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RESEARCH ARTICLE

MICROBIOLOGICAL AND MOLECULAR GENETIC ASPECTS IN THE CLINICAL COURSE OF ALLERGIC DERMATOS IS IN UZBEKISTAN

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ABSTRACT

The article presented molecular genetic studies of genotypes of St.aureus isolated from biosubstrates of the persistent opportunistic skin of the organism in patients with allergic dermatoses. Results of the study showed development of persistent opportunistic skin infections caused by persistent opportunistic skin infections in patients with allergic dermatoses caused by MRSA and toxic shock syndrome (TSST) by strains of S.Aureus in 37.5% of cases.

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INTRODUCTION

Allergic dermatoses are from most distributed chronically inflammatory and multifactorial which development is related with interaction of genetic factors and external environment. At the present in many countries including Uzbekistan is noted stable tendency to increase in the number of allergic dermatoses especially among the younger generation (Mavlyanova Sh.Z., 2017). We have noted more cases of complicated forms of allergic dermatoses associated with opportunistic infections of bacterial, fungal or viral etiology [Al-TalibH1, ?; Armeding, 1993]. It was proven by numerous scientific studies of domestic and foreign authors that staphylococci are underlying development of complicated forms of allergic dermatoses against the background of immunologic disorders. According to literature data conditional-pathogenic microorganism *St. Aureus* belongs to heterogenic and polymorphic species in which present not only gens of antibiotics resistance but also many gens of pathogenicity in chromosome as a part of genome islets of different types: islets of "pathogenicity" staphylococci chromosome cassettes (SCC), prophages [Belousova , 2013; Carlsen, 2011]. It should be noted that for majority of staphylococci natural media of habitat is surface of human skin, mucous membranes where they persisting without rendering harmful effects. But it was revealed by numerous studies that in chronic dermatoses occurred changes in state of skin microbioceonosis as in quantitative and qualitative interrelations. In this connection the question arises about etiopathogenetic role of these bacteria in development of skin pathologies, because main striking factors of effect of staphylococci of eukariotyc cells and tissues are factors of virulence and pathogenicity secreting (toxins) [Carlsen, 2011]. The purpose of study was research of variability of genome complexes of staphylococci isolated from skin of patients with allergic dermatoses.

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MATERIAL AND METHODS OF STUDY

Ninety six patients with allergic dermatoses aged from 9 to 57 were examined.

In their nosology patients with allergic dermatoses formed 38 (39,6%) and atopic dermatitis – 58 (60,4%). All the patients were underwent clinical, microbiology and molecular-genetic investigations. To identify culture Staphylococcus spp. was used medium Endo, medium Mueller-Hinton, salt broth with mannit, medium Klegr. Material for DNA served scraping of cultures of microbial cells from Petri dish. Separation of DNA from samples was made by set of reagents «RIBO-prep» (production OOO «InterLabService», Moscow, Russia). The principle of operation is based on lysis of cells and denaturation of cellular proteins for lysis, containing chaotropic agent (guanidinthiocinat) with the subsequent deposition of nuclein acids by isopropanol and their following extraction into solution. Genotypes of aureus Staphylococcus are differentiated by a presence of one or some specific products of amplification: for gene *mecA*- in size of 163 base pair, for gene *pvl* – 433 base pairs, for gene *tst*- in size of 540 base pairs. Detection of results of PCR was conducted by method of electrophoresis in 3% agar gel during 40 minutes in voltage 120 B, coloring by bromide ethidium and visualization in UV-light (Fig.1).

RESULTS OF STUDY

Results of microbiologic studies exhibited that Stapylococcus spp. was sown in 83 that formed 86,5 cases among 96 patients with allergic dermatoses on skin in lesion focus. In species identification of Staphylococci the largest number amounted to seeding of pathogen flora - St. aureus in 44,8% (43 from 96), St. epidermidis – 30,2% (Wen, 2011), St. haemolyticus – 11,5% (Chen, 2011). It should be noted that among 58 patients with atopic dermatitis, 14 patients revealed M.furfur, which amounted to 24.1%. Molecular-genetic research was conducted in 42 cultures St. aureus, isolated from skin of lesion focus in patients with allergic dermatoses. The age of patients was from12 to 54. In nosologic forms among 42 patients was diagnosed atopic dermatitis in 22 (AD) and allergodermatiis – in 20 (AlD) patients . Results of research showed DNA was separated in 100% of cases. By Method of PCR was confirmed also presence of marker gen nuc St.aureus in 100% (42 cultures) cases (Table 3). As can be seen from the table methicillin as resistant staphylococcus (mec A) was detected in 39 samples that accounted 92,8% cases. At the same time staphylococci producing toxin of syndrome of toxic shock (Tsst) were detected in 27 patients (64,3%), and staphylococci producing leukocidin of Panton-Valentine-Luk – 433 bp were detected in 7, that accounted 16,6% respectively.

It should be noted that combined genotypes of methicillin resistant staphylococcus (mecA) and toxin of syndrome of toxic shock (Tsst) observed, were revealed in 26 patients that accounted 61,9% cases and in 7 patients was noted combination of MRSA+Tsst+Luk – 433 bp, that made 16,6% cases. Clinical analysis of detectability of genotypes of St.aureus taking into account the nosological form of AlD showed the following peculiar properties (Table 4). As follows from the table toxin of syndrome of toxic shock (TSST) in 35,7% (15 from 42) of cases was manifested in patients with atopic dermatitis and in 28,6% (12) – in patients with allergic dermatoses. Methicillin resistant *St. aureus* (MRSA) in 47,6% (20) cases was detected in AD patients, and in 45,2% (19) cases – in patients with allergic dermatoses. It should be noted that pore-forming toxin Panton-Valentine leukocidin (Panton-Valentine leukocidin, PVL) in 14,3% (6) cases was revealed in AD patients and in 1 (2,4%) patient with complicated form of AlD - toxicoderma. As it is seen from the Table contaminants of strains MRSA and Tsst *St.aureus* were detected in 26 patients that made 61,9%, MRSA and Tsst + Luk – 433 bp *St. aureus* – in 7 (16,6%). Whereas taking into account nosology in a group of AD patients these contaminants were detected in15 patients (68,5%) cases and in a group of AlD patients – in 11 (55%) cases. Whereas contaminants MRSA and Tsst + Luk – 433 bp *St. aureus* in group of Ad patients were revealed in 6 (27,3%), and in group of AlD patients – in 1 (5%). Analysis of results of study taken into account sex of patients revealed a high seeding rate of strains of female subjects that made 71,4% cases (Table 6). As follows from the table strain Tsst was most frequent stood out in subjects of male gender – 40,5%, more over in group of patients with atopic dermatitis (44,4%). At the same time in subjects of female gender it made – 23,8% (10 cultures), but more frequent it stood out in a group of AlD patients (26,9%). Strain MRSA in subjects of male gender stood out in 47,6% (20) and female gender – in 45,2% (19) respectively. And the genotype MRSA in group of AD stood out in 35,9% (14), and in group of AlD in female gender – in 33,3% (13). And by their sex aspect contaminant strains more frequent stood out in subjects of female gender – 14,3% (3). Pore-forming toxin Panton-Valentine (PVL) leukocidin was revealed in 6 from 7 patients with AD. It should be noted that more often was stood out MRSA – 23,8% depending on organism bio substrates from mucosal membrane of urogenital system – 23,8%, whereas strain Tsst – in 9,5% cases.

Careful analysis of clinical course of allergodermatoses taking into account of strains isolated *St. aureus* exhibited that clinical picture of skin-pathologic process in AD group with MRSA was characteristic for erythematous-squamous form with lichenification. General condition of patients was medium heavy, as noted temperature rises up to $38,6^0$, an increase in submandibular lymph nodes, discomfort of the gastrointestinal tract. Skin-pathologic process in patients with strain St. aureus had prevalent infiltrative character caused by erythematous vesicular eruptions, large lamellar desquamation in scalded skin was found on upper and low extremities. In patients with genotype of the pore-forming toxin Panton-Valentine leukocidin (PVL) skin pathologic process had prevalent, infiltrative inflammatory character with duration of disease more than 10 years with oft relapses and resistance to standard therapy conducted.

Therefore, analysis of clinical-microbiological and molecular-genetic studies showed in 37,5% development of persistent opportunistic infections caused by MRSA and toxin of syndrome of toxic shock (TSST) of trains of St. aureus. At that etiologic factor of development of opportunistic infection in AlD patients in 92,8% was fixed methicillin-resistant staphylococcus, staphylococci producing toxin of syndrome of toxic shock (Tsst) were detected in 64,3% cases. Toxin of Panton-Valentine leukocidin (Panton-Valentine leukocidin, (PVL)) St. aureus was sown in 16,6% cases. Contamination of pathogen strains of methicillin-resistant staphylococcus and toxin of syndrome of toxic shock Tsst was noted in 61,9% (26) cases and in 16,6% (7) – contamination of MRSA and Tsst + Luk – 433 bp *St. aureus* cases respectively. As follows from the table strain Tsst was most frequent stood out in subjects of male gender – 40,5%, more over in group of patients with atopic dermatitis (44,4%). At the same time in subjects of female gender it made – 23,8% (10 cultures), but more frequent it stood out in a group of AlD patients (26,9%).

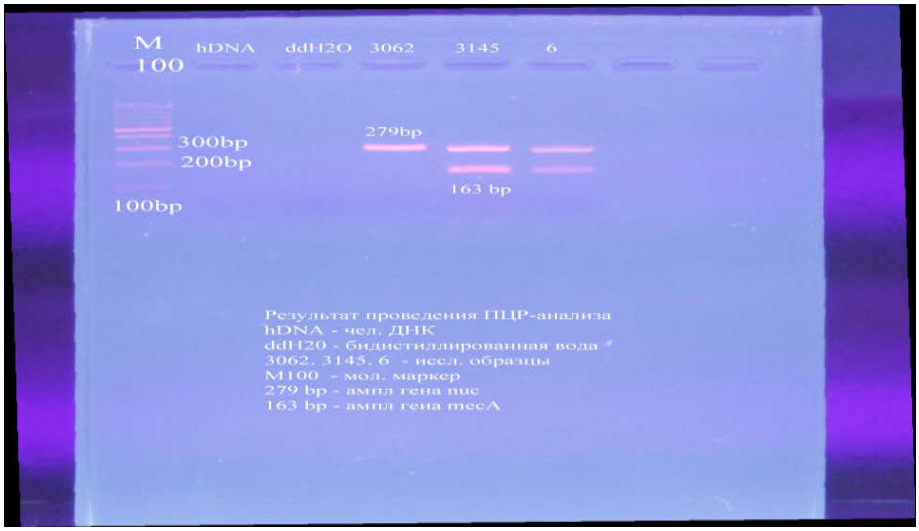

Fig.1. Electroforegram of results of PCR for determination of genotypes St. aureus

Table 2. Sequence specific* oligonucleoid primers for multiplex PCR-amplification to genes of virulence *pvl and tst and gene of resistanceto methicillinum mec A

luk-PV	Sequence of oligonucleotide
Вперед	ATCATTAGGTAAAATGTCTGGACATGATCCA
Обратно	GCATCAAGTGTATTGGATAGCAAAAGC
mecA	
Вперед	ACTGCTATCCACCCTCAAAC
Обратно	CTGGTGAAGTTGTAATCTGG
tsst1	
Вперед	ACCACCCGTTTTATCGCTTGAACG
обратно	AGCCCTTTGTTGCTTGCGACA

Table 3. Indicators of genotypes St. aureus, isolated from biosubsubstrates of AlD patients

Culture of St. aureus	Nuc – 279 bp	Tsst – 540 bp	mecA – 163 bp	Luk – 433 bp
All cultures n=42	42	27	39	7
%	100	64,3	92,8	16,6

Table 4. Indicators of detectability of genotypes St. aureus in AlD patients taking into account clinical form

Nosology	Nuc – 279 bp	Tsst – 540 bp	mecA – 163 bp	Luk – 433 bp
AD n=22	22 (52,4%)	15 (35,7%)	20 (47,6%)	6 (14,3%)
AlD n=20	20 (47,6%)	12 (28,6%)	19 (45,2%)	1 (2,4%)
In total n=42	42	27	39	7

Table 6. Seeding rate of strains of St. *aureus* in patients with allergodermatoses taking into account sex of patients (%, abs)

Culture St. aureus	Nuc		Tsst		mecA		Luk – 433 bp	
	male	female	male	female	male	female	male	Female
AD n=22	16	6	12	3	14	6	6	
AlD n=20	5	15	5	7	6	13	1	
In total n=42	21(50%)	21(50%)	17(40,5%)	10(23,8%)	20(47,6%)	19(45,2%)	7(16,6%)	

Strain MRSA in subjects of male gender stood out in 47,6% (20) and female gender – in 45,2% (19) respectively. And the genotype MRSA in group of AD stood out in 35,9% (14), and in group of AlD in female gender – in 33,3% (13). And by their sex aspect contaminant strains more frequent stood out in subjects of female gender – 14,3% (3). Pore-forming toxin Panton-Valentine (PVL) leukocidin was revealed in 6 from 7 patients with AD. It should be noted that more often was stood out MRSA – 23,8% depending on organism bio substrates from mucosal membrane of urogenital system – 23,8%, whereas strain Tsst – in 9,5% cases. Careful analysis of clinical course of allergodermatoses taking into account of strains isolated *St. aureus* exhibited that clinical picture of skin-pathologic process in AD group with MRSA was characteristic for erythematous-squamous form with lichenification. General condition of patients was medium heavy, as noted temperature rises up to $38,6^0$, an increase in submandibular lymph nodes, discomfort of the gastrointestinal tract. Skin-pathologic process in patients with strain St. aureus had prevalent infiltrative character caused by erythematous vesicular eruptions, large lamellar desquamation in scalded skin was found on upper and low extremities. In patients with genotype of the pore-forming toxin Panton-Valentine leukocidin (PVL) skin pathologic process had prevalent, infiltrative inflammatory character with duration of disease more than 10 years with oft relapses and resistance to standard therapy conducted. Therefore, analysis of clinical-microbiological and molecular-genetic studies showed in 37,5% development of persistent opportunistic infections caused by MRSA and toxin of syndrome of toxic shock

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