World J Surg (2010) 34:1811–1816
DOI 10.1007/s00268-010-0569-2

World Journal of Surgery

Hyperparathyroidism in Pregnancy: Options for Localization and Surgical Therapy

Todd P. W. McMullen · Diana L. Learoyd · David C. Williams · Mark S. Sywak · Stan B. Sidhu · Leigh W. Delbridge

Published online: 13 April 2010

Abstract
Background Hyperparathyroidism in pregnancy is a threat to the health of both mother and fetus. The mothers suffer commonly from nephrolithiasis, hyperemesis, or even hypercalcemic crisis. Untreated disease will commonly complicate fetal development and fetal death is a significant risk. Treatment options, including medical and surgical therapy, are debated in the literature.
Methods This is a case series comprising seven patients with primary hyperparathyroidism in pregnancy. Data collected included symptoms at diagnosis, biochemical abnormalities, pathologic findings, treatment regimes, and subsequent maternal and fetal outcomes.
Results Seven women, aged 20 to 39 years, presented with hyperparathyroidism during pregnancy. The earliest presented at 8 weeks and the latest at 38 weeks. Four of seven patients experienced renal calculi. Calcium levels were 2.7–3.5 mmol/l. All were found to have solitary parathyroid adenomas, of which two were in ectopic locations. Fetal complications included three preterm deliveries and one fetal death with no cases of neonatal tetany. Maternal and fetal complications could not be predicted based on duration or severity of hypercalcemia. Three patients were treated during pregnancy with surgery, and two of these had ectopic glands that required reoperations with a novel approach using Tc-99m sestamibi scanning during pregnancy to assist in localizing the abnormal gland. Four cases were treated postpartum with a combination of open and minimally invasive approaches after localization. No operative complications or fetal loss related to surgery were observed in this cohort.
Conclusions Primary hyperparathyroidism in pregnancy represents a significant risk for maternal and fetal complications that cannot be predicted by duration of symptoms or serum calcium levels. Surgical treatment should be considered early, and a minimally invasive approach with ultrasound is best suited to mitigating risk to mother and fetus. Equally important, Tc-99m sestamibi imaging may be used safely for localization of the parathyroids after negative cervical explorations.

Keywords Endocrine · Head and Neck

Introduction

Primary hyperparathyroidism in pregnant women presents a threat to the health of both mother and fetus [1–6]. Often presenting with subtle and nonspecific findings, the reported prevalence of hyperparathyroidism in pregnancy varies from 0.15 to 1.4% [5, 7]. The most common symptoms that prompt investigation in the general population, including fatigue, lethargy, and proximal muscle weakness, may be dismissed by patient or physician in pregnant women [7]. A relative state of maternal hypocalcemia with high fetal calcium requirements and increased maternal urinary excretion also may mask the presence of this disease and

T. P. W. McMullen (✉) · D. C. Williams
Department of Surgery 2D, Walter C. Mackenzie Health Science Centre, 8440-112 Street, Edmonton, AB T6G 2B7, Canada
e-mail: todd.mcmullen@ualberta.net

D. L. Learoyd
Department of Endocrinology, Royal North Shore Hospital, St Leonards, University of Sydney, Sydney, NSW, Australia

M. S. Sywak · S. B. Sidhu · L. W. Delbridge
Department of Surgery, Royal North Shore Hospital, St Leonards, University of Sydney Endocrine Surgical Unit, Sydney, NSW, Australia

thus account for the wide variations in reported prevalence [7, 8]. In the mother, untreated parathyroid disease can lead to nephrolithiasis, hyperemesis, or potentially life-threatening complications, including hypercalcemic crisis and pancreatitis [5, 7, 9]. Fetal complications, which may occur in up to 80% of fetuses in untreated mothers, include intrauterine growth retardation, low birth weight, preterm delivery, intrauterine fetal demise, or postpartum neonatal tetany [5, 10–13].

A solitary parathyroid adenoma accounts for more than 85% of all cases of primary hyperparathyroidism in pregnancy [5–7]. The dilemma for most physicians is how to balance the risks of medical treatment versus surgical removal of the adenoma at different stages of pregnancy. Conservative medical treatment typically consists of low calcium diet, high fluid intake, and oral phosphates. Pharmacologic options are limited in pregnancy because the use of calcitonin and bisphosphonate therapy to lower serum calcium is not advised [7, 14–16]. When surgery is considered for hyperparathyroidism in pregnancy, the approach will depend on whether the diseased gland can be localized preoperatively [17, 18]. If localized by ultrasound, the surgeon may choose a minimally invasive incision under a local anesthetic, but the chance of success as outlined by the Kebebew score is likely improved in more advanced disease with calcium levels >3 mmol/l and PTH values at least two times normal [18]. The second option is a four gland open neck exploration performed in the second trimester. Preoperative localization with Tc-99m sestamibi is not typically offered in pregnancy [5, 7, 17–21]. The timing of surgery is debated in the literature as to whether surgery can be delayed until postpartum in "mild" cases of hyperparathyroidism with no symptoms and calcium levels <3 mmol/l. Treatment is typically avoided in pregnancy due to concern for fetal outcomes. The inability to utilize Tc-99m sestamibi scans to localize hyperfunctioning glands not identified by ultrasound also may encourage physicians to delay surgical treatment until after delivery, thus allowing for a minimally invasive approach [22–26].

Recent reviews of the different treatment options for primary hyperparathyroidism in pregnancy advocate disparate views. Conservative therapy has been suggested as the best option, bridging patients to surgery postpartum [5–7]. Others advocate surgical treatment, even in the third trimester providing that the patient's calcium levels exceed 3 mmol/l or when patients are experiencing symptoms [7, 27, 28]. No prospective data are available and many reports are typically limited to the experience of one to three cases. In one of the largest reviews in the literature, Kelly found that conservative therapy through pregnancy resulted in significant maternal complications as well a significant incidence of neonatal tetany at term [5]. Moreover, when treated surgically, the overall neonatal complication rate is much lower than that documented for conservative therapy, at 10–20% [5, 7]. There are virtually no reports on the surgical management of ectopic glands or persistent disease and the timing for surgery in pregnancy remains a debated issue [29, 30]. In this report, we review seven cases of primary hyperparathyroidism in pregnancy and discuss the role of parathyroid localization and parathyroid surgery in pregnant women.

Patients and methods

This is a case series for the years 1992 to 2007 for surgical cases for hyperparathyroidism in pregnancy. The New South Wales Health Human Research Ethics Committee and the University of Alberta Health Ethics Review Board approved the research protocol. All patients gave consent to the acquisition and storage of such data for research purposes. Patient demographics, presentation, biochemistry, imaging, and pathology results were collected as well as fetal outcomes. Diagnosis of hyperparathyroidism was made on the basis of biochemical determination of elevated calcium levels and inappropriately nonsuppressed PTH levels. Data were obtained from the University of Sydney Endocrine Surgical Unit and University of Alberta medical records database. In all cases an endocrinologist, obstetrician, and surgeon were consulted in patient management. When performed surgery consisted of a traditional four gland exploration of parathyroid glands or a directed, minimally invasive procedure using preoperative ultrasound and Tc-99m sestamibi scans to localize the parathyroid adenoma. All pathology results were reviewed to confirm histologic diagnosis of parathyroid adenoma.

Results

The case series sampled the surgical cases of four surgeons during a 15-year period in which 3,395 patients were treated for primary hyperparathyroidism. During this timeframe, seven women, varying from 20 to 39 years of age, presented with primary hyperparathyroidism. A summary of the demographics, patient symptoms, and complications as well as the clinical biochemistry is shown in Table 1. The earliest diagnosis was at 8 weeks with the latest at 38 weeks, and there did not seem to be a predisposition in relation to trimester. All of the cases presented as an incidental finding or as part of the workup for hypertension or renal calculi. The levels of serum calcium in four of the cases exceeded 3.0 mmol/l and PTH values were all significantly elevated, in one case more than five times normal (Table 1). Urine calcium determinations

Table 1 Patient demographics and clinical biochemistry

Gestation (wk)	Symptoms	Serum calcium (mmol/l) (2.1–2.5[a])	PTH (pmol/l) (1.1–6.8[a])	Fetal outcome	Surgical treatment
8	Renal calculi	2.7	12	Fetal demise	Postpartum: four gland exploration
20		3.2	13	Preterm labor	Postpartum: MIP
34		2.7	10	Preterm labor	Postpartum: MIP
38	Renal calculi	3.1	40	Preterm labor	Postpartum: two surgical attempts, second with Tc-99m localization
10	Renal calculi	3.5	25		Second trimester: two surgical attempts, second with Tc-99m localization
21		2.8	15		Second trimester: 4-gland exploration
23	Renal calculi	3.2	19		Second trimester: two surgical attempts, second with Tc-99m localization

[a] Reference range

demonstrated increased fractional excretion of calcium. On detailed questioning, no patient had a previous endocrine tumor or family history of thyroid or parathyroid disease.

The surgical case histories follow two patterns, as outlined in Table 1. In four cases, patients had a diagnosis of primary hyperparathyroidism but surgical treatment was completed postpartum. In the first case the diagnosis was at 8 weeks, but before treatment could be initiated the patient suffered an unfortunate spontaneous abortion and a four gland exploration was completed postpartum. In the cases identified at 20 and 34 weeks, conservative therapy was attempted comprising hospital supervised hydration, low calcium diet, and oral phosphates. However, both cases had preterm delivery within 2 weeks of medical therapy. In these cases both fetuses were healthy and, although requiring critical care, neither infant suffered any sequelae related to elevated maternal calcium levels. The management in these cases was a minimally invasive parathyroidectomy after successful localization with ultrasound and Tc-99m sestamibi scans. The fourth case managed postpartum was a consequence of an emergent preterm delivery at 38 weeks of a healthy infant with normal calcium metabolism. The patient first had a four gland surgical exploration that failed. After ultrasound, CT and Tc-99m sestamibi scans she was found to have a thoracic parathyroid adenoma that was removed subsequently via a thoracotomy.

In the second set of cases, surgical therapy was mandated during pregnancy due to patient symptoms and high calcium levels. Also, one case (21 weeks), multiple previous lost pregnancies were thought possibly to be caused by unrecognized primary hyperparathyroidism and the patient requested early operative intervention. The patient had a successful open procedure in the second trimester (24 weeks) with biochemical cure and a normal fetal delivery at term. In the other two patients (10 and 23 weeks gestation), a standard four gland cervical exploration was completed in the second trimester—in one case by a surgeon outside this study. Despite a comprehensive exploration of all parathyroid-bearing areas in the neck, no abnormal parathyroid tissue was identified between the carotid bifurcation and the anterior mediastinum. The persistence of high calcium levels in the initial postoperative period prompted further attempts to localize the abnormal parathyroid tissue. In both cases, a parathyroid scan using Tc-99m sestamibi was performed with a CT scan of the neck and chest. In performing the sestamibi study, dosimetry was carefully calculated and a number of measures were adopted to reduce the radiation dose to the fetus, including a 50% reduction in the administered dose of Tc-99m sestamibi with a corresponding increase in scanning time, increased maternal hydration, and urinary catheterisation for 24 h after tracer administration. The combined techniques were able to localize adenomas concordantly in the mediastinum at the level of the aortic arch (10 weeks) and in the thymus (21 weeks). Figure 1 shows the parathyroid scan for the thoracic parathyroid adenoma. The thymic gland was removed through the neck and a thoracotomy removed the diseased gland in the mediastinal tumor, both demonstrating biochemical cure. After birth, there were no complications. In all cases, there was no evidence of neonatal tetany, hypocalcemia, or maldevelopment. All adenomas, between 95 mg and 2 g in size, were described pathologically as fat-depleted glands with nodular hyperplasia and trabecular architecture.

Discussion

This cohort, the largest single published series of primary hyperparathyroidism in pregnancy, demonstrates some important facets of the natural history of this disease. Consistent with previous reports, the majority of this cohort demonstrated symptoms, notably nephrolithiasis.

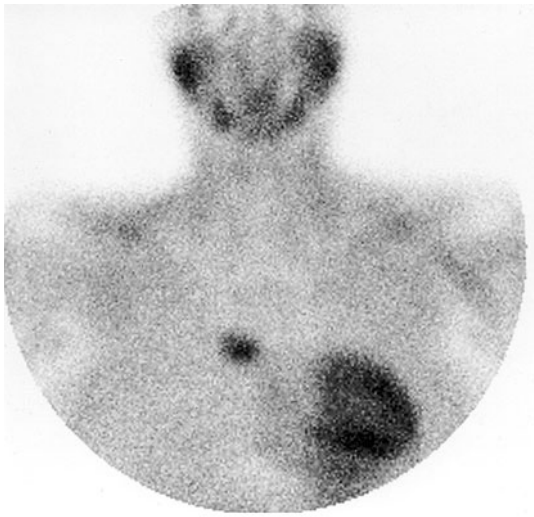

Fig. 1 Tc-99m sestamibi parathyroid scan demonstrating the mediastinal focus from where a parathyroid adenoma measuring 5 cm in diameter was removed

Hypertension also was seen in three of the cases but this can be attributed to a number of different causes other than hyperparathyroidism [5, 7]. Hyperemesis and other more severe, but less commonly reported complications, including pancreatitis and crisis hypercalcemia, were not seen [5, 7, 31]. In two cases subclinical hyperparathyroidism was thought to be a possible contributing factor in previous spontaneous abortions, but a lack of available data on calcium and PTH levels prevented confirmation. A shift in maternal calcium homeostasis artificially lowers calcium levels in pregnancy, which may have obscured the diagnosis in previous pregnancies [5, 32, 33]. We also note that the calcium levels vary significantly in our cohort, from 2.7 to 3.5 mmol/l, and that relatively mild hypercalcemia did not prevent or preclude maternal complications. Hyperparathyroidism was diagnosed with similar frequency in all trimesters. Three of the seven patients did not have symptoms and it was screening of serum calcium levels that led to the diagnosis. Thus, recognizing the limitations of a retrospective case series, we believe that the rate of subclinical disease may be significant as suggested by Schnatz and Curry [7]. Fetal complications observed in our study, including three preterm deliveries and a fetal demise in a total of seven pregnancies, mirror the high level of overall complications documented in previous studies, nearing 80% [5, 7, 34, 35]. However, neonatal tetany, a common complication in previous studies, was not seen in any of the infants postpartum. This possibly reflects the relatively short exposure of the fetus to hypercalcemia because all the mothers delivered or were surgically treated within 6 weeks of diagnosis as opposed to previous cohorts where the hypercalcemia was treated medically through pregnancy. There is no cohort that has been followed at our institutions that was treated medically; thus, it is not possible to truly compare outcomes. However, in previous historical cohorts, 37% had neonatal tetany in patients treated medically with an overall neonatal mortality rate nearing one in five [5]. It also is important to note that the fetal complications that we observed—notably preterm delivery and fetal demise—can be the result of many other factors, including genetic abnormalities.

The optimal management of hyperparathyroidism in pregnancy has been debated in the literature, especially in cases diagnosed in the first or third trimester. Previous studies have attempted to stratify disease severity and present a choice of medical or surgical therapy as reviewed by Schnatz and Curry [7]. Conservative therapy, considered for "mild" hypercalcemia of varying definitions, is limited to hydration and oral phosphates and may require a long period of close medical attention with a significant risk of preterm delivery. Advocates of conservative therapy quote the surgical dangers of operating during the first, third, and even second trimester with concerns for the teratogenic effects of general anesthesia and the risk of triggering preterm labor. For those patients with symptoms and/or signs of renal or bone disease uncontrolled by therapy, or for calcium levels in excess of 3 mmol/l, urgent control is advocated with the addition of diuretics and the consideration of surgery, preferably after the first trimester. Based on our results, we believe that this approach to hyperparathyroidism in pregnancy is flawed for two reasons. First, it is not possible to predict complications, in maternal or fetal terms, based on calcium levels. In the present study attempts at conservative therapy in two cases were unsuccessful even when mild hypercalcemia was present (calcium 2.7 mmol/l). Fetal complications soon after diagnosis led to the decision for surgery. Further review of the literature confirmed that both maternal and fetal complications are difficult to predict based on maternal serum calcium levels [5, 7]. Previous studies examining medical therapy demonstrated a significant increased risk of complications to both mother and fetus, in up to 80% of cases overall. Moreover, options for pharmacologic lowering of calcium levels using bisphosphonates or calcitonin, class X and B drugs, are not considered safe, especially during early pregnancy or for long-term therapy [15, 36–38]. Second, the argument that surgery should be reserved for advanced or symptomatic disease is based on overestimated dangers of the teratogenic effects of general anesthesia. Recent evidence suggests that the risks of surgery in the pregnant patient are much diminished compared with experience in a previous era of anesthesia [22–24, 39, 40]. Large cohorts examining nonobstetrical open and laparoscopic surgery during pregnancy have not shown an association with preterm labor, fetal loss, or teratogenicity [22–24]. Surgery also offers the

possibility of a definitive treatment, eliminating the risks of hypercalcemia, which clearly has a high morbidity as outlined in this and previous studies. In this cohort we observed no maternal or fetal complications relating to surgery. Consideration of surgery in the second trimester of pregnancy, the safest time to proceed, may be warranted in select cases but patients early or late in pregnancy should not be denied consideration of surgery. We suggest that surgical treatment should be considered from the outset, mindful of the stage of gestation, the presence or absence of symptoms, and patient preference.

In pregnancy surgical choices include both minimally invasive parathyroidectomy (MIP) and the standard four gland exploration. MIP success relies on preoperative localization through ultrasound or Tc-99m sestamibi, or both. Accuracy rates vary for each technique and local expertise is an important part of the success for either choice [18, 19]. In cases where ultrasound identifies an abnormal gland, MIP may be used with a local anesthetic to minimize impact on mother and fetus. This approach also may be utilized outside of the second trimester in cases deemed to be high risk for mother and fetus and has minimal impact on maternal and fetal physiology. However, it is understood in the general population that up to 15–20% of parathyroid glands may exist in ectopic locations, which likely applies to the pregnant population [41]. Thus, there will be a small but significant expected failure rate in pregnancy and the question arises of what to do under the circumstances. In this cohort there were two cases with ectopic glands not identified at the initial surgery that also were not amenable to removal via a cervical incision. In the situation of persistent hyperparathyroidism after surgical attempt at cure, the frequency of ectopic parathyroid glands is greatly increased and accurate preoperative localization using various imaging techniques seems to be mandatory to increase the chances of successful reoperation [41–43]. Intraoperative PTH measurements were not routine for this cohort; however, it should now be considered in cases with equivocal preoperative imaging [18].

If an experienced endocrine surgeon has performed the initial failed operation, then there is a high probability that the adenoma is in the mediastinum. Although 50% of such tumours can be removed through a neck incision, the patient must be aware of the possibility that a median sternotomy or a video-assisted thoracoscopic approach may be required for extirpation of the gland [43]. There have been only two reports of negative neck explorations during pregnancy, one of which required a median sternotomy to remove the abnormal parathyroid gland [4, 30]. The surgery was guided by MRI and CT scanning, which can utilize shielding, because it was believed that isotope imaging was absolutely contraindicated. However, CT and MRI alone are relatively insensitive in the detection of normally located and ectopic parathyroid adenomas. Uptake of Tc-99m sestamibi is observed in nearly 75% of these lesions and when coupled with MRI or CT, most abnormal gland(s) can be detected before reoperation [29]. The extent of fetal irradiation from maternal nuclear scanning must be addressed. In our two cases, the mothers were administered 400 MBq of Tc-99m sestamibi, which is a 50% reduction in radiation dose. This equates to a dose of 4.8 mGy to the fetus in case 1 (0.012 mGy/MBq at 12 weeks) and 3.36 mGy to the fetus in case 2 (0.0084 mGy/MBq at 24 weeks) [44]. The effects of fetal irradiation are divided into deterministic effects (caused by damage to a number of cells in tissues) and stochastic effects (caused by mutations in cells). At the levels of exposure in the above cases, the fetuses are not at risk for significant deterministic or stochastic effects, and thus, sestamibi scanning should be considered a valuable adjunct to localization in difficult cases [25].

Conclusions

This case series illustrates that hyperparathyroidism in pregnancy has significant maternal and fetal morbidity and that surgical intervention should be considered as an early therapeutic option, even in cases with only moderate calcium elevations. Minimally invasive surgery with preoperative ultrasound is a safe option. In cases with failed localization using ultrasound, Tc-99m sestamibi scanning during pregnancy can be performed safely provided that careful strategies reduce fetal irradiation are included.

References

1. Ludwig GD (1962) Hyperparathyroidism in relation to pregnancy. N Engl J Med 267:637–642
2. Wagner G, Transhol L, Melchior JC (1964) Hyperparathyroidism and pregnancy. Acta Endocrinol 47:549–564
3. Delmonico FL, Neer RM, Cosimi AB et al (1976) Hyperparathyroidism during pregnancy. Am J Surg 131:328–337
4. Salem R, Taylor S (1979) Hyperparathyroidism in pregnancy. Br J Surg 66:648–650
5. Kelly TR (1991) Primary hyperparathyroidism during pregnancy. Surgery 110:1028–1034
6. Carella M, Gossain V (1992) Hyperparathyroidism and pregnancy: case report and review. J Gen Intern Med 7:448–453
7. Schnatz PF, Curry SL (2002) Primary hyperparathyroidism in pregnancy: evidence-based management. Obstet Gynecol Surv 57:365–376
8. Hosking DJ (1996) Calcium homeostasis in pregnancy. Clin Endocrinol 45:1–6
9. Amaya Garcia M, Acosta Feria M, Soto Moreno A et al (2004) Primary hyperparathyroidism in pregnancy. Gynecol Endocrinol 19:111–114

10. Cemeroglu AP, Bober E, Buyukgebiz A (2001) Prolonged hypocalcemia in a 2 month-old boy unmasking maternal diagnosis of primary hyperparathyroidism. J Pediatr Endocrinol Metab 14:785–787
11. Ziegler R (2001) Hypercalcemic crisis. J Am Soc Nephrol 12:S3–S9
12. Clark D, Seeds JW, Cefalo RC (1981) Hyperparathyroid crisis and pregnancy. Am J Obstet Gynecol 140:840–842
13. Graham EM, Freedman LJ, Forouzan I (1998) Intrauterine growth retardation in a woman with primary hyperparathyroidism—a case report. J Repro Med 43:451–454
14. Montoro MN, Collea JV, Mestman JH (1980) Management of hyperparathyroidism in pregnancy with oral phosphate therapy. Obstet Gynecol 55:431–434
15. Briggs GG, Freeman RK, Yaffe SJ (1998) A reference guide to fetal and neonatal risk: drugs in pregnancy and lactation, 5th edn. Williams & Wilkins, Baltimore, pp 131–132
16. Levy HA, Pierucci L, Stroup P (1981) Oral phosphates treatment of hypercalcemia in pregnancy. J Med Soc NJ 78:113–115
17. Whitson BA, Broadie TA (2008) Preoperative ultrasound and nuclear medicine studies improve the accuracy in localization of adenoma in hyperparathyroidism. Surg Today 38:222–226
18. Kebebew E, Hwang J, Reiff E, Duh QY, Clark OH (2006) Predictors of single-gland vs. multigland parathyroid disease in primary hyperparathyroidism: a simple and accurate scoring model. Arch Surg 141:777–782
19. Mihai R, Simon D, Hellman P (2009) Imaging for primary hyperparathyroidism—an evidence-based analysis. Langenbecks Arch Surg 394:765–784
20. Hsieh YY, Chang CC, Tsai HD et al (1998) Primary hyperparathyroidism in pregnancy—report of 3 cases. Arch Gynecol Obstet 261:209–214
21. Kort KC, Schiller HJ, Numann PJ (1999) Hyperparathyroidism and pregnancy. Am J Surg 177:66–68
22. Duncan PG, Pope WD, Cohen MM et al (1986) Fetal risk of anesthesia and surgery during pregnancy. Anesthesiology 64:790–794
23. Visser BC, Glasgow RE, Mulvihill KK, Mulvihill SJ (2001) Safety and timing of nonobstetric abdominal surgery in pregnancy. Dig Surg 18:409–417
24. Jackson H, Granger S, Price R, Rollins M, Earle D, Richardson W, Fanelli R (2008) Diagnosis and laparoscopic treatment of surgical diseases during pregnancy: an evidence-based review. Surg Endosc 22:1917–1927
25. Steenvoorde P, Pauwels EK, Harding LK et al (1998) Diagnostic nuclear medicine and risk for the fetus. Eur J Nucl Med 25:193–199
26. Stalberg P, Delbridge L, van Heerden J et al (2007) Minimally invasive parathyroidectomy and thyroidectomy—current concepts. Surgeon 5:301–308
27. Gidiri M, Lindow SW, Masso EA, Philips K (2004) Parathyroidectomy in pregnancy for primary hyperparathyroidism with successful pregnancy outcome: a report of two pregnancies. J Obstet Gynaecol 24:318–319
28. Schnatz PF, Thaxton S (2005) Parathyroidectomy in the third trimester of pregnancy. Obstet Gynecol Surv 60:672–682
29. Pattou F, Huglo D, Proye C (1998) Radionuclide scanning in parathyroid diseases. Br J Surg 85:1605–1616
30. Rooney DP, Traub AI, Russell CF et al (1998) Cure of hyperparathyroidism in pregnancy by sternotomy and removal of a mediastinal parathyroid adenoma. Postgrad Med J 74:233–234
31. Iqbal N, Aldasouqi S, Peacock M et al (1999) Life-threatening hypercalcemia associated with primary hyperparathyroidism during pregnancy: case report and review of literature. Endocr Pract 5:337–342
32. Kristoffersson A, Dahlgren S, Lithner F et al (1985) Primary hyperparathyroidism in pregnancy. Surgery 97:326–330
33. Ammann P, Irion O, Gust J et al (1993) Alterations of calcium and phosphate metabolism in primary hyperparathyroidism during pregnancy. Acta Obstet Gynecol Scand 72:488–492
34. Peschgens T, Stollbrink-Peschgens C, Merz U et al (1994) Primary hyperparathyroidism and pregnancy. Aspects of neonatal morbidity. Z Geburtshilfe Perinatol 198:96–99
35. Cherry TA, Kauffman RP, Myles TD (2002) Primary hyperparathyroidism, hypercalcemic crisis and subsequent seizures occurring during pregnancy: a case report. J Matern Fetal Neonatal Med 12:349–352
36. Nudelman J, Deutsch A, Sternberg A et al (1984) The treatment of primary hyperparathyroidism during pregnancy. Br J Surg 71:217–218
37. Gelister JSK, Sanderson JD, Chapple CR et al (1989) Management of hyperparathyroidism in pregnancy. Br J Surg 76:1207–1208
38. Haenel LC 4th, Mayfield RK (2000) Primary hyperparathyroidism in a twin pregnancy and review of fetal/maternal calcium homeostasis. Am J Med Sci 319:191–194
39. Mazze RI, Kallen B (1989) Reproductive outcome after anesthesia and operation during pregnancy: a registry study of 5405 cases. Am J Obstet Gynecol 161:1178–1185
40. Cohen-Kerem R, Railton C, Oren D et al (2005) Pregnancy outcome following non-obstetric surgical intervention. Am J Surg 190:467–473
41. Phitayakorn R, McHenry CR (2006) Incidence and location of ectopic abnormal parathyroid glands. Am J Surg 191:418–423
42. Gough I (2006) Reoperative parathyroid surgery: the importance of ectopic location and multigland disease. ANZ J Surg 76:1048–1050
43. Russell CF, Edis AJ, Scholz DA, Van Heerden JA (1981) Mediastinal parathyroid tumors. Experience with 38 tumors requiring mediastinotomy for removal. Ann Surg 193:805–809
44. Russell JR, Stabin MG, Sparks RB (1997) Placental transfer of radiopharmaceuticals and dosimetry in pregnancy. Health Phys 73:756–769