5 years of age.

The girl was vaccinated with BCG vaccine at maternity hospital on the 3rd day of life. There are no data on preventive vaccination in further life, including PPD tests.

*Case history* was recorded according to the girl, as her mother does not speak Russian well and was living in a different town when the disease was developing. There had been no medical documentation by the first visit to the FSBI “Scientific Center of Children’s Health”. The girl received BCG revaccination at the polyclinic at place of residence at 7 years 6 months of age in the setting of insignificant catarrhal phenomena. Ulcerous defect started forming on the 2nd-3rd day on the vaccine administration site – on the lateral surface of the left shoulder’s upper third. Similar ulcerous lesions started forming on facial skin on sites of cat scratches within the first week; the girl started experiencing pain in the left eye.

The girl reported these complaints to the polyclinic at place of residence, where she received unsuccessful external treatment (application of dressings soaked with unknown solutions). Ulcers on shoulder and facial skin were becoming larger within the subsequent 2-3 weeks; multiple bluish-red tubercles appeared on hand and leg skin with hyperemic phenomena around them; these tubercles burst within 5-10 days forming fresh ulcers disposed to peripheral growth.

Multiple ulcers and general intoxication phenomena indicated the girl’s hospitalization to a surgical, then – to a resuscitation unit of the hospital at place of residence, where she received treatment of disseminated pyoderma (sepsis, according to the girl), which was unsuccessful as formation and peripheral growth of ulcers continued. All injection measures led to the formation of new ulcerous defects.
The girl stayed in resuscitation units of 3 Kishinev (Republic of Moldova) municipal hospitals for 6 months; no improvement was noted. Relatives took the girl home on request; there she was treated with popular means by a healer (intake and external therapy). By the moment that treatment started, ulcers had been vast and deep, with abundant (up to 1 glass) purulent discharge. In the setting of the 4-5-month-long treatment using popular means, the old ulcerous defects started closing, general condition improved, although fresh nidi continued to form.

Medical commission was convened on the insistent demand of relatives; the commission involved Professor K.M. Yavorsky – phthisiatrician of the Kishinev research institute of phthisiology, where the girl had been being treated for the subsequent 2 years – from 2006 to 2008.

According to the information received from Professor K.M. Yavorsky, the girl’s condition by the time therapy began had been extremely severe. Vast ulcerous defects with abundant purulent discharge and stinking odor were localized on the skin of face, buttocks, hands and legs (pic. 1, 2).

![Pic. 1. Ulcerous defects on shin skin](image)

![Pic. 2. Ulcerous defects on leg skin](image)
Combinations of different anti-tuberculous drugs were being selected throughout therapy. Fresh nidi stopped appearing after 4 months of therapy, however, old ulcerous defects on limb skin became finally covered with healing tissue only after 1.5 years of therapy (pic. 3, 4).

Pic. 3. Cicatrical alterations remaining after ulcerous defects on shoulder skin

Pic. 4. Cicatrical alterations remaining after ulcerous defects on hand and facial skin

In 2009 the girl moved to Moscow and remained under observation of a TB dispensary’s phthisiatrician with the diagnosis “keloid disease after BCGitis”. Examination – clinical blood and urine analyses, chest radiography (December 2009) and magnetic resonance tomography (May 2012) did not reveal any deviations.

**Status localis.** By the moment of examination skin process has been disseminated and represented by multiple extensive cicatrical lesions. Cicatrical defects of irregular torn form of flesh and pink color with visible vessels are identified on facial skin; cutaneous outgrowths (papillae, “bridges” and “crosspieces”) are identified on the surface of cicatrices.
Deep drawn-in cicatrical defects are localized on shoulder, forearm, buttock, thigh and shin skin; they are primarily of roundish outlines, 3-15cm in diameter; of flesh or bluish color with atrophy phenomena (pic. 5-8).

**Pic. 5.** Deep cicatrical defect on shoulder skin

**Pic. 6.** Deep drawn-in cicatrical defects on leg skin

**Pic. 7.** Multiple defects on facial and cervical skin, 2006

**Pic. 8.** Cicatrical alterations of facial skin, 2012
When analyzing spread and clinical peculiarities of different tuberculosis forms, it is important to note that the share of skin tuberculosis is small – 5.6% of all extrapulmonary tuberculosis forms, i.e. 4-5 times smaller than shares of any of its primary localizations. Small rate of skin tuberculosis is caused by a range of morphological, physiological and immunological skin properties, which make skin an unfavorable environment for tuberculous mycobacteria: “grave for bacilli Kochii”, as several authors wittily put it.

The main factors which may favor development of extrapulmonary tuberculosis forms, including skin tuberculosis, are large-scale infection, mycobacterial virulence and immune reactivity of body in whole and of skin in particular [3, 4].

Endogenous infection spread out of the first-affected organs (lymph nodes, lungs etc.) is prevalent in the skin tuberculosis development.

Clinical presentation of scrofuloderma (pic. 9) attracted our attention when we were studying clinical presentations of various skin tuberculosis forms (lupus, tuberculosis cutis papulonecrotica and colliquativa, Bazin’s erythema induratum).

At this affection, the process evolves through the following stages (according to E.N. Bellendir) [5]:

- 1-5cm subcutaneous nodes;
- merger of nodes, with subjacent tissues and covering skin acquiring crimson-red color; dissolution and ulceration of certain nodes;
- softening of merged nodes, skin defect enlargement, ulceration and formation of fistulas; creeping (serpiginous) process;
- recurrent course of many years; formation of extensive ulcerative affection zones; deforming, disfiguring cicatrization with surface “bridge-like” outgrowths, papillae and crosspieces.
Differential diagnostics of this form of tuberculosis is conducted with syphilitic gummas, infiltrative ulcerative pyoderma, ulcerative actinomycosis and sporotrichosis gummas on the basis of data of microbiological, serological studies and of results of tuberculin tests [3, 5]. Anamnestic data, clinical presentation of the disease and study of materials on skin tuberculosis allowed establishing a provisional diagnosis: “Post-vaccinal BCG revaccination complication. Skin and hypodermic tuberculosis of scrofuloderma type, cicatrization stage?”

Council of specialists of the FSBI “Scientific Center of Children’s Health” resolved to conduct an advanced examination of the child involving a phthisiatrian to cut out tuberculous infection’s activity and an immunologist to assess the immune system’s condition, which, if deviated, could favor generalization of the infectious process. Diaskin and Quantiferon tests were included in the examination plan; they confirmed lack of tuberculous process’s activity. We also conducted phagocytosis examination, immunophenotyping of blood lymphocytes and determined the level of blood immunoglobulins and found no deviations; this allowed us to rule out an immunodeficiency state.

CONCLUSION

We may assume that such a rapid development of tuberculous infection in skin may have been caused by vaccination technique violations (incorrect administration, overdose) or biological properties of BCG strain. Taking into account the fact that the reaction to vaccination is a “petty disease” of a kind, it is possible that the concurrent pathology (catarrhal phenomena during vaccination) may have favored complications, thus disturbing general immunity in that period.

Analysis of special studies of post-vaccinal BCG complications allows stating that specific tuberculosis vaccination is the main method of protecting children from the development of severe disease forms and reduces mortality from this infection. In order to reduce risk of post-vaccinal complications, neonatologists and pediatricians should carefully select children subject to immunization within strictly decreed time limits.

Vaccination and revaccination should be conducted by qualified personnel strictly observing the vaccination technique [2].

Ruling out an immunodeficiency state in the girl in this clinical case allowed plastic surgeon’s consultation and suggesting consecutive cosmetic and surgical rehabilitation measures for esthetic correction of the present alterations.

REFERENCES