A case of pulmonary carcinoid in pregnancy and review of carcinoid tumours in pregnancy

D Kevat^{1,2}, M Chen¹, D Wyld^{1,3}, N Fagermo¹ and K Lust¹

Abstract

Carcinoid tumours are rare slow growing tumours which arise from primitive neuroendocrine cells. The effect of the pregnant state on carcinoid tumours and vice versa remains unclear, as does the optimal management of carcinoid tumours during the pregnancy including labour. We report the rare case of a 36 year old primigravida woman with large bilateral pulmonary carcinoid tumours. The patient's disease was minimally symptomatic with no clinical suspicion of carcinoid syndrome. Under close observation, the pregnancy progressed well and the patient proceeded to a spontaneous vaginal delivery of a healthy child. We conduct the first literature review in 30 years of all reported cases in this area and make suggestions as to assessment and monitoring of cases of carcinoid during pregnancy.

Keywords

High-risk pregnancy, endocrinology, oncology

Date received: 6 October 2016; accepted: 28 November 2016

Case report

We report the case of the successful first pregnancy of a 36-year-old lady, notable for the presence of large bilateral pulmonary carcinoid. Five other reports of pulmonary carcinoid during pregnancy were found in the literature (1984–2014) with this case having more extensive disease and longer follow-up than other published reports in pregnancy.

The patient was referred to the obstetric medical department for co-management during her pregnancy. Carcinoid had been diagnosed incidentally three years earlier following an episode of pneumonia requiring inpatient treatment with intravenous antibiotics. Imaging had revealed a 4 cm mass in the left hilum and a 7 cm mass in the anterior right upper lobe causing complete obstruction of the bronchi and atelectasis (Figure 1). Bronchial washings stained positive for neuroendocrine markers (neuron-specific enolase (NSE), protein gene product 9.5 (PGP9.5), synaptophysin, chromogranin and CD56). Serum chromogranin A levels were significantly elevated at 62 U/L (reference range 0–17.2 U/L). There was no clinical suggestion of carcinoid syndrome and 5-hydroxyindoleacetic acid (5-HIAA) levels were in the normal range. Other than an elevated body mass index (BMI) and acne rosacea, her medical history was unremarkable.

Clinically the patient's disease had been minimally symptomatic from the time of diagnosis, with a single episode of haemoptysis and occasional central chest discomfort on deep inspiration. Cardio-thoracic review concluded that surgery was not desirable because the extent of disease would require both a left pneumonectomy and right upper lobe resection. Bi-annual imaging did not reveal growth of the pulmonary lesions or the development of metastases or the development of carcinoid syndrome. Somatostatin analogue therapy was not indicated in the absence of carcinoid syndrome/symptoms or disease progression. Potential treatment with lutecium octreotate was also considered but not indicated in the absence of evidence of disease progression.

The patient did not report any symptoms at the initial obstetric medical review at 10 weeks' gestation. On subsequent review at 15 weeks' gestation, the patient did report mild shortness of breath. Clinical assessment at the time was unremarkable. An echocardiogram was performed at 20 weeks to exclude a cardiac cause for dyspnoea and was normal with an ejection fraction 62%, chromogranin A levels at 26 weeks and 32 weeks' gestation were 76 and 89 U/L respectively

(reference range 0–17.2 U/L), compared with 68 U/L two years prior with the rise being considered consistent with pregnancy rather than disease progression. 5-hydroxyindoleacetic acid (5-HIAA) levels were measured at 26 weeks (23 µmol/24 h, reference range <40 µmol/24 h), and 32 weeks (43 µmol/24 h).

Respiratory function tests were initially declined by the patient as she felt her symptoms were not severe enough to warrant this investigation. They were performed prior to the delivery and were normal. The patient's preference was for vaginal delivery, which was supported by treating clinicians. Spontaneous rupture of membranes occurred at 36 weeks, with a vacuum delivery of a healthy female under epidural anaesthesia. An octreotide infusion was not used, as there was no prior evidence of hormonal secretion. The patient was observed in the intensive care unit for 24 h of monitoring and discharged home after 48 h. The patient has now been followed for 12 months post-partum and her disease remains stable. At her next assessment, magnetic resonance imaging (MRI) showed a 10 × 11 × 13 mm solitary liver lesion and was non-specific. Nuclear imaging with (fluorodopa (FDOPA) positron emission tomography scan (PET) was done and did not show abnormal uptake prompting a plan for observation. Further imaging at five years post-pregnancy showed very minimal progress of her disease and she remained asymptomatic.

Discussion

Carcinoid tumours are rare slow growing tumours which arise from primitive neuroendocrine cells. The most common sites for growth are the gastro-intestinal tract (66%) and the pulmonary system (10%). The incidence of the condition has been reported at approximately

¹Division of Medicine, Royal Brisbane and Women's Hospital, Brisbane, Australia

²School of Public Health, Monash University, Melbourne, Australia

³Faculty of Medicine, University of Queensland, Brisbane, Australia

Corresponding author:

D Kevat, Monash University School of Public Health, 99 Commercial Road, Melbourne 3004, Australia.

Email: dev.kevat@monash.edu

Figure 1. Computerised tomography image of chest prior to pregnancy, showing bilateral pulmonary carcinoid tumours.

2.0 to 3.0 per 100,000 using national registry data in Sweden, the United Kingdom and the United States, but may be rising.¹ The sex distribution is approximately equal and diagnosis is most often made in those aged between 55 and 65. Ten per cent of cases are associated with Multiple Endocrine Neoplasia – Type 1 (MEN1). MEN1 is an autosomal dominant disease characterized by parathyroid, pancreatic islet and anterior pituitary tumours, but may also cause other tumours such as adrenocortical and carcinoid tumours.²

Patients with pulmonary carcinoid may be asymptomatic and be incidentally diagnosed or present with obstructive pneumonia, pain, shortness of breath or cough. Less than 10% of patients with carcinoid tumours present or develop carcinoid syndrome which is associated with flushing, diarrhoea, vomiting, abdominal cramps and bronchoconstriction. Diagnosis in pregnancy can be made more challenging by attribution of symptoms such as shortness of breath and vomiting to physiological changes of pregnancy rather than pathology. Furthermore, normal pregnancy is associated with increased levels of the key carcinoid tumour marker chromogranin A, partly due to a contribution from the placenta, an organ with neuroendocrine activity.³ Decisions regarding imaging and biopsy procedures may be influenced by pregnancy, with a desire to minimise exposure to ionising radiation and procedural risk. In the absence of a histological sample, clinicians will have to consider all features of symptomatic, biochemical and radiological evidence in making a diagnosis.

Reported survival rates vary depend on whether the disease is localised or metastatic, with recent data reporting 80 to 95% survival at five years post-diagnosis.^{4–7} Surgical resection may be curative and is the treatment of choice where possible. Surgery (and required anaesthesia) during pregnancy is not associated with any increase in fetal malformations but is associated with an increase in fetal loss rates. Risks will vary according to trimester and type of surgery.⁸ Somatostatin analogues such as octreotide and lanreotide and, more rarely, external beam radiotherapy are also used depending on symptomatology and location. The former therapy is generally recommended in carcinoid syndrome with recent evidence suggesting growth restraint with longer time to progression.^{9,10} However, the safety of octreotide in pregnancy is yet to be established with conflicting case reports published with both poor and positive outcomes.^{11–13} Both the long- and short-acting forms cross the placental barrier, with data indicating short acting octreotide is found in lower concentrations in umbilical cord serum, amniotic fluid, and newborn serum. Hepatic artery embolisation and radiofrequency ablation (RFA) are potential options for patients with liver lesions, with a median survival of five years.¹⁴ Both treatments have been utilised in pregnancy, though RFA is best avoided during organogenesis.^{15,16} Treatments which are yet to develop a strong evidence base include inhibition of mTOR (mechanistic target of rapamycin) for non-functioning pancreatic, gastrointestinal and lung neuro-endocrine

Table 1. Summary of cases of carcinoid in pregnancy by site and other features.

Total cases	24
Appendix	7
Bronchial	4
Pancreas	5
Ovary	3
GIT	2
Pelvic	1
Trachea	1
Uterus	1
Cases with metastases:	7
outcomes:	Death: 1
Cases with hormone secretion	4
Outcomes:	Treatment for carcinoid syndrome: 2 Ceased octreotide: 1/4: carcinoid symptoms worsened Treated with octreotide: 1 case throughout 3 pregnancies, Treated with octreotide in labour: 1/4
Cases diagnosed before pregnancy	8
Outcomes:	Worsening of carcinoid symptoms during pregnancy: 1/8
Maternal survival	23/24
Fetal survival	17/23 1 ectopic 1 elective termination 2 spontaneous abortions: 10 weeks, 12 weeks 1 hysterectomy required at 13 weeks 1 stillbirth

tumours. Radioisotope therapy with lutecium octreotate has been used in patients with progressive disease and has a growing evidence base.^{17,18}

Durkin reviewed 18 cases of carcinoid during pregnancy in 1983,¹⁹ half of which were appendiceal carcinoids, and one case of pulmonary carcinoid which spontaneously regressed post-partum.²⁰ Intra-uterine death occurred in three cases – two had liver metastases, and the third had carcinoid tumour diagnosed in the body of the uterus. We located a further 26 other cases of carcinoid during pregnancy reported in the literature in the two decades since Durkin's report (1984–2014) (Table 2). Whilst appendiceal tumours remained common, they represented a smaller proportion of cases reported (7/26 cases). Bronchial (5) and pancreatic (5) sites of carcinoid tumour were also commonly reported in the last 20 years. Seven of the 24 cases had metastatic disease, and only four cases reported evidence of hormonal secretion (see Table 1).

The effect of carcinoid upon pregnancy is not clear. Given the array of hormones associated with carcinoids such as serotonin, adrenocorticotrophic hormone and cortisol, it is plausible that carcinoids could have an effect on smooth muscle (including uterine) function and placental growth. Whilst the effect of appendiceal carcinoids was not noted to be significant in Durkin's series, primary uterine and metastatic hepatic carcinoid disease were associated with fetal loss. In our review of the 26 subsequently reported cases, five cases resulted in fetal loss and two in early delivery. Jurica et al.'s report²¹ was of a small appendiceal tumour and a 21-week delivery of a 315g infant; Chlamydia infection was thought to be the cause of fetal demise rather than carcinoid tumour. Gilboa et al. reported a case of spontaneous first trimester miscarriage five days after surgery for an appendectomy which resulted in a histological diagnosis of carcinoid.²² In an ectopic pregnancy, Thompson and Hawe reported a case of dual pathology of acute inflammation and appendiceal carcinoid.²³ Poiana

Table 2. Clinical details of cases of carcinoïd in pregnancy.

Paper	Year	Pre-existing or discovered during pregnancy	Site and size	Secretory and/or metastatic?	Management during pregnancy	Maternal outcome	Fetal outcome	Immunohistochemistry staining	Patient symptoms
Dombrowski M et al ³²	1986	Diagnosed at 30 weeks of pregnancy	Ovary – left 10 × 7.5 × 7 cm	Nil	Patient presented in labour at 30 weeks. Primary caesarean section performed under spinal anaesthesia	Maternal survival	Fetal survival, 30 weeks Caesarean	Positive	Patient presented in labour at 30 weeks' gestation
Jurica JV et al ²¹	1989	Diagnosed at 21 weeks of pregnancy	Appendix – distal 2.0 cm	Nil	Appendectomy	Maternal survival	Terbutaline given to suppress labour before surgery, however, patient delivered a 315 g stillbirth (attributed to Chlamydia infection), 21 weeks Caesarean	Not mentioned	18-h history of fever; abdominal pain, uterine contraction
Gough IR et al ²⁵	1991	Diagnosed 22 months prior to pregnancy	Pancreas probable primary site	Multiple liver metastases, small bowel nodule, lymph nodes in hilum of left kidney	Had been treated prior to pregnancy with total colectomy. Tumour monitored by serial HPP estimations and liver ultrasound during pregnancy	Tumour did not progress during pregnancy. Patient remained asymptomatic post-partum	Healthy baby with normal delivery, 39 weeks – Vaginal delivery	Staining negative	Chronic constipation since childhood
Venu K et al ²⁶	1997	Diagnosed first trimester	Bronchial – right middle and lower bronchus	Nil – only mechanical obstruction	Laser therapy	Symptoms resolved, tumour recurred after two years.	Not specified, but fetal survival implied	Not specified	Productive cough, SOB, wheeze, chest pain, fever
Abraham P et al ¹⁸	2002	Diagnosed at 29 weeks' gestation	Pancreas	PTP-IP secretions causing hypercalcaemic crisis	Laparotomy and removal of pancreatic mass and splenectomy	Maternal survival, nil complications	29 weeks –Caesarean. Baby noted to have hypercalcaemia after birth (3.03 mmol/l) but became hypocalcaemic (1.59 mmol/l) over next two days and required calcium supplementation for a month. Mild asymmetric cerebral palsy at follow-up, attributed to prematurity	Staining negative	Altered consciousness, headache, hypertension, proteinuria

(continued)

Table 2. Continued

Paper	Year	Pre-existing or discovered during pregnancy	Site and size	Secretory and/or metastatic?	Management during pregnancy	Maternal outcome	Fetal outcome	Immunohistochemistry staining	Patient symptoms
Yamamoto K ²⁷	2003	Diagnosed at 29 weeks' gestation	Trachea – above carina 4.5 cm lesion	Nil – 80% obstructed lumen	Patient put on ventilator and emergency caesarean done. Subsequent surgical resection and anastomosis of trachea	Maternal survival.	29 weeks Caesarean, 1.4 kg infant without complications	Not mentioned	Massive haemoptysis
Korkontzelos I ²⁷	2005	Diagnosed at 16 weeks' gestation	Appendix – 2.2 cm diameter	Nil	Surgical excision. At 36 weeks caesarean section after 12 mg of dexamethasone. Right hemicolectomy after birth of fetus	Maternal survival	Fetal survival, 36 weeks Caesarean	Positive	Acute right lower quadrant pain, nausea and vomiting
Hogan RB et al ²⁸	2007	Diagnosed at seven weeks' gestation	Jejunal – 1.2 cm ulcerated lesion	Nil	14 Units PRBC. EGD, VCE and laparotomy with surgical removal	Maternal survival, nil complication	Fetal survival	Positive	Acute hypotension, syncope and 'burgundy coloured' stool
Smaldone M et al ³³	2007	Diagnosed five years prior to pregnancy	Appendix – 1.7 cm	Metastasis include – sac nodule, uterine, sacral ligaments	Pt received IP cisplatin chemotherapy. IVF pregnancy five years later. Uncomplicated pregnancy	Patient had three spontaneous abortions (later she was diagnosed with MTHFR gene variant and treated with aspirin and folic acid). After treatment, had uncomplicated pregnancy and has been disease free for nine years.	One uncomplicated pregnancy with Caesarean delivery of healthy infant	Not mentioned	Discovered incidentally during investigation for infertility. Later had right lower quadrant pain
Gilboa Y et al ¹⁴	2008	Diagnosed at nine weeks' gestation	Appendix	Nil	Surgical removal. Five days after surgery, spontaneous incomplete miscarriage diagnosed. Treated by metergin	Maternal survival.	Spontaneous incomplete miscarriage, 10 weeks	Staining positive	Right lower abdominal pain, tenesmus, diarrhoea
Pitiakoudis M et al ³⁰	2008	Diagnosed at 32 weeks' gestation	Appendix – located at tip 0.5 cm diameter	Nil	Appendectomy	Maternal survival	Normal vaginal delivery with fetal survival, 39 weeks	Not mentioned	Vomiting and pain in right iliac fossa

(continued)

Table 2. Continued

Paper	Year	Pre-existing or discovered during pregnancy	Site and size	Secretory and/or metastatic?	Management during pregnancy	Maternal outcome	Fetal outcome	Immunohistochemistry staining	Patient symptoms
Thompson RJ et al ¹⁵	2008	Ectopic pregnancy, acute appendicitis and carcinoid of appendix diagnosed together	Appendix	Nil	Appendectomy	Patient well at six-month follow-up	Ectopic pregnancy	Nil	Sudden onset lower abdominal pain
Kamphues CH et al ³¹	2009	Diagnosed at 19 weeks	Pancreas – tail 10 × 4.5 × 6.5 cm	Thrombosis of splenic vein and infiltration of portal vein	Distal pancreatectomy, splenectomy, resection of portal vein	Patient discharged 14 days post-op. Nil complications at six-year follow-up	39 weeks vaginal delivery, healthy baby	Staining positive	Hypertension of unknown origin
Kamphues CH et al ³¹	2009	Diagnosed at 16 weeks	Pancreas – head 5 × 5 cm	Nil	Pancreaticoduodenectomy with a pancreaticogastrostomy was performed	Eight weeks after surgery mother and fetus in excellent health.	No delivery at time of publication	Positive	Persisting vomiting and weight loss (8 kg since start of pregnancy)
Le et al ²²	2009	Diagnosed six years prior to pregnancy	Site stated as gastrointestinal with liver metastases	Liver metastases and carcinoid syndrome	Pt presented at 37 weeks in labour: given single doses of ranitidine, diphenhydramine, octreotide. Epidural analgesia and vaginal birth	Patient observed to have flushing after delivery but no other symptoms of carcinoid syndrome.	Healthy vaginal delivery, 37 weeks	Not mentioned	When presenting in labour, describes one-week history of carcinoid syndrome after discontinue octreotide (without medical consultation)
Woo KM et al ³²	2009	Diagnosed six years prior to pregnancy	Pancreas	Liver metastases	Induced labour at 38 weeks. Octreotide prepared in case of symptoms of carcinoid crisis but not used	Maternal survival	Vaginal delivery without complications, 38 weeks	Negative at time of pregnancy	Nil at time of pregnancy
Cornell RL et al ²⁰	2010	Diagnosed 36 weeks	Bronchial – left main bronchus	Nil	Caesarean at 37 weeks followed by sleeve resection of tumour	Tumour removed without complication	37 weeks Caesarean, fetal survival	Staining negative	Acute SOB at rest
Chahajed PN et al ²¹	2011	Diagnosed at nine months of pregnancy	Bronchial – right lower lobe	Nil	Emergency caesarean and then emergency pneumonectomy	Maternal survival with no complications at three-month follow-up	Fetal survival, Caesarean at term	Immunohistochemistry staining positive	Haemoptysis (>200 mL in 24 h), chronic productive cough (seven months)
Komiyama S et al ³³	2011	Diagnosed at 13 weeks of pregnancy	Uterine cervix – 50 × 45 mm	Vascular invasion – metastasis to left breast, multiple lung metastases, pancreatic, mediastinal lymph node,	Radical surgery, multiple drug chemotherapy (paclitaxel, etoposide, cisplatin, irinotecan, carboplatin).	Patient died at 19 months after initial operation and 10 days after diagnosis of meningeal carcinomatosis	Radical hysterectomy required at 13 weeks	Staining positive	Initially presented with atypical vaginal bleeding. Later developed disorientation, convulsions, impaired

(continued)

Table 2. Continued

Paper	Year	Pre-existing or discovered during pregnancy	Site and size	Secretory and/or metastatic?	Management during pregnancy	Maternal outcome	Fetal outcome	Immunohistochemistry staining	Patient symptoms
Naccache DD et al ³⁴	2011	Diagnosed and surgically removed prior to pregnancies	Bronchial – left lower lobe 22 mm × 15 mm - 10 mm	meningeal carcinomatosis Cushing's syndrome with high ACTH and cortisol	Whole brain radiotherapy Left lower lung lobectomy before pregnancy. Octreotide LAR treatment given through three pregnancies	Maternal survival with no complications 10 years after diagnosis	Three healthy Caesarean deliveries at term	Staining positive.	abduction of right eye Headache, flaring acne and hirsutism, facial puffiness, weight gain, paroxysmal myopathy, paranoid thoughts of rape and sexual intimidation
Pistilli B et al ¹⁷	2012	Diagnosed seven years prior to pregnancy	Ovarian (right)	Liver metastases and carcinoid syndrome	Cisplatin + etoposide, octreotide LAR, surgical removal, PRRT with Lu-DOTATATE. During pregnancy: octreotide LAR ceased, oxatomide + ranitidine for carcinoid syndrome symptoms	Maternal survival	Spontaneous abortion at 12 weeks	Nil	Carcinoid syndrome symptoms worsened during pregnancy (recurrent flushing, abdominal cramping, diarrhoea, severe orthostatic hypotension)
Poiana C et al ³⁵	2012	Diagnosed one month prior to pregnancy	Appendix tip – 1 cm diameter	Nil	Surgical removal one month prior to pregnancy. Elective termination of fetus	Maternal survival	Elective termination of pregnancy	Staining positive, but stayed negative from three-month follow-up	Right lower quadrant abdominal pain
Binesh F et al ³⁶	2013	Diagnosed at 34 weeks	Bronchial – right lower lobe	Nil	2 bouts of bronchoscopic electrocautery after patient refused pregnancy termination	Maternal survival with no complications at 6 months follow-up	Fetal survival, 38 weeks Caesarean	Staining positive	Haemoptysis (100 mL six times a day), chronic productive blood-tinged cough (six months)
Yamaguchi M et al ³⁷	2013	Diagnosed at eight weeks pregnancy (but was symptomatic for 12 years prior)	Ovary – right 10 × 8 × 12 cm	Nil	Right salpingo-oophorectomy at 13 weeks' gestation	Maternal survival with no recurrence of disease at 11 months	Fetal survival with caesarean at 38 weeks	Staining positive	Worsening constipation for 12 years (BM every two to four weeks with laxatives)

et al.²⁴ reported a case of appendiceal carcinoid, where the patient decided upon an elective termination of pregnancy.

In one of four reported cases of secretory carcinoid, Pistilli et al. reported that a patient suffered a spontaneous late first trimester miscarriage of an unplanned pregnancy after previously receiving six cycles of radioisotope therapy for an ovarian carcinoid with hepatic metastases.²⁵ Abraham et al.²⁶ reported a case of pancreatic carcinoid with PTHrP secretion presenting with hypercalcaemic crisis. The baby was delivered at 29 weeks and noted to suffer from hypercalcaemia followed by hypocalcaemia requiring calcium supplementation for a month. Mild asymmetric cerebral palsy was noted at follow-up, attributed to prematurity. The mother underwent laparotomy for removal of the mass and survived the pregnancy. Yamamoto et al.'s²⁷ case of bronchial carcinoid also presented at 29 weeks with massive haemoptysis requiring emergency caesarean section and then resection of the tumour and tracheal anastomosis. Cornell and Chhajer reported separate cases of pulmonary carcinoid diagnosed close to term (36 and 38 weeks, respectively).^{28,29} Both cases were successfully managed by caesarean section and then surgical intervention to remove the carcinoid tumour.

The effect of pregnancy upon carcinoid tumour progression is also unclear. Only eight cases were diagnosed prior to pregnancy, and with the possible exception of the case reported by Le where the patient self-ceased therapy,³⁰ no case reported significant disease progression. This stability was evident in all three cases of bronchial carcinoid diagnosed prior to pregnancy. Sewpaul et al. reported a case of spontaneous regression of a pelvic carcinoid, cautiously postulating that changes to B and T cell cytotoxicity during pregnancy could be a potential mechanism.³¹ Limited weight can be put on these cases, as it may be that small carcinoids grow during pregnancy and thus present during gestation as per the majority of reported cases. Complicating this issue further is the fact that most women have significant contact with health professionals during pregnancy which allows scope for investigation of pre-existing but previously uninvestigated stable symptomatology. Diagnosis during pregnancy in such cases may have no relationship with disease progression. Interestingly, the majority of seven cases of metastatic disease did not have adverse outcomes. In one case of extensive metastatic disease, the mother passed away from meningeal carcinomatosis.

Anaesthetic reports demonstrate the potential management option of octreotide that may assist in a successful and safe delivery for secretory tumours, though this was not necessary in our case.³⁰ However, despite the extent of disease in our case, the pulmonary carcinoid remained stable during and after pregnancy.

Although reported cases of carcinoid in pregnancy are heterogeneous, we would suggest that management of such cases is aided by considering (1) whether the disease is a new diagnosis or a pre-existing one, (2) where disease course to date is known, any available histological information (low or high grade), (3) disease sites and bulk, and (4) determining if the tumour is secretory or non-secretory. Large tumours, such as our case, or metastatic disease do not necessarily portend a poor prognosis or likely disease progression. It seems unlikely that bronchial carcinoids have a negative impact on the pregnancy as fetal survival was reported in all cases except for one mentioned in the original Durkin series.³² Of the bronchial cases discussed, including our patient, none of the three cases in which carcinoid was diagnosed prior to pregnancy showed any progression of the tumour during pregnancy. Although a fifth (6/23) of pregnancies were associated with fetal demise, most were first trimester losses, and not inconsistent with the spontaneous miscarriage rate in all pregnancies. In cases where fetal losses occurred, there was not a strong link to carcinoid as a contributing factor. Of the eight cases in which carcinoid was diagnosed prior to pregnancy, only one case showed worsening after pregnancy.³⁰ This may suggest that pregnancy has little effect on the progression of carcinoid tumours. We would therefore suggest that clinicians looking after women with carcinoid in pregnancy should be cautiously optimistic rather than pessimistic regarding positive maternal and fetal outcomes, though regular monitoring for progression in symptoms and disease is essential.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethical approval

Written patient consent was obtained for publication.

Guarantor

DK.

Contributorship

DK and MC drafted the report. NF, DW and KL reviewed and provided references.

References

1. Yao JC, Hassan M, Phan A, et al. One hundred years after "carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. *J Clin Oncol* 2008; 26: 3063–3072.
2. Thakker RV, Newey PJ, Walls GV, et al. Clinical practice guidelines for multiple endocrine neoplasia type 1 (MEN1). *J Clin Endocrinol Metab* 2012; 97: 2990–3011.
3. Syversen U, Opsjon SL, Stridsberg M, et al. Chromogranin A and pancreastatin-like immunoreactivity in normal pregnancies. *J Clin Endocrinol Metab* 1996; 81: 4470–4475.
4. Asamura H, Kameya T, Matsuno Y, et al. Neuroendocrine neoplasms of the lung: a prognostic spectrum. *J Clin Oncol* 2006; 24: 70–76.
5. Filosso PL, Oliaro A, Ruffini E, et al. Outcome and prognostic factors in bronchial carcinoids: a single-center experience. *J Thoracic Oncol* 2013; 8: 1282–1288.
6. Fink G, Krelbaum T, Yellin A, et al. Pulmonary carcinoid: presentation, diagnosis, and outcome in 142 cases in Israel and review of 640 cases from the literature. *Chest* 2001; 119: 1647–1651.
7. Soga J and Yakuwa Y. Bronchopulmonary carcinoids: an analysis of 1,875 reported cases with special reference to a comparison between typical carcinoids and atypical varieties. *Ann Thoracic Cardiovas Surg* 1999; 5: 211–219.
8. Duncan PG, Pope WD, Cohen MM, et al. Fetal risk of anesthesia and surgery during pregnancy. *Anesthesiology* 1986; 64: 790–794.
9. Rinke A, Muller HH, Schade-Brittinger C, et al. Placebo-controlled, double-blind, prospective, randomized study on the effect of octreotide LAR in the control of tumor growth in patients with metastatic neuroendocrine midgut tumors: a report from the PROMID Study Group. *J Clin Oncol* 2009; 27: 4656–4663.
10. Caplin ME, Pavel M, Cwikla JB, et al. Lanreotide in metastatic enteropancreatic neuroendocrine tumors. *N Engl J Med* 2014; 371: 224–233.
11. Fassnacht M, Capeller B, Arlt W, et al. Octreotide LAR treatment throughout pregnancy in an acromegalic woman. *Clin Endocrinol* 2001; 55: 411–415.
12. Maffei P, Tamagno G, Nardelli GB, et al. Effects of octreotide exposure during pregnancy in acromegaly. *Clin Endocrinol* 2010; 72: 668–677.
13. Skajaa GO, Mathiesen ER, Iyore E, et al. Poor pregnancy outcome after octreotide treatment during pregnancy for familial hyperinsulinemic hypoglycemia: a case report. *BMC Res Notes* 2014; 7: 804.

14. Pavel ME, Hainsworth JD, Baudin E, et al. Everolimus plus octreotide long-acting repeatable for the treatment of advanced neuroendocrine tumours associated with carcinoid syndrome (RADIANT-2): a randomised, placebo-controlled, phase 3 study. *Lancet* 2011; 378: 2005–2012.
15. Wilson CH, Manas DM and French JJ. Laparoscopic liver resection for hepatic adenoma in pregnancy. *J Clin Gastroenterol* 2011; 45: 828–833.
16. Bröker MEE, Ijzermans JNM, van Aalten SM, et al. The management of pregnancy in women with hepatocellular adenoma: a plea for an individualized approach. *Int J Hepatol* 2012; 2012: 3.
17. Davi MV, Bodei L, Francia G, et al. Carcinoid crisis induced by receptor radionuclide therapy with 90Y-DOTATOC in a case of liver metastases from bronchial neuroendocrine tumor (atypical carcinoid). *J Endocrinol Invest* 2006; 29: 563–567.
18. Strosberg WE Jr and Chasen B. NETTER-1 phase III: progression-free survival, radiographic response, and preliminary overall survival results in patients with midgut neuroendocrine tumors treated with 177-LU-Dotatate. *J Clin Oncol* 2016; 34: 194.
19. Durkin JW Jr. Carcinoid tumor and pregnancy. *Am J Obstet Gynecol* 1983; 145: 757–761.
20. Luosto R, Koikkalainen K and Sipponen P. Spontaneous regression of a bronchial carcinoid tumour following pregnancy. *Ann Chirurgiae et Gynaecologiae Fenniae* 1974; 63: 342–345.
21. Jurica JV and Baumgardner DJ. Chlamydia and incidental carcinoid tumor in spontaneous abortion. *J Am Board Fam Pract* 1989; 2: 126–129.
22. Gilboa Y, Fridman E, Ofir K, et al. Carcinoid tumor of the appendix: ultrasound findings in early pregnancy. *Ultrasound Obstet Gynecol* 2008; 31: 576–578.
23. Thompson RJ and Hawe MJ. A rare pathological trinity: an appendiceal ectopic pregnancy, acute appendicitis and a carcinoid tumour. *Irish J Med Sci* 2011; 180: 579–580.
24. Poiana C, Carsote M, Trifanescu R, et al. Case study of appendiceal carcinoid during pregnancy. *J Med Life* 2012; 5: 325–328.
25. Pistilli B, Grana C, Fazio N, et al. Pregnant with metastatic neuroendocrine tumour of the ovary: what now? *Ecancermedicalscience* 2012; 6: 240.
26. Abraham P, Ralston SH, Hewison M, et al. Presentation of a PTHrP-secreting pancreatic neuroendocrine tumour, with hypercalcaemic crisis, pre-eclampsia, and renal failure. *Postgraduate Med J* 2002; 78: 752–753.
27. Yamamoto K, Alarcon JP, Armengod EB, et al. Tracheal carcinoid during pregnancy. *J Cardiovas Surg* 2004; 45: 525.
28. Cornell R, Wilkens J, Cooper T, et al. Bronchial carcinoid tumour in pregnancy. *Scottish Med J* 2010; 55: 57.
29. Chhajed PN, Kate A, Chaudhari P, et al. Massive hemoptysis during pregnancy. *J Assoc Phys India* 2011; 59: 660–662.
30. Le BT, Bharadwaj S and Malinow AM. Carcinoid tumor and intravenous octreotide infusion during labor and delivery. *Int J Obstet Anesth* 2009; 18: 182–185.
31. Sewpaul A, Bargiela D, James A, et al. Spontaneous regression of a carcinoid tumor following pregnancy. *Case Rep Endocrinol* 2014; 2014: 5.
32. Dombrowski M, Chan J, Malviya V, et al. Ovarian carcinoid and pregnancy. A case report. *J Reprod Med* 1986; 31: 732–733.
33. Smaldone GM, Richard SD, Krivak TC, et al. Pregnancy after tumor debulking and intraperitoneal cisplatin for appendiceal carcinoid tumor. *Obstet Gynecol Int* 2007; 110: 477–479.