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Hemoptysis during pregnancy: a comprehensive review of literature and an unprecedented case report of oropharyngeal carcinoma

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ABSTRACT

Objectives: Hemoptysis in pregnancy is a very rare finding causing diagnostic and therapeutic difficulties. The case report of hemoptysis by a 29 years old patient in the 31st week of pregnancy is presented and discussed along with the diagnostic process and treatment provided. Upon pharyngeal cancer occurrence in a pregnant patient a multidisciplinary medical team performed appropriate treatment along with delivery of a healthy newborn at term. Patients and fetal conditions and outcomes were analyzed and compared to available literature in this newly created literature review.

Material and methods: After MEDLINE database analysis using formula "hemoptysis" AND "pregnancy" more than 125 results were found published during the period 2002–2022. Almost 30 papers about hemoptysis were found and included for full analysis.

Results: The review of literature revealed 32 cases of patients with hemoptysis during pregnancy. The two most common causes were vascular abnormalities and neoplastic tumors. The treatment comprised of chemotherapy and surgical procedures during the pregnancy or after delivery. Almost 35% of pregnancies ended prematurely. The conducted research did not provide a description of any other case of pharyngeal cancer during pregnancy.

Conclusions: The literature review offers a detailed description of previously reported incidents of hemoptysis in pregnancy to gain understanding of the etiology, differential diagnosis, available treatment and predicted future outcomes for both patient and fetus.

Key words: hemoptysis; pseudohemoptysis; pregnancy; oropharyngeal carcinoma; minor salivary gland carcinoma

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INTRODUCTION

Hemoptysis occurs very rarely in pregnancy and may be initially linked to emergency medical conditions such as pulmonary embolism [1, 2], which can be induced and exacerbated by pregnancy [3–6]. Alternatively, due to physiological blood dilution during pregnancy [7, 8] and a lower platelet count which is common during pregnancy [9–11], oral cavity bleedings [12, 13] linked to gingival abnormalities may mimic hemoptysis [14, 15].

The incidence of malignant neoplasms diagnosed during pregnancy is constantly rising with melanoma, breast and cervical cancer at the forefront [16–18] yet other types of malignancies cannot be excluded in pregnancy and have to be considered [19, 20]. This includes a choriocarcinoma [21–25], which in our review proved to be the most common neoplastic process resulting in hemoptysis during pregnancy.

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Objectives

Currently, there are no systematic literature reviews available upon the subject of hemoptysis in pregnancy, with no noted case reports of hemoptysis in pregnancy due to oropharyngeal carcinoma. Authors of this paper wanted to sum up the current state of knowledge and draw attention of other professionals on multidisciplinary problem which could be omitted being in fact, sometimes the first, symptom of live-threatening conditions.

MATERIAL AND METHODS

On 07.05.2022 MEDLINE (PubMed) database was searched manually by two authors (J.O. and N.M.). Eligibility criteria were hemoptysis that occurred during the course of pregnancy and date of publication in the last 20 years (2002–2022). Bleeding manifesting in the post-partum period and during the cesarean section was excluded. Search formula was "hemoptysis" AND "pregnancy". The database search provided 126 unique results. After title and abstract screening, 88 papers got rejected and 38 selected for full-text analysis. In the next step 9 papers were rejected due to incomplete data or because English version of article was not available Finally 29 articles were included in the literature review.

RESULTS

The texts included in the literature review describe 32 patients with occurrence of hemoptysis during pregnancy (Tab. 1). The two most common causes of hemoptysis are pulmonary vascular abnormalities (n = 9; 28.1%) and malignant neoplasms (n = 8; 24.9%), amongst which, the most common is lung metastatic choriocarcinoma (n = 5; 15.6% of all causes). Other malignant neoplasms included carcinoids Benign and inflammatory tumors occurred with the same frequency as choriocarcinoma (n = 5; 15.6%). Detailed clinical presentation of the hemoptysis during pregnancy and clinical outcome of cases included in this literature review is presented in Table 2. The description of laryngeal pyogenic granuloma must be noted. These changes often occur during pregnancy as a result of hormonal fluctuations and the majority of them are localized within the oral cavity [26].

Most common treatment strategy was surgery (n = 18), mainly conducted after the delivery (12 patients, 37.5%). Chemotherapy was administered in 3 patients (9.4%), in all of them after delivery. Other pharmacological treatment during pregnancy (for example steroids for primary disease) was used in 7 cases (21.9%). Both treatment strategies (surgery and chemotherapy) were used in 3 patients (9.4%). There were no notable cases of chemotherapy used during pregnancy and other non-chemotherapy based pharmacological treatment after delivery.

In 9.37% (n = 3) of patients included in the review, termination of pregnancy was induced, 8 (25%) continued pregnancy until term and 11 (34.38%) had a preterm birth. Two cases (6.25%) of intrauterine death and 8 patients (25%) with no information provided. In two patients (6.25%), the outcome was fatal. Out of 8 term births, 1 (3.13%) was vaginal delivery, 1 (3.13%) C-section due to obstetric indications and 6 (18.75%) C-sections due to primary disease. Among the 11 preterm deliveries, 1 (3.13%) C-section from obstetric indications and 10 (31.25%) C-sections due to primary disease must be noted. There was no preterm vaginal delivery described in any of the cases.

A course of steroids to fasten the development of fetal lungs was administered in 5 (17.9%) of review patients. Two patients (7.1%) received steroids as treatment for primary disease (Goodpasteure syndrome and vasculitis). Steroid treatment was not administered in 6 (21.4%) cases, whilst in 15 (53.6%) there was no information about it (Tab. 2).

Case description

A 29 years old patient, with chronic asthma, in her first pregnancy, dating 30 weeks and 3 days, presented to the emergency department of a tertiary hospital due to hemoptysis which occurred for the first time 2 weeks prior to seeking medical advice. A routine gynecological and obstetric examination were performed with normal findings. An ear, nose and throat (ENT) examination has been performed and findings included a mass in the oropharynx with a presumed source of bleeding which was located in the proximity of the left tonsil. A diagnosis of tonsil or oropharyngeal carcinoma was considered, as the exact site of tumor origin was difficult to establish. At 30 weeks and 5 days of pregnancy, a biopsy specimen was taken from the ulcerated mass. Histopathological examination revealed a low-grade mucoepidermoid carcinoma, mitotic index Ki67 ~0.5%. Rearrangement of MAML2 gene was confirmed. In an MRI study (Siemens Magnetom Aera 1.5T), the $22 \times 20 \times 14$ mm oval, exophytic, polycyclic lesion originating from the left vallecula was described (Fig. 1A–C). Diffusion was not restricted in diffusion-weighted imaging (DWI) sequence.

An interdisciplinary consultation of ENT surgeons and obstetricians was planned to decide upon the patient's treatment.

Within a week the patient was admitted for a planned hospitalization at the pathology of pregnancy ward where a full course of intramuscular steroid treatment to fasten the development of fetal lungs was administered along with regular fetal ultrasonography, cardiotocography (CTG) and laboratory tests which were all normal.

A partial left-side pharyngectomy and tonsillectomy were performed on 33 weeks and 5 days of pregnancy. The tumor originated from the base of the tongue, just below

Table 1. Review of the literature

Reference	Age	GA [weeks]	Diagnosis	Treatment	Pregnancy complications	GA at end of pregnancy [weeks]	Fetal/child well being [yes/no]	Steroids administered for fetal lung development [yes/no]	Follow-up
[33]	28	34	Typical carcinoid tumor of bronchus	Surgical (after delivery)	Absent	38 (elective C-section, due to disease)	–	–	6 months, no chemotherapy, no recurrence
[22]	22	34	Choriocarcinoma - pulmonary metastasis	Chemotherapy (after delivery)	–	34 (urgent C-section due to disease)	–	Yes	6 months, no recurrence
[34]	38	8	Microscopic polyangiitis	Pharmacotherapy (methylprednisolone, cyclophosphamide after termination)	Absent	8 (termination due to disease)	–	–	Remission after cyclophosphamide
[35]	23	17	Systemic Lupus Erythematosus	Pharmacotherapy (methylprednisolone during pregnancy)	Present	17 (termination due to disease)	–	–	Several months, persisted seizures and headaches
[36]	22	34	Cavitating tuberculosis (HIV+)	Surgical (after delivery)	Absent	36 (urgent C-section due to disease)	No	No	14 months, TB remission
[21]	22	36	Choriocarcinoma — pulmonary metastasis	Both (surgical and chemotherapy after delivery)	Absent	37 (C-section due to disease)	Yes	No	No information, ended during chemotherapy
[37]	28	I trimester	Inflammatory myofibroblastic tumor of the lung	Surgical (after termination)	Absent	I trimester termination (due to disease)	–	–	Asymptomatic, follow-up time not specified
[38]	21	28	Mature teratoma of mediastinum	Surgical (after delivery)	Present	28 (C-section, obstetric indications)	Yes	Yes	No information
[39]	23	20	Pyogenic granuloma of the larynx	Surgical (after delivery)	Absent	38 (elective induction due to disease)	Yes	No	Remission after excision
[40]	29	26	Adenocarcinoma of the lung	Both (chemotherapy during pregnancy, surgery after delivery)	–	30 (elective C-section due to disease)	Yes	Yes	Died 17 months after diagnosis
[41]	27	II trimester	Lymphangioma — pulmonary	Surgical (after delivery)	–	–	–	–	–
[42]	43	25	Rheumatic mitral valve stenosis	Surgical (during pregnancy)	–	–	–	–	–
[25]	22	31	Choriocarcinoma — pulmonary metastasis	Chemotherapy (after delivery)	Absent	32 (elective C-section due to disease)	Yes	Yes	B-hCG normalized after 51 days
[43]	36	34	Cystic fibrosis, bronchiectasis	–	–	–	–	–	–

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Table 1. (cont.) Review of the literature

Reference	Age	GA [weeks]	Diagnosis	Treatment	Pregnancy complications	GA at end of pregnancy [weeks]	Fetal/child well being [yes/no]	Steroids administered for fetal lung development [yes/no]	Follow-up
[44]	34	28	Right lower bronchial artery bleeding	Surgical (during pregnancy)	Present	28 (intrauterine death during therapy)	–	–	3 months follow-up, no recurrence of bleeding
[45]	29	20	Dissection of an anomalous systemic artery in the lung	Both (surgery after delivery)	Absent	Elective c-section (due to disease)	–	–	6 months follow-up, asymptomatic
[46]	33	III trimester	Unilateral pulmonary artery agenesis	Pharmacotherapy (during pregnancy)	Absent	–	–	–	Emergency CT was not performed in AnE due to pregnancy , one week postpartum CT
[47]	17	13	Goodpasteure syndrome	Pharmacotherapy (methylprednisolone during pregnancy)	Present	Death	No	Yes (as therapy for primary disease)	Death of patient: could probably have been avoided if pregnancy was terminated earlier
[48]	33	18	Pulmonary TB (HIV-)	Pharmacotherapy (anti tuberculosis treatment during pregnancy)	Absent	42 (spontaneous,vaginal delivery)	Yes	No	10 month follow up: healthy patient and child
[49]	41	29	Pulmonary AV malformation	Surgical (after delivery)	Present	34 (urgent C-section due to disease)	–	–	–
[50]	25	28	Rheumatic mitral valve stenosis	Surgical (during pregnancy)	Present	38 (elective C-section, obstetric indications)	Yes	–	1.5 year follow up, asymptomatic
[51]	29	37	Pulmonary tuberculosis	Pharmacotherapy (anti tuberculosis therapy after delivery)	Present	37 (urgent C-section, due to disease)	–	No	–
[24]	22	36	Choriocarcinoma — pulmonary metastasis	Chemotherapy (after delivery)	Present	36 (urgent C-section due to disease)	–	–	–
[52]	1. 32 2. 19 3. 27	1. 17 2. 16 3. 24	1, 2, 3 Anomalous right pulmonary artery	1, 2, 3. Surgical (during pregnancy)	1, 2, 3 Absent	1. 38 2, 3 -	1, 2 Yes, 3 -	1, 2,-	1. 2 year follow-up, asymptomatic, 2. 6 months follow-up, asymptomatic, 3.10 months follow-up, asymptomatic
[53]	–	29	Tracheal carcinoid	Surgical (after delivery)	Present	29 (emergency C-section due to disease)	-	Yes	–

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Table 1. (cont.) Review of the literature

Reference	Age	GA [weeks]	Diagnosis	Treatment	Pregnancy complications	GA at end of pregnancy [weeks]	Fetal/child well being [yes/no]	Steroids administered for fetal lung development [yes/no]	Follow-up
[54]	30	34	Tracheal inflammatory myofibroblastic tumor.	Surgical (after delivery)	Absent	34 (emergency C-section due to disease)	–	–	1 year follow-up, no recurrence or metastasis
[55]	1. 29; 2. 37	1. 33; 2. 27	1. Bronchial artery bleeding, 2. Pulmonary hypertension	1, 2. Surgical (after delivery)	Absent	1. 29; 2. 37 (both emergency C-section due to disease)	1. No, 2. Yes	–	1. 16 months follow-up, no recurrence of bleeding, 2. 11 months follow-up, no hemoptysis
[23]	35	36	Choriocarcinoma — pulmonary metastasis	Surgical (after delivery)	Present	36 (elective C-section due to disease)	Yes	No	Death due to massive hemoptysis
[56]	25	I trimester	Anti-neutrophil cytoplasmic antibodies (ANCA) vasculitis after propylthiouracil	Pharmacotherapy (corticosteroids during pregnancy)	–	–	–	Yes (as vasculitis) therapy	6 months follow-up, remission

GA — gestational age; "–" — not given

Table 2. Clinical presentation of the hemoptysis during pregnancy and clinical outcome

Cause of hemoptysis/primary disease	Number [n]	Percentage [%]
Connective tissue disorder and vasculitis (excluding rheumatic fever)	4	12.5
Choriocarcinoma	5	15.6
Malignant tumors (excluding choriocarcinoma)	3	9.3
Pulmonary vessels abnormalities	9	28.1
Tuberculosis	3	9.3
Heart defects (including rheumatic fever)	2	6.25
Benign and inflammatory lesions	5	15,6
Bronchiectasis, Cystic Fibrosis	1	3,1
Steroid administration for fetal lung development prior to preterm delivery	**Number [n]**	**Percentage [%]**
Yes	5	17.9
No	6	21.2
Steroid administered as treatment for primary disease	2	7.1
No information	15	53.6
Treatment strategy	**Number [n]**	**Percentage [%]**
Surgery during pregnancy	6	18.75
Surgery after delivery	12	37.5
Chemotherapy after delivery	3	9.4
Other pharmacological (non-chemotherapy) during pregnancy	7	21.88
Surgery and chemotherapy	3	9.40
No information	1	3.2
End of pregnancy time	**Number [n]**	**Percentage [%]**
Preterm birth (C-section obstetric indications)	1	3.13
Preterm birth (C-section due to primary disease)	10	31.25
At-term birth (vaginal)	1	3.13
At-term birth (C-section obstetric indications)	1	3.13
At-term birth (C-section due to primary disease)	6	18.75
Termination	3	9.37
Intra-uterine death	2	6.25
No information	8	25.00

the glossotonsillar sulcus. For the duration of surgery a constant cardiotocography was performed in the presence of an obstetrician and a neonatology team on stand-by in case of emergency cesarean section.

Postoperatively the patient was transferred to ENT ward and 3 days later to pathology of pregnancy ward for

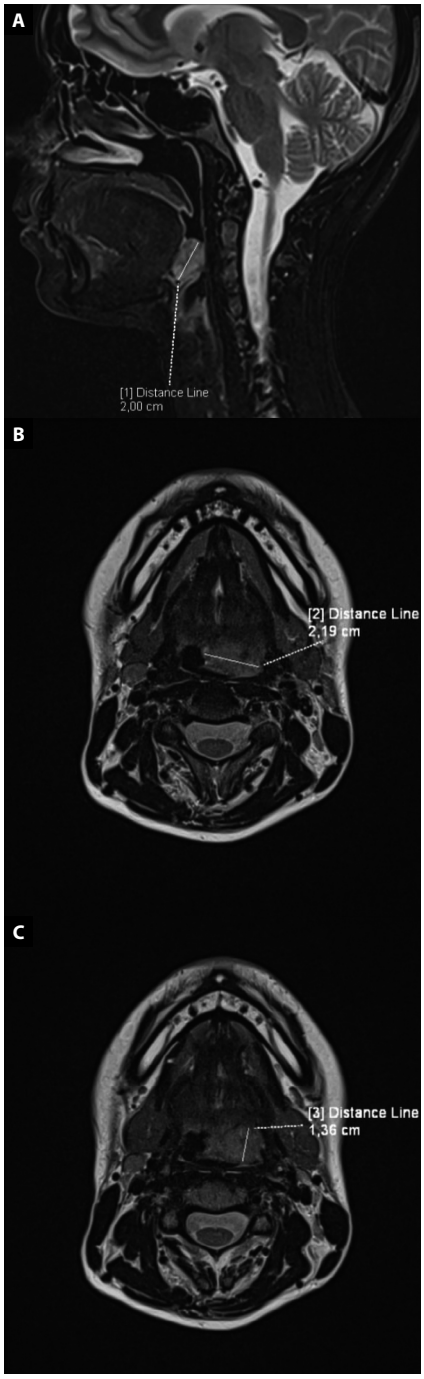

Figure 1. A–C. A magnetic resonance imaging (MRI) study: 22×20×14 mm oval, exophytic, polycyclic lesion originating from the left vallecular

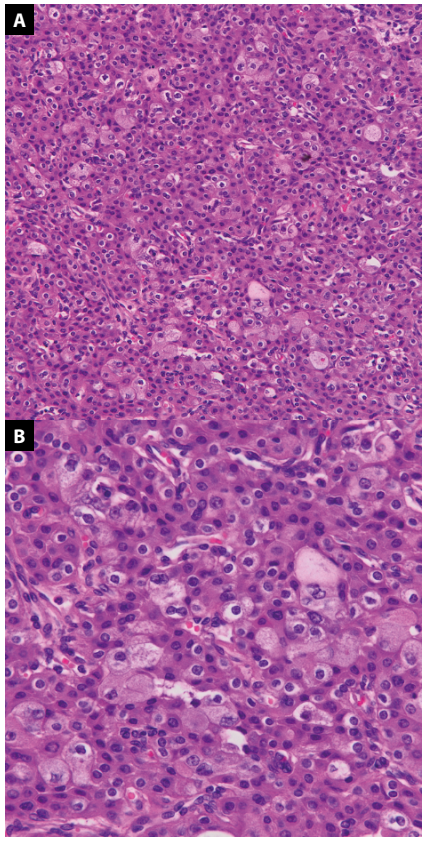

Figure 2. A, B. Classical images of a low grade mucoepidermoid carcinoma, composed mostly of intermediate cells (hematoxylin and eosin stain, 400× (2a) 200× (2b) magnification)

further observation which proved uneventful and later discharged home. Histopathological examination of the excised lesion confirmed a low grade mucoepidermoid carcinoma, arising from minor salivary glands (Fig. 2A, 2B**)**. Growth of the cancer was expandable, no necrosis or invasion of nearby tissues and neurovascular bundles were found. Histological level of malignancy was low (AFIP 0 points, Brandwein 0 points). Excision of the mass was radical (R0), with the smallest margin of 2 millimeters. Pathological TNM was pT1a, NX.

Upon the end of 38th week of pregnancy the patient was readmitted and an elective cesarean section was performed due to ENT indications of early post-operative period and the risk of bleeding from resection site. A healthy newborn girl, weighing 2651 g was born, scoring 10 points on the Apgar scale. After 3 days of uneventful hospitalization mother and child were discharged home with standard post cesarean section recommendations. Interdisciplinary consultation of ENT surgeons and oncology specialists recommended observation. Control MRI study has been scheduled 6 months after surgery and showed no sign of recurrence. Follow-up is carried out in an outpatient ENT clinic specializing in head and neck cancers. Nasofiberoscopic examination is a standard part of the visit.

DISCUSSION

Oropharyngeal carcinoma is not the most common malignant neoplasm of the head and neck region, its incidence is approximately 0.5% of new cancer cases [27]. In the population of pregnant women, this cancer is probably even less frequent, but there is no relevant statistical data

confirming this thesis. Majority of oropharyngeal carcinomas are squamous cell carcinomas, arising from the mucosal epithelial cells. These tumors are widely described because of their frequency and etiological links with HPV infection. However, tumors originating from other cells or structures within oropharynx (like minor salivary glands) could also occur. Among other minor salivary gland malignant tumors, the adenoid cystic carcinoma and adenocarcinoma, must be noted. As mentioned earlier, the most common malignant neoplasms during pregnancy are melanoma, breast and cervical cancers [16–18]. Each malignancy that occurs in a pregnant woman presents a therapeutic challenge that requires careful consideration of the benefits and risks of the treatment process. For this reason, decisions regarding the further procedures should be made in a multidisciplinary team consisting of obstetricians, oncologists, radiotherapists and other specialists, depending on the type of tumor. Multidisciplinary team was involved in establishing the treatment plan in the case described above.

Hemoptysis is coughing up blood along with sputum. The source of bleeding may be localized in the respiratory system or digestive tract. Depending on the localization of bleeding site, "true hemoptysis" (lungs or lower respiratory tract), "pseudo-hemoptysis" (outside the lungs and lower respiratory tract) and "hematemesis" (bloody vomiting, a source of bleeding within the gastrointestinal tract) have to be listed [31]. According to this classification, the case described in the article should be classified as pseudo-hemoptysis, as the source of the bleeding was in the oropharynx. Any case of hemoptysis should be diagnosed to determine the source of the bleeding, as the underlying cause may be a life-threatening condition. Massive hemoptysis (also described as pulmonary hemorrhage) is characterized by coughing up 100–1000 mL of blood during 24 hours and is an emergency condition (flooding of the lower respiratory tract with blood and subsequent cardiopulmonary failure leading to death) [32].

Depending on the gestational age a careful consideration and discussion with multidisciplinary team and patient, providing extensive information on outcomes of treatment, risks associated with continuation of pregnancy or possibility termination should be conducted. In the literature review presented above, most of the cases managed by surgical treatment had surgery conducted after the delivery (12 of 18 cases). The case report presented in this article belongs to the less quantitative group of surgery carried on during pregnancy.

In patients with hemoptysis that may result in preterm birth when possible a course of steroids to fasten the development of fetal lungs should be considered if patients' parameters allow for such treatment.

CONCLUSIONS

The novel case report of a carcinoma of the minor salivary glands in a pregnant woman that manifested as hemoptysis and first of a kind literature review offer a comprehensive description to gain understanding of the causes of hemoptysis during pregnancy, their treatment and outcomes for both patient and fetus.

Oral cavity and oropharynx is accessible by any physician for routine examination, thus thorough inspection of this site should be included in any routine check-up especially upon patient's concerns.

Every suspicious lesion should be biopsied and examined histopathologically as it is more sensitive than image-based technologies in identifying malignant changes. This should be considered the "golden standard", also in pregnant patients.

A multidisciplinary approach in diagnosis and treatment of hemoptysis in pregnancy is recommended to achieve the highest standard of care and best outcomes for patient and fetus to maximize their survival rate and ensure minimal long term consequences.

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Conflict of interest

Authors declare no conflict of interest.

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