



Clinical and Immunological Evaluation of Patients with Painful Pulpitis

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Annotation: Atypical facial pain can be caused by pulpal pathology, most commonly manifested by chronic pulpitis. The pain of pulpitis is known to be one of the most severe and distressing for the patient. The ongoing study would allow the dentist to consider the pulpitis pain not only as a symptom of dental disease, but also as a systemic syndrome, in which the patient's nervous system, mental health, ability to work and quality of life are affected. Clinical and immunological studies have clarified the clinical and pathophysiological features of atypical facial pain in pulpitis. Treatment of pulpitis cannot be limited to endodontic and restorative measures, it should include a complex of diagnostic and rehabilitative measures aimed at restoration of neuropsychological and immunological health of the patient.

Key words: painful pulpitis; nervous system; facial pain; pain syndrome

Introduction: The relevance of studying mechanisms of pain and analgesia is determined by its general medical and social-economic importance to the society [2,5,6,12]. In recent decades intensive research was conducted on pain mechanisms, searching for effective means of its suppression and pathogenetic treatment. Facial pain is a symptom complex, characterized by sensory, autonomic and motor disorders in the face or oral cavity [1,3,8,9].

Unlike physiological pain that plays the role of organism's protective reactions trigger mechanism, pathological pain has maladaptive and pathogenic meaning and differs significantly in its characteristics and mechanisms. In persistent chronic pain syndromes, prolonged use of medications often leads to drug intoxication, allergy, immunodeficiency. It is obvious that further search of ways of prevention and treatment of pain syndromes should be connected with carrying out basic researches revealing the essence of pathological pain.

The International Classification of Diseases (ICD-10) currently classifies painful facial and oral symptoms as follows:

➤ Typical neuralgia of the fifth pair of cranial nerves;

- atypical facial neuralgia;
- craniofacial pain secondary to other extracranial and intracranial pathologies.

Thus, atypical facial pains are painful syndromes in the face and organs of the mouth associated with pathology of the teeth, temporomandibular joint, masticatory muscles, bone tissue, and mucous membrane. According to the literature, atypical facial pain occurs more frequently in women after 40 years of age [7,11,13,15].

Among neurodental diseases, atypical facial pain averaged 6.4% [19]. Atypical facial pain can also be caused by pulpal pathology, most commonly manifested by chronic pulpitis. The pain of pulpitis is known to be one of the most severe and distressing for the patient. It often prevents you from sleeping, chewing food, makes you irritable and short-tempered. However, fear of treatment at the dentist or other reasons make people endure this pain for a long time, use all kinds of means of self-treatment, which often turn out to be temporary and ineffective [14,15]. Despite a long study of the problem of odontogenic facial pain, the clinical and pathophysiological features of atypical facial pain in pulpitis have not yet been elucidated. Such a study would allow the dentist to consider pulpitis pain not only as a symptom of dental disease, but also as a systemic syndrome, in which the nervous system, the patient's psyche, ability to work and quality of life are affected [17].

The aim of the investigation was to study complex of clinical and immunological parameters in patients with pulpitis.

Materials and methods of research.

107 patients with facial pain caused by inflammation of dental pulp were examined at the age of 18 to 64 years. Mean age was $36 \pm 1,2$ years. The bulk of patients (87.9%) were aged 20-49 years, less often below 20 years (3.7%) and after 50 years (8.4%). The male to female ratio was 48 (44.9%) to 59 (55.1%).

Individuals with typical facial pain characteristic of trigeminal neuralgia, as well as those with a history of demyelinating or rheumatic diseases, were excluded from the analysis of the present study. Facial pain was often detected on the right side, in 60.7% of cases. Bilateral pain was detected in only 1 case (Table 1).

Table 1: Distribution of patients by side of pain (abs., %)

Side of the pain	Number of patients		
	women	men	Total
right	39	26	65 (60,7%)
left	31	10	41 (38,4%)
both	0	1	1 (0,9%)
Total	70 (37,4%)	37 (34,6%)	107 (100%)

The "immunological study" compared the results with those of healthy volunteers. The comparison group consisted of 20 people with a sanitised oral cavity and no acute or chronic somatic or neuropsychiatric pathology. There were 8 males and 12 females. Their age varied, like in the main group, from 18 to 62 years. The average age was $34,2 \pm 3,1$ years.

Methods of immunologic research

They included detection of serum levels of antibodies to myeloperoxidase (MPO) and antibodies to myelin basic protein (MBP) by immunofemoral assay (ELISA) [11,13]. Test-systems from "Navina" (Russia) were used for this purpose.

The content of myeloperoxidase was determined using monospecific polyclonal antibodies in enzyme

immunoassay. The principle of the method consists in interaction of myeloperoxidase with antibodies to it on a slide, followed by optical density determination using Multiscan spectrophotometer at a wavelength of 492 nm. The results were compared with those of the comparison group.

If assayed correctly, the mean OD value of the positive control serum wells should be higher than the negative control serum wells by at least 0.5 OD units. It is known that myelin is one of the major components of the human nervous system and is a part of both nerve cells and nerve fibers. Studying the level of antibodies to its main constituent allowed us to judge about autoimmune processes directly affecting the human nervous system at pulpitis, accompanied by destruction of myelin.

Antibodies to the common myelin protein were determined by immunoassay using a set of reagents developed by N.E. Yas-trebova and N.P. Vaneeva.

The determination was carried out due to specific interaction of the OBM sorbed on the plate with antibodies to it, contained in blood serum. Registration was done using spectrophotometer "Multiskan" at wavelength 492 nm. ELISA was performed using automatic micro-pipettes. The kit includes the following components: immunosorbent - polystyrene slides with a preparation of cBM from rabbit, bull or human brain sorbed in wells; positive control - human serum preparation containing antibodies to cBM above diagnostic level; conjugate - diagnostic antibodies against human peroxidase O immunoglobulin, OFD, FSB-D, CFB-P; "stop - reagent" - 2M sulfuric acid solution.

The assay consists of washing the immunosorbent with at least 0.2 ml of FSB-D and incubating the plate at room temperature for 2-6 min. The contents of the wells were then removed by shaking. Washing was repeated twice. A serum sample was then added and incubated at 36.5-37.5° C for 60 minutes. The next step was to wash off the excess antibodies. The conjugate, 0.1 ml of diagnostic antibodies against human peroxidase-labelled immunoglobulin G was then added. After incubation the conjugate was washed off for 60 minutes and the substrate-indicator mixture was added. The reaction was stopped by adding 0.05 ml of stop reagent - 2M sulfuric acid solution to the wells of the plate.

Immunological study was performed in Laboratory of Reproductive Immunology, Institute of Human Immunology and Genomics, Research Center.

The obtained data were statistically processed using a Pentium-IV computer using Microsoft Office Excel-2003 software package, including the use of built-in statistical processing functions.

Results: All 107 patients with painful symptoms examined by us required oral hygiene treatment. Oral hygiene was assessed in all examined patients using the Fyodorov-Volodkina hygiene index. Table 2 shows that poor and bad hygienic state of oral cavity was found in the majority of patients:

Table 2: Results of oral hygiene assessment of the examined patients (abs., %)

Hygienic condition of the mouth	Number of patients		
	women	women	women
Good	6.	2	8 (7,4%)
Satisfactory	16	9	25 (23,4%)
Unsatisfactory	22	15	37(34,6%)
Poor	15	22	37(34,6%)
Total	"59 (55,1%) "	48 (44,9%)	107(100%)

Periodontal disease was diagnosed in 59 (55,1 %) patients; failure of orthopaedic constructions at the loss of teeth was found in 14 of 37 examined patients (37,8%); bite pathology was revealed in 28 (26,2%) out of all examined patients. Prevalence of carious process in the examined patients was 100%. Painful symptoms of different duration, localisation and intensity were the leading complaint of

all patients. With the progression of the inflammatory process in the dental pulp pain intensified, became nagging and excruciating, localized in the projection area of the affected tooth plexus. The pain encompassed the tooth, gingiva and alveolar process. In most cases (53.7%), the upper dental plexus was affected. A 19.6% of patients experienced a paroxysmal exacerbation of pain lasting from a few seconds to 1 minute against a background of nagging pain. Pain paroxysms occurred with varying frequency, from 3 to 4 times a day to 5 to 7 attacks per hour. Localisation of pain corresponded to the affected dental plexus. Most frequently the pain was localized in molars (61.1%) and premolars (36.1%), rarely in canines (0.9%) and incisors (1.9%). During the onset, pain radiated through the alveolar plexus and to the hard palate, cheek and temple. When the inferior plexus was affected, pain spread to the floor of the mouth, the cheek and the parotid region. Patients were passive during the attack, lying horizontally and applying heat to the cheek. At the end of the attack the pain was localized in the area of the corresponding tooth, where the affected dental plexus was located. The duration of the painful symptom varied from 3 days to 7 months. A detailed neurological examination of patients with pulpitis pain revealed symptoms of nervous system damage. The most common symptoms were tinnitus and ringing in the ears, hearing loss, dizziness of systemic and non-systemic nature, headache, unsteadiness when walking, nausea and vomiting. The examined patients complained of general weakness, decreased efficiency, rapid fatigue, sweating (especially at night), increased body temperature ($37.1^{\circ} - 37.7^{\circ} \text{C}$), decreased body weight.

In some patients with prolonged pain symptoms, we observed (both subjectively and objectively) impaired salivation. In some cases, hyposalivation was detected, with patients complaining of dry mouth. However, on the contrary, most of these patients reported increased salivation, especially during an attack of pain.

Painfulness when moving the eyeballs was observed in 11.2% of patients. Impaired innervation of the facial nerve was manifested by a unilateral smoothing of the nasolabial fold in 45.8% of patients, indicating a central nature of the lesion. Deviation of the tongue was observed in 17.8% of patients.

Disseminated cerebral microsymptomatology syndrome was detected in 37.4% of patients, with 28.0% of patients diagnosed with grade I dental neuralgia and 34.6% of patients with grade II dental neuralgia. This syndrome is characterized by the presence of subjective neurological symptomatology and focal microsymptoms as insufficiency of eyeball convergence, reduction of corneal reflexes, smoothness of nasolabial folds, tongue deviation, reflexes of oral automatism.

Syndrome of focal affection of the brain was in 24.3% of patients, moreover, 1st degree dental neuralgia was revealed in 4.7% of patients, and P degree - in 19.6% of patients. This syndrome is characterized by the presence of focal neurological symptoms associated with circulatory disturbances in a particular vascular basin. Focal symptoms were mostly mild and transient or persistent, most often manifesting as an altering syndrome, systemic vertigo, hemihypesthesia, hemiparesis, and aphasia.

Results of an immunological study. We determined the content of antibodies to myeloperoxidase in the blood serum of patients with subjective and objective signs of dental neuralgia (main group). The results were compared with those of the comparison group. The results are presented in table 3.

Table 3: The content of antibodies to myeloperoxidase in patients with facial neuralgia of the comparison group ($M \pm t$, units OP).

Indicator	Main group (n=107)	Comparison group (n=20)
Antibodies to myeloperoxidase	$0,8 \pm 0,002$	$1 < 0,00001$

Immunological studies revealed a significant increase in indicators in patients with atypical facial pain compared to those in the comparison group. The difference was 6.2 times (Table 3).

One can see from Table 3 the highest values of antibodies to myeloperoxidase were registered at the affection of the dental plexus of the molars. Dental plexus lesions are accompanied by high titers of antibodies to myeloperoxidase, indicating microvascular inflammation.

The presence of exudative and productive vasculitis at histological examination of the pulp of the patients is proved by microscopic examination data. The revealed increase of titers of antibodies to myeloperoxidase in patients with dental neuralgia proves the presence of systemic vasculitis as these antibodies are one of the markers of inflammatory damage of small vessels.

Thus, dental neuralgia is the result of a systemic vascular process of vasculitis due to allergy to infectious and allergic factors. We also studied antibodies to myelin total protein in blood serum of patients with dental neuropathy in comparison with analogous parameter of the control group (Table 4).

Table 4: Antibody content to myelin total protein in patients with facial pain and control group patients (M±t, units OD)

Indicator	Main group (n=107))	Comparison group (n=20)
Antibodies to myeloperoxidase	0,06±0,001*	0,02±0,007*

* - difference between values $p < 0.00001$

Determination of the level of antibodies to myelin total protein also revealed its significant increase in the group of patients with dental neuropathy in comparison with similar indicators in the comparison group. As can be seen from the table above, the highest content of the studied antibodies was determined at exacerbation of chronic pulpitis, which indicates, in our opinion, a higher degree of autoimmune process at this stage of dental plexopathy. This is due to the association of chronic inflammatory and autoimmune processes in atypical facial pain with pathology of the terminal branches of the trigeminal nerve.

The number of myeloperoxidase antibodies in the venous blood of patients with pulpitis pain symptoms is 6,2 times higher than in healthy patients, indicating a direct link between inflammatory and autoimmune processes in atypical facial pain and pathology of the trigeminal nerve terminal branches. The studied immunological parameters have direct statistically significant dependence on the duration and phase of the disease and the size of the dental plexus. Patients with pulpitis and severe pain symptoms must be referred to the risk group of dental diseases, in connection with which in 100% of cases they require sanitation of oral cavity. The obtained results of the study are recommended for use in the activities of dentists-therapists to prevent the development of pain symptoms and prevent the development of a neurological picture of the process.

Conclusions

1. Inflammation in dental pulp of examined patients is accompanied not only with painful symptom, features of which are conditioned by series of pathophysiological processes, but also with disorders of immune, nervous system, manifested in 42,1% of patients with hege-vascular dystonia syndrome, 24,3% with focal lesions of brain, combined with dental plexopathy.

2. The number of antibodies to myeloperoxidase in the venous blood of patients with pulpitis pain symptom is 6,2 times more, and to the common myelin protein - 3 times more than that of healthy patients, that indicates a direct connection of inflammatory and autoimmune processes at atypical facial pain with pathology of the trigeminal nerve terminal branches.

3. The studied immunological parameters have direct statistically significant dependence on the duration and phase of the disease, the size of the dental plexus.

4. Treatment of pulpitis cannot be limited to endodontic and restorative measures only, it should

include complex of diagnostic and rehabilitation measures aimed to restore neuropsychological and immunological health of patient.

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