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CLUSTER-TIC SYNDROME

REPORT OF FIVE NEW CASES

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ABSTRACT - The so-called short lasting primary headaches include heterogenic entities that can be divided between those without pronounced autonomic activation and those where this activation is evident, which includes the cluster-tic syndrome. We report five new cases with age closer to the trigeminal neuralgia's one, and concomitance of cluster headache and trigeminal neuralgia, which is less frequent in the literature. We also discuss briefly the pathophysiology of these clinical entities, suggesting that the trigeminus nerve is a common pathway of pain manifestation.

KEY WORDS: cluster headache, trigeminal neuralgia, overlapping syndromes.

Síndrome da cefaléia em salvas – neuralgia do trigêmio: relato de cinco novos casos

RESUMO - As assim chamadas cefaléias primárias de curta duração incluem entidades heterogêneas podendo ser divididas entre aquelas sem importante ativação autonômica e aquelas onde esta ativação é evidente, nestas se inclui a síndrome cefaléia em salvas - neuralgia do trigêmeo (cluster-tic). Apresentamos cinco novos casos com faixa etária mais próxima da neuralgia do trigêmeo e com concomitância entre a cefaléia em salvas e a neuralgia do trigêmeo o que é muito menos frequente na literatura. Discute-se também brevemente a fisiopatologia desta entidade clínica sugerindo que o nervo trigêmeo é a via comum da manifestação dolorosa.

PALAVRAS-CHAVE: cefaléia em salvas, neuralgia trigeminal, síndromes de superposição.

The so-called short lasting primary headache syndromes include a heterogenic group of entities that can arise with remarkable autonomic activation, as in cluster headache, paroxystic chronic and episodic hemicrania, and in SUNCT (short lasting unilateral headache with conjuntival injection and tearing), oposed to those the autonomic features are virtually absent, as in continuous hemicrania and hypnic headache. This paper intends to discuss an uncommon affection, with just 39 reports in the literature, in which coexist trigeminal neuralgia and cluster headache, the so-called cluster-tic syndrome[1-3], aiming to add five new occurrences with overlapping symptoms, which does not occur in the majority of the reported cases.

The cluster-tic syndrome is characterized by the coexistence of two kinds of pain. One is strictly unilateral, usually periocular, with evident autonomic features, and daily attacks for weeks or months (cluster). The other is characterized by paroxysms similar to electric shocks (tics).

In the reported cases the diagnosis of the overlapping conditions was made based on the criteria of the International Headache Society. The discussion will refer to the involvement of the V cranial nerve as a probable common pathway of two affections. All patients were treated with drug associations for neuralgia of the V pair and cluster headache.

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CASES

Case 1. JA, 79 years old caucasian male. For six years he has a neuralgic kind of pain affecting the 1st and 2nd divisions of the right V nerve. The attacks were both spontaneous and triggered by tactile stimulation of the nose, had a very short duration and ceased spontaneously. About one year later, pain paroxysms started to occur with nasal congestion and ipsilateral tearing, ensued by deep pain, predominantly periocular, for an hour, lasting in average for 60 days and recurred at regular intervals of six or seven months, between which a neuralgic pain persisted, but with much less intensity. In 1993, at the beginning of a new attack, he came to the Ambulatory of Headache at Santa Casa de São Paulo, already taking carbamazepine, 300 mg daily, without success. Phenytoin, 300 mg daily, and baclofen, 15 mg daily were added, with improvement of the neuralgiform picture. The cluster component remitted during the time of the treatment above described. Currently the patient has no specific medication, has no symptoms of cluster headache eversince about three years ago, persisting the neuralgic component slightly intense on the second division of the right trigeminus. He was submitted to a brain computerized axial tomography (CT), which showed signals of cortical involution, compatible with his age, had normal blood biochemistry and laboratory tests for inflammation.

Case 2. TMO, 65-year-old caucasian female. For 16 years she had paroxystic neuralgic pain affecting the 2nd divison of the right V nerve. In other occasions she had pain predominantly periocular, on the right side, very intense, pulsatile with nasal congestion and ipsilateral conjunctional injection; the attacks were daily and predominantly nocturnal, lasting from one to two hours and very intense, recurring in about one month with asymptomatic periods of variable duration. In several occasions (more than 50%) there was overlapping of the two kinds of pain. When she was admitted for ambulatory treatment in August 1994 she was taking carbamazepine, 400 mg daily, without remission of any symptomatology. She had diagnosis of facial algia and the neurologic examination showed tactile hypoesthesia on the second division of the rigth trigeminus. Brain CT with and without contrast, media blood biochemistry and laboratory tests for inflammation were normal. In August 1996 a cardiac arrythmia was diagnosed, being added verapamil, 160 mg daily, and increased the dose of carbamazepine to 600 mg daily. Both components improved, with the overlapping decreasing to levels under 20%, without autonomic signals related to headache, being associated baclofen, in increasing doses until 30 mg daily, when both symptoms remitted almost completely. She is in ambulatory follow-up.

Case 3. JPN, 59-year-old caucasian male, For ten years he had paroxysms of pulsating left frontal pain of short duration, sparing the periocular region, followed by very short duration "tics" on the same region. Five minutes after he had a periocular ipsilateral pain of great intensity, with nasal congestion and tearing. This picture recurred four or five times by day and in the last years has become each time more frequent, with increasing intensity, what made him to come to the specialized service. It is important to stress that during the periods of pain intensification the stimulation of the trigger zones, like the nasal margin and the upper lip, triggered the painful picture with all features described above. He was taking carbamazepine, 800 mg daily without any clinical improvement. It was added verapamil, 240 mg daily, without succes. In a new period there was introduction of fenitoine, 300 mg daily and baclofen, 30 mg daily. He was admitted in the hospital and submitted to CT with and without contrast, which was normal, as well as blood biochemistry and laboratory tests for inflammation. The symptoms remitted three days after the new drug association. Presently he is in ambulatory follow-up taking baclofen, 15 mg daily, fenitoin, 200 mg daily and verapamil, 240 mg daily, with good clinic control.

Case 4. OB, 79-year-old caucasian male. About one year ago, without any posterior remission period, he started to have right periorbital pulsatile pain of great intensity, with great conjunctional injection, tearing, and nasal congestion, lasted for about 120 minutes, invariably followed by a short lasting neuralgic kind of pain on the 1st and 2nd division of the ipsilateral trigeminus, already been with carbamazepine 1 g daily and baclofen, 15 mg daily, without any evident improvement. Short before at the Ambulatory of Headache of Santa Casa of São Paulo (two days) he had been prescribed verapamil 240 mg daily and quinidine, 120 mg daily, during admission in emergency service because of cardiac arrythmia. Brain CT with and without contrast, blood biochemistry and laboratory tests for inflammation were normal, being added prednisone, 60 mg daily. In 15 days the cluster pain remitted, remaining symptoms compatible with trigeminal neuralgia. Corticosteroid was tapered. Presently he has only neuralgic pain on the 1st and 2nd divisions of the trigeminal nerve, with long periods of remission that cease at the attempt of reducing the medication.

Case 5. JBS, 60-year-old caucasian female, from Pernambuco. About one year ago (1996) she had a sudden strong neuralgic pain of very short duration affecting the 1st divison of the left trigeminus. In the following

months the pain increased in frequence and intensity. It raised spontaneously but could also be triggered by contact with the left nasal wing, the zygomatic region and by activities such as chewing and verbalization, and during the periods of greater susceptibility, by any tactile stimulation of the face. The patient came to the medical service, being prescribed carbamazepine, 400 mg daily, which controlled the pain for several months, with only five short sporadic attacks. In July 1997, after suspension of the drugs, the painful symptoms described recurred, with pain on the same topography but with different features. The new pain, of great intensity, lasted for about 60 minutes, was pulsatile, spared the ocular globe, came along with tearing, nasal congestion, conjunctional injection, rhinorrhea and palpebral ipsolateral semiptosis, could reccur several times during the day, and could be triggered concomitantly by tactile stimulus. She used thyroid hormone for subclinical hypotyroidism. She came to our service where we observed an attack of pain triggered by a very ligth tactile stimulation. In that occasion the pain had the features above described and the physical examination showed all related autonomic activities, early reported, besides important pain at the palpation of the left carotid artery. At the same time any ligth tactile stimulation tiggered a neuralgic pain disproportionately intense, which even overcame the cluster one. The attack partially remitted with inhalation of 100% oxygen and ceased with 2% intranasal lidocaine instilation. Brain CT with and without contrast, media blood biochemistry and laboratory tests for inflammation were normal. She was discharged without pain, being prescribed carbamazepine 600 mg daily, baclofen 30 mg daily, and verapamil 240 mg daily. She is in ambulatoty follow-up.

DISCUSSION

Report on the literature, the mean age for the beginning of pain was 44.6 years, 60% of patients are female, pain was always unilateral, and in 60% affected the left hemiface[4]. Two great groups of patients with this syndrome are described, the first without concurrent clinical mainfestations (28 patients or 65%) and the second with concurrent manifestations (11 patients or 35%). In the five cases hereby reported the mean age in the beginning of the symptoms is 61.5 years, 60% are males and in 60% the rigth side is affected. The age range in these cases, different from the literature[1,2], is closer to the trigeminal neuralgia than to the cluster headache. Since the association of the two kinds of pain is very narrow, it is likely not fortuitous, being a distinct clinical entity, with the pathophysiologic basis probably superimposed. In this casuistic, as in literature[4,5], the laboratory tests and the brain CT did not any contribution to the diagnosis.

The trigeminal neuralgia is probably caused by changes in the myelinated fibers of small caliber, whereas the cluster headache is related to changes in non-myelinated trigeminal fibers of the trigeminal-vascular system at the level of the nervous plexus of the cavernous sinus[6]. Currently it was proposed the division of the primary headaches between those without pronounced autonomic activation and those where this activation is evident, thus forming the so called group of the "trigeminal-autonomic" cephalalgias[7].

A "reflex-arc" is proposed as a common pathway, defining connections at the level of the brainsteam and the parasympathetic portion of the VII cranial nerve, although the true underlying mechanism is still unknown. Cholinergic cells disseminated through the dorsal lateral reticular pontine formation constitute the superior salivatory nucleus, from which depart general efferent visceral fibers that follow as components of the intermedius nerve, reaching the pterygopalatine ganglion as secretory and vasomotor fibers which inervate the lacrimal gland and the oral and nasal mucosa[8]. Several authors[9,10] have demonstrated that an stimulation intense enough of the trigeminal fibers can cause liberation of trigeminal markers (CGRP - calcitonin gene related peptide and P substance) and parasympathetic markers (VIP - vasoactive intestinal polypeptide)[10,11]. This means an autonomic reflex activation of the connections of the central trigeminal vascular system, highly somatotopic and functionally organized. Furthermore, several ganglions, as for instance the sphenopalatine, contain a constitutive enzime, the NO-synthase, which through the conversion of L-arginine into L-citruline leads to the production of a potent vasodilator, the nitric oxyde (NO), which has its activity modulated by the intracellular increase of calcium, which in turn is mediated by excitatory neurotransmitters as the glutamate. Besides causing intense vasodilation, the liberation of NO inhibits the platelet aggregation and decreases the expression of the molecules mediators of the cellular adhesivity (ICAMs), being the vasodilation probably a result of the autonomic disturbs associated with this kind of pain.

Future efforts will be necessary to the stablishment the real mechanism of the integration between the trigeminal impulses and the marked parasympathetic activation in this clinical entity. Even more difficult is to explain how the activation of those pathways can cause pain with different features.

We consider that, as the example of the range proposed by Raskin between migraine and chronic daily headache[12], this clinical entity now refered should be seen as a continuous of algic manifestations that begin with trigeminal neuralgia and progress depending on the intensity and quality of the impulses in the involved pathways.

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