Case Report

Management of a Multiple Endocrine Neoplasia 1 Patient in Pregnancy

Deepanshu Dhiman, Summit Dev Bloria, Pranshuta Sabharwal, Rashi Sarna, Rajeev Chauhan

Department of Anaesthesia, PGIMER, Chandigarh, India

Abstract

Multiple endocrine neoplasia (MEN) syndrome has rarely been reported during pregnancy. The multiple manifestations of the syndrome along with the normal body changes associated with pregnancy can prove to be difficult to manage. We describe our experience of the diagnosis and management of MEN1 syndrome in a pregnant female.

Keywords: *In vitro fertilization, multiple endocrine neoplasia 1, pregnancy*

Introduction

Multiple endocrine neoplasia 1 (MEN) 1 is an autosomal dominant disorder with a prevalence of 0.25%.[1] It is characterized by the presence of tumors in at least two of the following three organs: the parathyroids, pancreatic islets, and anterior pituitary. In addition, there is an increased incidence of carcinoid tumors, adrenal adenomas, and other nonendocrine features, including the development of angiofibroma, lipomas, and ependymomas in MEN1 patients.[2]

The present literature is evidenced by very few case reports on MEN 1 syndrome during pregnancy.[3,4] Although there are no clear guidelines for medical or anesthetic management of these patients, these case reports direct toward an interdisciplinary management of such patients. We present a case report on the medical and anesthetic management of a primigravida with precious pregnancy (conceived after *in vitro* fertilization [IVF]), diagnosed with MEN 1 syndrome during the antenatal period and later posted for an elective cesarean section.

Case Report

A 37-year-old healthy primigravida, post-IVF conception for unexplained primary infertility presented at 25 weeks of gestation with complaints of epigastric pain (radiating to back) and multiple episodes of vomiting. The complaints were investigated and the patient was diagnosed to be a case of acute pancreatitis on the basis of abdominal ultrasound (USG) findings and raised serum amylase (372 IU/L) and lipase levels (1082 IU/L). The other significant laboratory findings in the patient were leukocytosis (18,900/mm^3) and raised serum calcium levels (13 mg %). She was subsequently referred to our institute for further evaluation and follow-up for her pregnancy.

We reviewed the clinical history; examination and laboratory investigations of the patient. The patient had a history of renal stone disease in the past. There was no significant family history, the patient was nonalcoholic, and drug history was negative as well (except for iron and folate supplementation during pregnancy). We admitted the patient and ordered fresh blood investigations.

Her repeat serum calcium (14.3 mg%) and intact parathyroid hormones (PTHs) (263 pg/ml) were found to be raised while serum Vitamin D levels were normal. Following this, a magnetic resonance imaging (MRI) of the neck was done which showed an inferior (cystic) parathyroid adenoma. Hence, a diagnosis of primary hyperparathyroidism (PHP) was performed.

Furthermore, she started to have episodes of headaches, sweating, and sudden hunger. On one of such episodes, her sugar was checked and found to be 39 mg/dl. The hypoglycemia was found to be insulin-dependent, with the insulin of 10.6 mIU/ml and a c-Peptide of 2.19 ng/ml at a random blood sugar of 40 mg/dl indicating toward

Address for correspondence: Dr. Rajeev Chauhan, PGIMER, Chandigarh, India.
E-mail: dr.rajeevchauhan@gmail.com

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a possibility of insulinoma. Insulinoma was further confirmed using a 72 h starvation test. The patient became symptomatically hypoglycemic after 7 h of starvation with blood glucose levels of 37 mg/dl. The starvation test was then discontinued after taking blood samples for insulin and C-peptide levels; the insulin and C-peptide levels were found to be raised thus confirming the diagnosis of insulinoma.

We also performed an MRI of the head in the patient to rule out the presence of a pituitary tumor, which was normal. Serum insulin-like growth factor 1 and serum gastrin levels were also tested (to rule out other entero-pancreatic tumors) and were found to be within the normal limits.

On the basis of the presence of PHP and insulinoma, the patient was labeled to be suffering from MEN1. It was decided to manage the patient conservatively.

For the management of hypercalcemia, she was started on tablet cinacalcet 30 mg BD (a calcimimetic). For the treatment of hypoglycemia, she was advised of frequent meals with complex carbohydrates and injection octreotide. The fetal well-being was ensured throughout the hospital stay with ultrasonography and doppler. She was discharged at 29 weeks of gestation with an advice to continue octreotide, progesterone, and cinacalcet and follow-up every 4 weeks.

A month into treatment, her serum calcium levels were still high and USG guided alcohol ablation of the parathyroid adenoma was performed with 2 ml of absolute alcohol. Cystic fluid aspirate showed an intact parathyroid hormone (iPTH) of 3233 pg/ml. The calcium and iPTH values decreased subsequently.

On her regular follow-ups at 37 weeks of pregnancy, the patient was found to have blood pressure of >140/100 mmHg, she was started on tablet labetalol 100 mg twice daily and was admitted for induction and delivery in view of hypertension.

After a trial of failed induction of labor, elective lower segment cesarian section was considered. After a thorough preanesthetic evaluation and review of all recent investigations, including serum ionized calcium and blood glucose levels, we decided to administer spinal anesthesia.

Nil per oral (NPO) orders were strictly followed while hypoglycemia prevention done using 10% dextrose infusion in titrated doses and hourly blood glucose monitoring. The American Society of Anesthesiologists standard monitoring was placed. A subarachnoid block (SAB) was given under strict asepsis using 26 G Quinke's spinal with 7.5 mg of 0.5% bupivacaine dextrose and 25 μg of Fentanyl citrate. A sensory block for cold sensation was achieved till T4 dermatome. The procedure commenced and after the delivery of the baby, inj. Oxytocin 25 IU infusion was started. Intraoperative hemodynamics remained between 20% of the baseline. Intraoperative blood sugar was 139 mg/dl. The procedure lasted for 1 h and the patient was shifted to postanesthesia care unit. Hourly blood sugar monitoring was done postoperatively and orally allowed after 2 h of surgery. She gave birth to a healthy child weighing 3.2 kg, with an APGAR (Appearance,Pulse, Grimace, Activity, and Respiration) score of 10/10 at 5 min. The rest of her hospital stay was uneventful and she was attached to the endocrinology outpatient department after her discharge from the hospital for further management.

Discussion

MEN I syndrome comprises any of the two or more tumors of parathyroid, pituitary, and enteropancreatic origin. The patients with this syndrome can present at different age groups with a number of varying symptoms.[1] The present patient presented with pain abdomen and hypercalcemia, later on, the presence of insulin-dependent hypoglycemia helped in clinching the diagnosis of MEN 1 syndrome.

The medical management of the patient followed the recent guidelines laid down for the treatment of MEN 1 syndrome.[1] The patient was started on tablet cinacalacet for treatment of hyperparathyroidism. Cinacalcet directly lowers PTH levels by increasing the sensitivity of the calcium-sensing receptors to activation by extracellular calcium, resulting in the inhibition of PTH secretion. The reduction in PTH is associated with a concomitant decrease in serum calcium levels.

Previous case studies of asymptomatic women with PHP in pregnancy suggest a conservative approach with a eucalcemic diet, good hydration and regular monitoring of maternal blood tests and fetal growth can produce a good outcome for mother and baby. Surgery is recommended only in the postpartum period, although minimally invasive surgery with prior USG localization of parathyroid tissue is thought to be a safe option in pregnancy.

As medical management of hypercalcemia did not normalize calcium levels, ablation of the parathyroid adenoma was done in our patient.

The patient was also investigated for entero-gastrointestinal tumors when she was found to have recurrent episodes of hypoglycemia. The diagnosis of Insulinoma was confirmed using the 72 h starvation test in our patient, which is considered to be

the most reliable test for diagnosing insulinoma. As the hypoglycemia was insulin-dependent therefore, she was started on tablet octreotide and a carbohydrate-rich diet in order to avoid recurrent hypoglycemia. Although surgery is the first-line treatment for insulinoma, this patient was antenatal and had already passed her second trimester and therefore she was managed medically in form of treatment with octreotide. The patient did not have any other symptoms pertaining to other forms of tumor with rest all investigations within in a normal range.

The anesthetic plan was to completely evaluate her history, check all recent investigations, and monitor her blood sugar levels and maintain a euglycemic state and normal hemodynamics. As there were no contraindications for SAB, the patient was taken up for the surgery under regional anesthesia. Furthermore, general anesthesia might have concealed the symptoms of hypoglycemia. The intraoperative concern was to manage hypoglycemic episodes and monitor both blood glucose and serum calcium levels intraoperatively as well as postoperatively. All this was done and the patient had an uneventful course both intraoperatively and postoperatively. In MEN 1 patients though, neuraxial anesthesia should be administered only after ruling out raised intracranial pressure due to the presence of pituitary tumors.

Although none of the patient's relatives gave any similar history, they were advised to get themselves screened in view of the autosomal dominant nature of the syndrome. Furthermore, the patient was advised to remain in regular follow-up with the endocrinology department. Another consideration in this patient was the safety of the drugs used for MEN1 management considering the pregnant status of the patient. Octreotide comes under Food and Drug Administration (FDA) pregnancy category B drug (No risk in nonhuman studies) while cinacalcet comes under FDA pregnancy category C (Animal reproduction studies have shown an adverse effect on the fetus and there are no studies in humans, but potential benefits may warrant the use of the drug in pregnant women despite potential risks).

The present case report thus highlights the importance of an interdisciplinary management of patients with MEN 1 syndrome. The early recognition of the signs and symptoms of the syndrome is necessary to avoid any untoward complications both to the mother and growing fetus. Anesthetic management should be based on the clinical scenarios with complete knowledge of the presenting syndrome and its associated complications. The required monitoring and choice of anesthetic technique which best suits the patient must be always be a priority.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Thakker RV. Multiple endocrine neoplasia type 1 (MEN1). In: Robertson RP, Thakker RV, editors. Translational Endocrinology and Metabolism. Vol. 2. Chevy Chase, MD: The Endocrine Society; 2011. p. 13-44.
2. Brandi ML, Gagel RF, Angeli A, Bilezikian JP, Beck-Peccoz P, Bordi C, *et al*. Guidelines for diagnosis and therapy of MEN type 1 and type 2. J Clin Endocrinol Metab 2001;86:5658-71.
3. Mistry M, Gupta M, Kaler M. Pregnancy in multiple endocrine neoplasia type 1 equals multiple complications. Obstet Med 2014;7:123-5.
4. Daglar HK, Kirbas A, Biberoglu E, Laleli B, Danisman N. Management of a multiple endocrine neoplasia type 1 during pregnancy: A case report and review of the literature. J Exp Ther Oncol 2016;11:217-20.