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## Clinical Notes

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# Cluster Headache During Pregnancy: Case Report and Literature Review

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**A 32-year-old pregnant woman presented with cluster headache (CH) during the third trimester of a normal pregnancy. Pure oxygen mask inhalation was ineffective, and intranasal lidocaine applications were realized associated with oral methylprednisolone, given at 1 mg per kg once daily. These treatments rendered the pain tolerable and the pregnancy went to its term with no consequence on the baby. This case of CH attack during pregnancy raises the issues of the influence of sexual hormonal changes in women with CH and the way to treat this disease in such circumstance. To date, there are no therapeutic guidelines available; this case suggests some possibilities.**

**Key words:** cluster headache, pregnancy, sexual hormonal changes, facial pain

**Abbreviation:** CH cluster headache

(*Headache* 2008;●●:●●-●●)

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Cluster headache (CH) is a rare primary headache disorder well defined by the International Headache Society.<sup>1</sup> The estimated prevalence is less than 1/1000 in the general population and the disease affects mainly men with a sex ratio between 2.5 to 1 and 7.5 to 1.<sup>2</sup> Recently several studies pointed out the increase in the number of female cases bringing up new difficulties in terms of acute or prophylactic treatment, particularly when the condition occurs during pregnancy. In 2006 the European Federation of Neurological Societies (EFNS) published evidence-based guidelines for the treatment of CH,

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but there was no suggestion for a suitable and safe treatment in such a situation.<sup>3</sup> Even in the global campaign to reduce the burden of headache worldwide, we do not find a specific chapter on this topic.<sup>4</sup> We report below a single case of a woman with episodic CH, whose attacks reappeared during the third trimester of an otherwise normal pregnancy. In the absence of definite guidelines for the treatment in such a case, therapeutics strategy appeared more complex considering the raising anxiety for the mother and potential danger for the baby.

This uncommon case raises new questions about CH in women. To date, the link between hormonal events and CH and the management of CH during pregnancy have been poorly explored and to our best knowledge, there are no reports on such situation and no guidelines. We suggest a brief review of the available therapeutic options and literature.

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*Conflict of Interest:* None

## CASE REPORT

A 32-year-old pregnant woman was admitted because of severe, repeated, right-sided spontaneous peri-orbital pain, diagnosed as typical CH. She had suffered with previous episodes of this typical episodic nonfamilial right CH since the age of 24 years. Attacks were typical; however, because of the age of onset and the female sex, brain computerized tomography scan and magnetic resonance imaging scan were performed and were normal. During previous clusters, she had used sumatriptan 6 mg injections or pure oxygen inhalation as acute treatment, and verapamil, 120 mg 3 times daily associated with steroids as preventatives. When she was admitted, the new cluster had started 2 weeks earlier. She was 35 weeks pregnant, there was no baby complication. At admission, she was suffering with 2 attacks a day on average, described as a severe unilateral right orbital pain associated with autonomic symptoms including conjunctival injection and lacrimation. In between attacks, clinical and neurological examination remained normal. There were no hypertension and no general diseases. Neither rest nor nonopioid drugs were able to reduce the pain; opioid drugs were ineffective and caused an apparent reduction in baby motions which induced a stressful situation. Pure oxygen inhalation had no effect on pain. Sumatriptan injections were refused as it has not been tested for safety during pregnancy. At that point, obstetricians were considering inducing early delivery for therapeutic reasons in order to allow the use of sumatriptan injection for pain control. Before making this decision, intranasal lidocaine applications were tried and methylprednisolone was given at 1 mg per kg, once a day. Within 2 days and after 2 intranasal applications of the anesthetic solution, the pain was significantly reduced and considered by the patient as tolerable. Given the reduction in both intensity and frequency of attacks, the steroids were maintained, but with a lower dose of 0.5 mg/kg/day, and finally ruled out a few days before delivery. The delivery occurred on the due date without complications for the mother or baby. Clinical controls 3 months later proved normal with no recurrence of attacks. Episodic CH during the third trimester of pregnancy was the definite diagnosis.

## COMMENTS

This case of CH attacks during pregnancy draws questions in particular on the best way to treat CH when attacks appear during pregnancy, and on the link between hormonal changes in CH.

Classically, CH prevails among men, but recent works point out a progressive decrease in the male-to-female ratio of the disease.<sup>5</sup> Manzoni<sup>6</sup> observed that this fall in the male-to-female ratio was due to an increase in the number of female cases. In his retrospective study, he first looked for possible bias in their center such as bias of recruitment or demographic changes. But as he could not find any, he concluded there was an increase in the prevalence of CH in females. He suggested this was a consequence of the gradual change in the female lifestyle, for example the increase number of female smokers and the exposure to professional stresses. There is limited literature about the relationship between CH and female hormonal changes such as pregnancy, menstruation, or the use of oral contraceptives. Ekblom and Waldenlind<sup>7</sup> studied a population of 249 CH, 34 of which were women. They were compared with a control population of 99 consecutive women with migraine. Twenty-five of the 26 fertile female CH patients stated that their headaches had no relation to menstrual periods. Eight had had their pregnancies since the onset of CH. Six of them experienced remission of their headaches during pregnancy. A lower parity rate was observed in the CH female group. Furthermore, the number of childbirths was particularly lower with those who had suffered from CH as nulliparae in comparison with those who contracted CH after previous pregnancies. The authors suggested some explanations, not yet demonstrated. First, CH female patients may show a reduction in sexual activities because of pain. Second, the patients may be reluctant to have a baby as they might well be unable to take care of a child while having a cluster. Because this was a retrospective study and the numbers of CH cases were limited, such hypothesis should be verified by further prospective studies. Manzoni et al<sup>8</sup> studied 82 females suffering from CH with respect to clinical findings and reproductive history, and the results were compared with those of various control groups. The data seemed to confirm a hypofertility trend,

mostly after onset of CH, which previously had been noted by other authors. Recently, Van Vliet et al<sup>9</sup> in the Netherlands studied 224 cases of women with CH and tried to explore the influence of hormonal changes in CH. They found that menstruation, use of oral contraceptives, pregnancy, and menopause had a much smaller influence on CH attacks than in migraine, but confirmed that women who had suffered from CH before the first pregnancy had significantly ( $P < .01$ ) fewer children than those who already had children at the time of their first CH attack. As in Ekblom and Waldenlind's work, this study was retrospective; the results were obtained with a standardized, somewhat suggestive questionnaire, the answers being stereotyped. The implication of progesterone in CH had been recently documented with a case report by Gaul et al.<sup>10</sup> In that case, repeated progesterone injections during in vitro fertilization treatment provoked typical CH and suggested the possible implication of sexual hormone in CH. To date available studies evaluating the relation between hormonal changes in women and CH remain limited. Therefore, large prospective works appear necessary to improve our knowledge, especially as the prevalence of CH in females seems to increase according to various authors.<sup>2,5</sup>

Attack treatments or prophylactic treatments in CH during pregnancy have been poorly documented and we did not find extensive works studying this specific aspect. In 2006, an EFNS task force proposed guidelines for the treatment of CH but there was no specific mention of pregnancy. In this condition, data now available in literature on fetal toxicity and pharmacokinetic on drugs suggested some proposition. Inhalation of pure oxygen via a nonbreathing facial mask could be suggested as a first-line treatment in attacks because there are no obvious contraindications.<sup>11,12</sup> Therefore, this treatment could be suitable during pregnancy even if definitive data are lacking.<sup>9</sup> But when this treatment fails as it did in our case, sumatriptan, selective 5 HT<sub>1B</sub>/1D receptor agonists could be discussed. Sumatriptan has been largely studied and used over the last 15 years in migraine as well as in CH, in its subcutaneous form. Its safety during pregnancy has been largely documented particularly in the first trimester.<sup>13</sup> Loder<sup>14</sup> considered the

available data in 2003 as sufficient to rule out major problems if this drug is accidentally given during pregnancy. However, there is as of yet no positive recommendation on its use during pregnancy and caution is still recommended because there has been no controlled study of this drug in this condition. Because of this unclear situation, we did not use sumatriptan in our case. Other triptans show the same lack of trustable study; therefore, we do not consider them an alternative. Classified as grade B level recommendation in EFNS guidelines, local intranasal application of lidocaine is an interesting approach. It induces anesthesia of the pterygopalatine fossa region with a rapid relief, without significant general side effects.<sup>3</sup> In our case, the block appeared a simple and well-tolerated procedure, allowing a rapid relief of pain. An alternative could be the greater occipital nerve (GON) block, which has shown good efficacy in CH as a transitional preventative and in some instances may break a cluster cycle. Peres et al<sup>15</sup> treated 14 CH patients with GON block and reported 28.5% of good response and 35.7% of moderate response; the treatment was well-tolerated with no adverse events. Prophylactic drugs such as verapamil or corticosteroids are not formally contraindicated during pregnancy but maternal and fetal potential side effects outweigh the potential benefits. Side effects of verapamil may include asthenia, bradycardia, lower limb edema, or myocardial rhythmic abnormalities with potential consequences during pregnancy.<sup>3</sup> Similarly, steroids can induce various complications such as hypertension, diabetes mellitus, or facilitate infection. In our case and in accordance with gynecologists and pediatricians, a short course with a low dose of corticosteroids was given without consequence on the pregnancy, the delivery, or the baby. Other prophylactic drugs were not discussed because of the lack of definite innocuity in pregnancy.<sup>3</sup>

This case report underlines the importance of suitable guidelines for treatment of CH in pregnancy. As a first-line acute treatment, we suggest oxygen therapy. In case of resistance, intranasal application of a local anesthetic seems a suitable alternative, especially as, to date, there is no reported toxicity. GON blockade could also be considered in this population. At present, we cannot suggest a safe preventative

treatment for CH during pregnancy, and further discussion on this topic is essential for this distinct headache population. Furthermore, we believe that in most cases, a multidisciplinary consensus is essential to fit the most effective and safest treatment.

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