Clinical Reports

Peripartum management of a patient with Isaacs' syndrome

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Purpose: To describe the peripartum management of a patient with Isaacs' syndrome with specific reference to the anaesthetic implications of the disease process. Associated medical problems included obesity, pregnancy induced hypertension and a difficult airway.

Clinical features: This 30-yr-old gravida V para 0 woman presented to the anaesthesia consultation clinic at 37-wk gestation to discuss pain relief options for labour and delivery. She had a history of Isaacs' syndrome (a peripheral motor neuron disorder), congenital heart disease (ASD and VSD), treated Hashimotos thyroiditis, obesity and a family history of haemachromatosis. On the day of consultation, she was hypertensive and peripheral oedema was noted. Her urine showed trace protein. Four days later, she presented to the labour suite and her cervix was 9 cm dilated. An epidural anaesthetic was given without difficulty and she had an uneventful labour and delivery course. There were no subsequent neurological complications.

Conclusion: Isaacs' syndrome is an extremely rare peripheral motor neuron disorder. This patient was successfully managed with epidural analgesia for labour and delivered a healthy child with no congenital anomalies.

Objectif : Décrire la ligne de conduite adoptée à la période périgravidique chez une patiente affligée du syndrome d'Isaacs en mettant l'accent sur les répercussions potentielles du mécanisme pathologique sur l'anesthésie. Les problèmes médicaux associés incluaient l'obésité, la grossesse, l'hypertension gravidique et une difficulté d'accès aux voies aériennes.

Éléments cliniques : Cette patiente de 30 ans gravida V para 0 s'est présentée à la clinique de consultation anesthésique à la 37e semaine de gestation dans le but de discuter des méthodes de soulagement de la douleur pendant le travail et l'accouchement. Affligée du syndrome d'Isaacs (une affection du neurone moteur périphérique), elle souffrait aussi d'une maladie cardiaque congénitale (CIA et CIV), d'une thyroïdite d'Hashimoto traitée, d'obésité et avait des antécédents familiaux d'hémochromatose. Le jour de la consultation, elle était hypertendue et présentait un oedème périphérique. Son urine montrait des traces d'albumine. Quatre jours plus tard, elle était en travail avec une dilatation de 9 cm. Une anesthésie épidurale lui a été administrée sans problèmes et son travail ainsi que son accouchement se sont déroulés sans incidents. Il n'y a pas eu de complications neurologiques subséquentes.

Conclusion : Le syndrome d'Isaacs est une affection du neurone moteur périphérique extrêmement rare. La conduite adoptée pour le travail – une analgésie épidurale – a été couronnée de succès ; la patiente a accouché d'un enfant en bonne santé sans anomalies congénitales.

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ISAACS' syndrome, also known as Isaacs-Merten syndrome, Continuous Muscle Fibre Activity syndrome, Neuromyotonia or Quantal Squander, is an extremely rare peripheral motor neuron disorder. Involuntary continuous muscle fibre activity may cause stiffness, delayed relaxation in affected muscles and continuous fine vibrating muscle movements (myokymia).[1] Patients suffering from this disorder may also experience ataxia, staggering and reeling (titubation) and the inability to coordinate voluntary muscle movement. The exact aetiology of the disease is unknown, but autoantibodies to peripheral nerve K^+ channels may be causative.[2]

Diagnosis is based on history, physical findings, and increased concentrations of homovanillic acid and 5-hydroxyindoleacetic acid in the cerebrospinal fluid (CSF). Electromyographic studies demonstrate doublet, triplet or multiplet single unit discharges with a high intraburst frequency.[2] Treatment options include phenytoin, low dose acetazolamide, or carbamazepine which may inhibit the abnormal discharges.[3] Plasma exchange has also been used in cases resistant to pharmacologic therapy.[2]

Case report

A 30-yr-old woman presented to the Anaesthesia Consultation Clinic to discuss analgesia options for labour and delivery. She was a gravida V para 0 woman at 37 3/7-wk gestation. She had a past history of Hashimotos thyroiditis and a congenital ASD and VSD. Both of these defects closed spontaneously by the age of five years and repeat echocardiograms revealed no cardiac anomalies. The patient had four fetal losses associated with a cluster of fetal anomalies including bilateral renal agenesis, mild micrognathia, facial asymmetry and joint contractures. Before the current pregnancy she began taking 0.5 mg folic acid a day to decrease the chance of a fetal neural tube defect.

Isaacs' syndrome

At 14 yr, the patient began to experience problems walking, forcing her to walk on the outside edges of her feet. She developed muscle fasciculations that ascended to involve her hips to the point where she was unable to walk without first, a cane, then crutches. Associated symptoms included muscle spasms of her hands and difficulty in relaxing after forming a fist. At one point she was noted to have bilateral foot drop. The initial diagnosis was arthritis and various therapy yielded no improvement. Five years after her symptoms began, the diagnosis of Isaacs' syndrome was made and the patient began phenytoin therapy. After eight months, this was discontinued due to persistence of symptoms as well as nausea and vomiting. Therapy with carbamazepine was initiated. Within three days, her symptoms disappeared and she was able to walk. She had been asymptomatic for 11 years except for two occasions when the carbamazepine dosage was decreased due to pregnancy.

She had had general anaesthesia for wisdom teeth removal, tonsillectomy and D & Cs without untoward effects. Unfortunately, the details of the anaesthetic agents used, were unavailable. There were no problems related to anaesthesia in members of her family who had received general anaesthesia. Her family history was negative for malignant hyperthermia and Isaacs' syndrome. At the time of consultation, she had no neurological symptoms or signs. Her medications included 800 mg carbamazepine a day and 0.5 mg folic acid a day.

She had a family history of ischaemic heart disease and her father died from haemochromatosis. She was obese, pre-pregnancy weight 114 kg and present weight 121 kg. On the day of her anaesthesia consultation she was found to have an elevated blood pressure (150/100 mmHg), peripheral pedal oedema and a trace of protein in her urine. The remainder of her history was unremarkable.

Physical examination revealed an obese female. Her blood pressure was 150/90 mmHg, heart rate 90 bpm. She was 165 cm tall and weighed 121 kg. There were no abnormalities of her cervical spine or temperomandibular joint. She had good mouth opening but pharyngeal visualization was limited and classed as a Mallampatti III. The remainder of her physical examination was normal. There were no neurological deficits, sensory or motor and her reflexes were equal and normal bilaterally.

Available options for labour and delivery analgesia/anaesthesia were discussed with the patient. The considerable advantages of early placement of an epidural catheter which could be used for both labour analgesia and anaesthesia for an urgent or emergency Caesarean section were explained. She fully understood the discussion and wished to receive epidural analgesia for pain relief in labour.

The patient presented to the labour triage unit four days later complaining of painful contractions and bloody vaginal discharge. On examination, the cervix was found to be 9 cm dilated with bulging membranes but a high presenting part. She was immediately transferred to the delivery room. Her blood pressure on admission was 140/90 mmHg. A coagulation screen was normal with a platelet count of $320 \times 10^9 \cdot L^{-1}$ Using sterile technique, in the sitting position, an epidural catheter was placed without incident on the

first attempt using the loss of resistance to air technique. She was given a test dose of 3 ml lidocaine 1.5% followed by incremental doses of bupivacaine 0.125% with 10 μg sufentanil to a total of 12 ml. One and a half hours later, she complained of rectal pressure and began to push. She delivered a healthy 3480 g male infant 20 min later. Apgar scores were 9 at one and five minutes. There were no congenital anomalies. The patient had an uneventful postpartum course and was discharged home on the second postpartum day.

Discussion

Isaacs first described two cases of continuous muscle-fibre activity in 1961.[4] Symptoms included muscle fasciculations, stiffness which increased with voluntary muscle contraction, sweating, weakness and the inability to walk. Electromyographic studies were performed and spontaneous discharge was found to persist despite a brachial plexus nerve block and general anaesthesia with pentothal. Blocking and depolarization of the motor end-plate with *d*-tubocurarine and succinylcholine abolished the spontaneous discharge resulting in muscle relaxation. There was marked sensitivity at the motor end-plate to *d*-tubocurarine as assessed by ulnar nerve stimulation. Neostigmine did overcome the block but the response was slow. The aetiology at this time was felt to be an acquired defect at the level of the terminal network of the lower motor neuron resulting in an abnormal release of acetylcholine.[4]

Approximately 60 cases of Isaacs' syndrome have been reported to date.[5] Electromyographic studies are characterized by doublet, triplet or multiplet single unit discharges with a high intraburst frequency. The frequency of the bursts may be irregular and fibrillation potentials and fasciculations are often present.[2] The abnormal activity persists during sleep and general anaesthesia and may be unaffected, reduced or abolished by peripheral nerve block.[2,6,7] Epidural anaesthesia completely blocked the abnormal discharge pattern in one case as did spinal anaesthesia in a second case.[7,8] Due to the variable response with peripheral nerve blockade, it has been suggested that the neuromyotonic discharges may be generated from different sites, terminal and proximal, perhaps including the anterior horn cell itself.

Although the aetiology of the disease is unknown, several clinical reports have alluded to the involvement of the immune system. There has been an association with thymoma, myasthenia gravis, rheumatoid arthritis and the Eaton-Lambert syndrome.[2,5,9] Elevated titres of anti-thyroid antibodies were found in one case.[2] Clinical evidence from five case studies point to antibody-mediated autoimmunity as a cause, specifically autoantibodies to peripheral nerve K^+ channels.[2] The patient in this report had a history of Hashimotos thyroiditis as well as recurrent fetal losses which in itself may have an autoimmune cause. She had a normal antinuclear factor test as well as an anti-RO antibody. No other antibody testing was done.

Isaacs, in his original paper, described the abolition of abnormal muscle activity with the anticonvulsant drug sodium hydantoinate which acts by increasing the sodium pumping action of nerve and muscle tissue.[4] Phenytoin continues as a first line treatment today.[3,6] Other treatment regimens include carbamazepine and acetazolamide.[10,11] Dantrolene has had variable results.[10] Plasma exchange has also been used in the treatment of Isaacs' syndrome but further evaluation of this treatment modality is warranted.[2,12]

Isaacs' syndrome is a rare peripheral motor neuron disorder which may have an auto-immune aetiology. The abnormal discharges are abolished by succinylcholine and there is an increased sensitivity to *d*-tubocurarine. Isolated case reports have demonstrated that abnormal EMG findings disappear with epidural and spinal anaesthesia. The patient in this case report was asymptomatic. There were no untoward effects from the administration of an epidural anaesthetic for labour and delivery.

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