

Complex regional pain syndrome and gestation. Case report*

Síndrome complexa de dor regional e gestação. Relato de caso

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SUMMARY

BACKGROUND AND OBJECTIVES: Complex regional pain syndrome I (CRPSI) is characterized by pain, neurovegetative disorders, sub-motor and vascular function abnormalities in the absence of nervous injury. In this case, drug limitations due to gestation and lactation have made even more difficult the therapeutic management.

CASE REPORT: Female patient, 26 years old with CRPS for 5 years. She presented twinge pain and shock on left fingers and forearm, followed by weakness, edema, hair loss, cyanosis and temperature decrease. Pain intensity was from 9 to 10 by the verbal analog scale. Worsening factors were: cold, movements, touch and night period. Additional tests included normal cervical MRI and electroneuromyography.

The treatment was multidisciplinary with unsatisfactory results. She was followed during gestation and lactation, with adaptation of drugs, physical therapy, psychotherapy and anesthetic blocks. Currently, pain is controlled.

CONCLUSION: Complex regional pain syndrome I treatment, which is very complicated, becomes even

more difficult during gestation and lactation to offer analgesia with less risk for mother and fetus.

Keywords: Analgesics, Breastfeeding, Gestation, Nervous block, Pain.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A síndrome complexa de dor regional I (SCDRI) caracteriza-se pela presença de dor, anormalidades neurovegetativas, anormalidades da função submotora e vasculares, na ausência de lesão nervosa. No presente caso, as limitações medicamentosas, impostas pela gestação e lactação dificultaram ainda mais o manuseio terapêutico.

RELATO DO CASO: Paciente de 26 anos, com SCDRI havia 5 anos. Apresenta dor em fígada e choque nos dedos da mão e antebraço esquerdo acompanhado de fraqueza, edema, queda de pêlos, cianose e diminuição de temperatura. Intensidade da dor pela escala verbal analógica entre 9 e 10. Fatores de piora: frio, movimentos, toque e período noturno. Exames complementares, incluindo ressonância nuclear magnética de coluna cervical e electroneuromiografia normais. Tratamento multidisciplinar com resultados insatisfatórios. Acompanhada durante a gestação, lactação com adaptações na medicação, fisioterapia, psicoterapia e bloqueios anestésicos. Atualmente, o quadro doloroso está controlado.

CONCLUSÃO: O tratamento da síndrome complexa de dor regional I que é bastante complicado se torna mais difícil durante a gestação e lactação para oferecer analgesia com menor risco para a gestante e feto.

Descritores: Amamentação, Analgésico, Bloqueio nervoso, Dor, Gestação.

INTRODUCTION

Complex regional pain syndrome I (CRPSI) is characterized by a broad spectrum of sensory, neurovegeta-

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tive and motor signs and symptoms, predominantly in the extremities. Pain, characterized by burning, throbbing or weight, shock paroxysm or twinge, is generally associated to allodynia, hyperesthesia, hyperpathia and hyperalgesia in the affected region. Severe spontaneous pain and hyperalgesia are common symptoms which are exacerbated by moving the limb. Shivering, dystonia, muscle spasms, strength deficits and limitation of movements amplitude are part of motor symptoms, as well as edema, change in color, temperature and trophism of tegument and anexa. Trophic changes, such as tendon and ligament retraction and amyotrophy may occur in the chronic phase¹⁻³. Voluntary movements of upper limbs, particularly the execution of fine movements such as clamp pressure and function, are commonly impaired in such patients⁴. Major clinical heterogeneity makes diagnosis and treatment difficult.

The adoption of the pain-immobilization-disuse-pain pattern is very common. The chronic character of pain leads to motor function limitation and irreversible trophic, sleep, appetite and mood changes, in addition to family and professional relationships impairment⁵. Major sympathetic changes may be observed; there are cases of pain with dependent sympathetic component which may become independent sympathetic, which justifies the inefficacy of sympathetic blocks for treatment. The multidisciplinary treatment aims at controlling pain and at physical rehabilitation and analgesic techniques depend on pain intensity. Sleep abnormalities, anxiety and depression should be treated in association¹.

CASE REPORT

Female patient, 26 years old, salesperson, laid off from work with CRPS for five years. Clinical symptoms: sudden pain in twinge and shock in left fingers and forearm, with weakness, edema, hair loss, cyanosis and decreased temperature. Pain evaluated through the verbal analog scale (VAS) was between 9 and 10. Worsening factors: cold, movements and physical contact. Without improvement factors.

She referred fatigue, non-repairing sleep, lack of appetite, changes in personal relationships and leisure activities. Independent daily life activity (DLA), minor help to get dressed. Left-handed with predominance above 50%. Additional exams, including normal MRI of cervical spine and electroneuromyography of the cervical region and upper limbs.

Unsatisfactory treatment with amitriptyline (50 mg/day), carbamazepine (200 mg) every 8 hours, 4% chlorpromazine (10 drops) every 4 hours, psychotherapy and physical therapy.

She became pregnant and was followed-up during gestation and lactation with adaptation of medication, physical therapy, psychotherapy and anesthetic blocks, with difficult adherence to medications due to fear of interfering with fetal integrity.

Medicated with low-dose levomepromazin until the 6th month, paracetamol, pain desensitization technique with cotton, movements in room temperature water and acupuncture.

Sympathetic block of left stellate ganglion with ropivacaine, by the peritracheal technique without using radiology in the 8th month of gestation, with complete pain relief, which returned one week after with intensity similar to the pre-blockade period.

During breastfeeding VAS = 8. Treatment with kinesiotherapy and nortriptyline (10 mg/day), without improvement (VAS = 9.5), being prescribed 25 mg amitriptyline a day. Throbbing, continuous pain persisted in hand, irradiating to homolateral shoulder, skin paleness, DLA lower than 50%, anxious. Physical therapy, occupational therapy, desensitization, motor imagination were maintained. Six months after delivery continuous axillary anesthetic left brachial plexus block was induced with ropivacaine (10 mL) every 8 hours for three weeks. VAS = zero, allowing kinesiotherapy optimization. Four weeks after axillary block interruption, burning pain was back being prescribed physical therapy and psychotherapy.

When she stopped breastfeeding, tramadol (50 mg) every 6 hours, amitriptyline (75 mg/day) and chlorpromazine (15 drops) were prescribed and a new continuous anesthetic left brachial plexus block was induced (10 months after the first) with ropivacaine (10mL) every 8 hours for six weeks. VAS = zero. After axillary block interruption, she remained without pain for 5 weeks.

Dorsal thoracic sympathetic block of T2 and T3 by radiology, to the left, was induced with ropivacaine (75 mg) and triamcinolone (40 mg). VAS remained 3 for one month. After catheter removal pain has progressively increased. She evolved with VAS between 4 and 8. Scapular waist was manipulated and triggering points were inactivated, in addition to isometric strengthening. Three months after there was pain improvement, stable mood, improved sleep, independent DLA (left hand with no function), VAS varying between 6 at rest and 9 at movement. Left upper limb with amyotrophy,

skin paleness, decreased temperature, diffuse allodynia, ADM limitation, pain at wrist / proximal and distal MCF / IF flexion, strength 4. Medicated with amitriptyline (75 mg/day), 4% chlorpromazine (15 drops) every 8 hours, methadone (10 mg/day) and lamotrigine (25 mg) every 12 hours.

DISCUSSION

The difficulty to treat CRPS pain is due to pathophysiological complexity. A wide range of inflammatory mediators, cytokines, neuropeptides and eicosanoids seem to be involved in its genesis, as well as central and peripheral nociceptive neurotransmission and neuromodulation changes^{1,3}.

During gestation and lactation, therapeutic interventions are a major challenge to offer analgesia with lower risk to mother and fetus^{6,7}. There is a great concern of the mother with the health of the fetus and whenever possible, clear explanation should be given and non-pharmacological methods should be used for a better adhesion to treatment. Fetal malformations due to drugs vary between 1% and 2%. The pharmacological treatment should consider gestational age and maternal, placenta and fetus organism. In mother's organism, gestational changes influence drugs absorption, distribution, metabolism and excretion.

The placenta has well-defined transfer mechanisms and active enzyme systems which interfere with the behavior of drugs going to the fetus and with metabolites returning to the mother. The crossing of drugs is conditioned to low molecular weight, non-binding to serum proteins, liposolubility and slightly acid pH⁸.

Fetal exposure to some drugs before the fourth week of gestation has the effect of everything or nothing, that is, they may cause the loss of the fetus by blastocyte injury, or they may not determine abnormalities due to the totipotentiality of embryo cells. Organogenesis period, between the 18th and 55th day after conception, is the most critical period for drug exposure, causing irreversible malformations^{6,7}. Lately, drugs may influence fetal growth or physiological function. Drugs

may determine congenital malformations, perinatal syndromes or late neurobehavioral changes. In choosing the drug it is important to know the safety profile in different stages of gestation and breastfeeding, the level of protein binding, lipid solubility, molecular weight and maternal metabolic characteristics which influence maternal-fetal transfer of drugs. Some drugs do not directly affect fetal development, but may influence gestation dynamics and, except for major polar molecules, most of them cross the placenta and reach the fetus^{6,7}.

To orient drug prescription during gestation and lactation, the Food and Drug Administration in the USA has developed a risk classification based on the drug potential to cause fetal malformations, which although limited, is an orientation for prescription (Table 1).

Risks of drugs used to control pain in our case were: paracetamol and dipirone – risk is B/D for the former and B for the latter. Acetaminophen in doses higher than 4 g/day for a long time may determine liver and kidney injuries for mother and fetus^{6,8}.

Chlorpromazine: risk C/D, avoid using close to term for causing hypotension, lethargy and difficulty to suck in the neonate and breastfeeding⁹

Levomepromazin: risk C, potential risk for neurological interurrences, but there are no controlled studies^{6,7}.

Avoid using during breastfeeding.^{9,10}

Lidocaine and ropivacaine: risk B, no adverse effects for fetus and compatible with breastfeeding⁸.

Amitriptyline: risk D, may cause cardiovascular abnormalities^{6,7}. It should be carefully used during breastfeeding and newborn shall be monitored⁹.

Nortriptyline: risk D, potential determinant of congenital malformations⁸. It is excreted in the milk and there are no available data about its use during breastfeeding¹⁰.

CONCLUSION

CRPSI, normally of complex treatment, is even more difficult during gestation and lactation due to the limitation in the choice of analgesic and adjuvant drugs.

Table 1 – Classification of drugs risk during gestation

A - Controlled studies do not show risk	0.7%
B – There is no evidence of risk for humans	19.0%
C – Risk cannot be ruled out; recently launched and/or not yet studied drugs are included	66.0%
D – There is positive evidence of risk	7.0%
X – Counterindicated during gestation	7.0%

REFERENCES

1. Lin TY, Teixeira MJ, Rogano LA. Síndrome complexa de dor regional I e II. *Rev Med São Paulo* 1999; 78(2 pt 1):168-89
3. Van de Beek WJT, Schwartzman RJ, van Nes SI, Delhaas EM, van Hilten JJ - Diagnostic criteria used en studies of reflex sympathetic dystrophy. *Neurology* 2002;58:522-526.
4. Birklein F, Sittl R, Spitzer A, et al. Sudomotor function in sympathetic reflex dystrophy. *Pain* 1997;69(1-2):49-54.
5. Bruehl S, Harden RN, Galer BS, et al. Complex regional pain syndrome: are there distinct subtypes and sequential stages of the syndrome? *Pain* 2002; 95(1-2):119-24.
6. Cohen LS, Rosenbaum JF. Psychotropic drug use during pregnancy: weighing the risks. *J Clin Psychiatry* 1998;59(Suppl 2):18-28.
7. Friedman JM, Little BB, Brent RL, et al. Potential human teratogenicity of frequently prescribed drugs. *Obstet Gynecol* 1990;75(4):594-9.
8. Zacharias J. A rational approach to drug use in pregnancy. *JOGN Nurs* 1983;12(3):183-7.
9. American Academy of Pediatrics Committee on Drugs. Use of psychoactive medication during pregnancy and possible affects on the fetus and newborn. *Pediatrics* 2000;105(4):880-7.
10. American Academy of Pediatrics Committee on Drugs. The transfer of drugs and other chemicals into human milk. *Pediatrics* 1994,93(1):137-50.
8. Kaneko S, Otani K, Kondo T, et al. Malformation in infants of mothers with epilepsy receiving antiepileptic drugs. *Neurology* 1992;42(4 Suppl 5):68-74.

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