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Case Report

Iron pill aspiration syndrome: A case report and literature review

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ABSTRACT

Aspiration of iron pill containing ferrous sulfate into the airway can induce fulminant chemical burn and necrosis of the airway mucosa. Acute chemical burn and inflammatory response can result in life-threatening airway compromise. It can also result in long-term sequelae including but not limited to fibrosis and airway stenosis. Considering the common use of iron supplements, and the potential severity of aspiration related airway injury, clinicians should be fully cognizant of the interaction between aspirated iron and airway passages. Herein, we present a case report with pertinent review of the literature.

1. Introduction

Aspiration of chemically active compounds like Iron pill (Ferrous sulfate) disintegrates in the airway resulting in deep mucosal injury from a chemical-burn and intense inflammatory response [1,2]. It can present acutely with life threatening injury of the large airway, can involve small airways presenting with obliterative bronchiolitis, and result in long-term sequelae like airway stenosis [2–4]. Although iron pill aspiration syndrome has been recognized since 1975 [5], clinician awareness is limited, further literature is merely limited to a few anecdotal case reports. Herein, we present a case report of iron pill aspiration syndrome and have sought to perform a pertinent review of the literature.

2. Case presentation

A 48-year-old Caucasian female with a past medical history including but not limited to hypertension and hypothyroidism was in a usual state of health until the morning of presentation to the emergency room (ER). She mentioned that she accidentally aspirated her Iron pill (Ferrous sulfate). After about a couple of hours following aspiration, she developed an intractable cough. Cough appeared in short episodes lasting a few minutes and each episode was associated with the expectoration of yellowish sputum with occasional blood stains. She also developed retrosternal chest discomfort. Pain was localized with no radiation or referral. She described new on-set dyspnea at rest.

On evaluation in the emergency room, she was in acute distress. Blood pressure measured 100/70 mmHg; heart rate was 120 beats per minute in sinus rhythm. She was breathing 25–30 times per minute with the use of accessory muscles of breathing. Saturation was 81% on room air and improved to 93% with supplemental oxygenation using a face mask at 6 L per minute. Initial laboratory assessment in ER was essentially unremarkable except white blood cell count of 14 thousand per deciliter with 89% neutrophils.

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Serum electrolytes and renal function parameter were within normal limits. Plain x-ray of chest was otherwise unremarkable except for chronic elevation of the right hemidiaphragm. Given the history of Iron pill aspiration and strong consideration of airway injury, a decision was made to proceed with emergent bronchoscopy.

2.1. Bronchoscopy procedural details

Bronchoscopy was performed under general anesthesia. Immediately after crossing the vocal cords, diffuse erythema and inflammation of the trachea was noted starting at the superior end of the trachea distal to the vocal cords. We advanced to the left bronchial tree which had erythema but noticeably less that resolved after the first subsegment level. Washings were done and no abnormality was noted. On the right, however, we immediately encountered a mucous-coated plug with an obvious foreign body resembling a partially dissolved pill in the bronchus intermedius just past the take-off from the RUL. This was retrieved rather easily with an endobronchial basket, however tissue that was very necrotic. A second amount of pill was able to be taken out and at that point mucous and necrotic material came from the bronchi. Once this was removed, a severe amount of damaged mucosa was noted in the airway starting at the middle lobe take off from the bronchus intermedius but largely involving the orifice to the lower lobe. The scope was reintroduced to the affected area and the medial basal and superior segments were completely obliterated by shredded, necrotic material partially attached to the orifice of those respective airways, and pill fragments were noted in a granular state. The material was attempted to be suctioned but was unable to do so due to the necrotic material occluding the scope. Therefore, we attempted to retrieve the pill granular parts with forceps and the basket, but they were too friable. At that point, a number three endobronchial blocker was advanced into the airway past the pills and inflated slightly. This allowed the fragments to be pulled out of the area with the issue fragments and could then be suctioned out. Afterward, the extent of the damage to the bronchi was noted and there was a severe chemical burn with necrosis in this area that had weblike fragments hanging from the airway and partially occluding the medial basal and superior segments as well as the remaining lower lobe segments. Using forceps, this area was debrided partially, removing the fragments of tissue that were occluding the airway. There was minimal bleeding from the removal, but it did not require any intervention to control and stopped nearly immediately and spontaneously. After several fragments were removed and collected into a formalin container, the medial basal and lower lobe segments (anterior, lateral, and posterior) were able to open. A small fragment of granulated pill was seen and removed with suctioning only from the medial basal segments. The visible portion of the medial basal segment had less severe damage, but normal tissue could not be visualized. Flushing the segment returned clear fluid. The anterior, lateral, and posterior segments however were noted to have completely normal tissue just past the orifice to the individual segments. We were able to navigate past the damaged tissue there in each segment and washings in those area returned clear form as well. We then turned our attention to the superior segment of the lower lobe which had more damaged mucosa appearing more as macerated tissue. This was removed with forceps and minimal to no bleeding was noted. Following this, the segment had a visible split into two subsegments but was extremely inflamed and had more dead tissue. Because of the narrow nature of the segment and damage that would likely be caused by attempts at further tissue removal, we did not remove any additional tissue here and flushes of the area were clear of any obvious remaining pill fragments. After this, the area was largely open with all airways again in communication with the mainstem. No bleeding was noted. The middle lobe itself was then inspected again and other than some inflammation, no damage was noted past the initial take off to the middle lobe. Pictographic evidence of findings during bronchoscopy are summarized in Fig. 1.

At this point, the concern would be a collapse of that segment onto itself and healing in a stricture-type fashion as well as potentially life-threatening hemoptysis as the additional necrotic material cleared. For this reason, the decision was made to leave the patient intubated with a positive end-expiratory pressure (PEEP) of 10 to splint the airway open and monitor her for the next several days as the area healed.

2.2. Post bronchoscopy intensive care management

The patient was subsequently transferred to the intensive care unit. Received mechanical ventilator support along with supportive measures. Methylprednisone was administered at a dose of 1 mg per Kg body weight to suppress the inflammatory response. A revision bronchoscopy was performed 48 hours later. It revealed substantial resolution of inflammatory changes of the airway mucosa and overall airway wall. There was no evidence of airway collapse while using a low PEEP trial. Thus, the patient was successfully extubated after two days. The patient was subsequently discharged on the fifth day of hospitalization. She did not require supplemental oxygen at discharge.

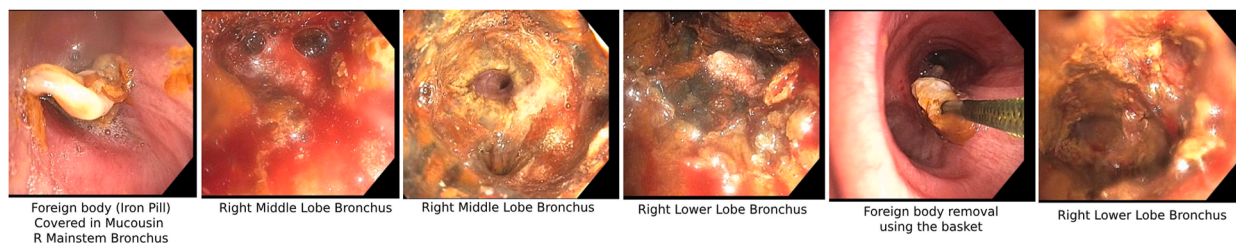


Fig. 1. Findings on bronchoscopy at the time of initial presentation.

2.3. Post discharge follow up

The patient was evaluated with a pulmonary function test (PFT) 4 weeks after discharge. It revealed mild restrictive physiology (total lung capacity: 4L-79% predicted) along with reduced DLCO (54% predicted) in setting of reduced VA (55% predicted). Collectively findings were likely suggestive of post-inflammatory fibrotic restriction along with parenchymal volume loss. Other PFT findings are summarized in [Table 1](#).

A follow-up bronchoscopy was performed at six weeks after discharge. Suctioning was performed in the bronchus intermedius and in the right lower lobe and the airway was cleared. There was a prior mucosal injury. There was evidence of some tissue necrosis in the bronchus intermedius as well as the medial basal segment of the right lower lobe. Otherwise, the right upper and middle lobes were clear as well as the anterior, lateral, and posterior segments (Fig. 2). The left side was clear.

The patient has had substantial clinical recovery. Her residual respiratory symptoms are unremarkable except for dyspnea on exertion equivalent to mMRC grade 0. She does not have residual orthopnea and cough. She continues to follow up at the pulmonary clinic.

3. Discussion

Foreign body aspiration can present with a potentially fatal respiratory emergency. It can diagnostic challenge especially because chest radiographs can be normal in up to 25% of patients [6]. Aspiration of medications present in various ways depending on the chemical property. Alendronate and tetracycline are known to dissolve within the airway producing marked mucosal edema, an inflammatory response to the extent of pseudo-membrane formation [7,8]. Non-dissolving compounds like Ciprofloxacin, Sucralfate, and Calcium carbonate are reported to present with airway obstruction [9,10]. Iron pills (ferrous sulfate), Nortriptyline, and Zinc are well known to cause chemical burn along with a profound inflammatory response [11–13]. Literature on iron pills aspiration is merely limited to a few anecdotal case reports with limited clinician awareness. Considering the common use of iron supplements, and the potential severity of aspiration related airway injury, clinicians should be fully cognizant of the interaction between aspirated iron and airway passages. Herein, we have sought to perform a brief literature review.

Iron supplements are commonly used to treat iron deficiency anemia or as a micronutrient supplement. Ferrous sulfate (FeSO_4) is the most common preparation reported in association with the “iron pill aspiration” (IPA). IPA associated with ferrous gluconate or ferrous fumarate have been previously reported in the literature. Iron deposits in the bronchial wall induce direct chemical burn, further acute intense inflammatory response eventually leading to granuloma formation, with a fibrotic response leading to stenosis [11,14]. The caustic property of iron results from exposure of Ferrous sulfate results to the acidic pH [3] of airway secretions. Ferrous ions are converted to a ferric state which promotes the formation of hydroxyl radicals. This results in free radicals mediated injury along with caustic chemical burn of the bronchial mucosa [12]. A shorter duration of contact can result in local irritation, while a pro-

Table 1

Results of Pulmonary function test performed at four weeks after discharge.

Parameter	Results
Forced expiratory volume in 1 s (FEV1)	Pre-Bronchodilator: 2.02L (71%) Post-Bronchodilator: 2.00 (70%)
Forced vital capacity (FVC)	Pre-Bronchodilator: 2.29L (65%) Post-Bronchodilator: 2.30L (65%)
FEV1/FVC (%)	Pre-Bronchodilator: 88% Post Bronchodilator: 87%
Slow vital capacity (SVC)	2.58 L (73%)
Expiratory reserve volume (ERV)	0.14L (11%)
Lung volumes measured using plethysmography	
Total lung capacity (TLC)	4.0L (79%)
Residual volume (RV)	1.42L (81%)
RV/TLC ratio	36 (103%)
Diffusion capacity	
DLCO (ml/min/mmHg)	13.32 (54)
VA (L)	2.8 (55%)

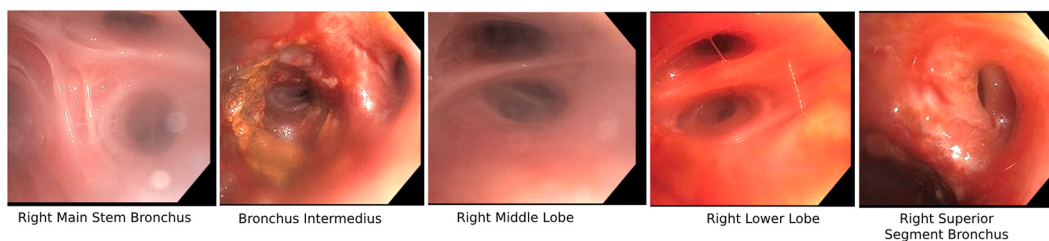


Fig. 2. Findings on follow-up bronchoscopy at six weeks following initial presentation.

longed duration of contact can result in airway and parenchymal destruction with a fibrotic healing response [12]. Since the extent of damage is determined by the duration of contact with the aspirated pill, it highlights the importance of early bronchoscopy [12]. A triad of history of aspiration of the pill, airway inflammation, and iron particles in bronchial biopsy specimens has been described as a triad of iron pill aspiration syndrome by Lee et al. [11]. Since, FeSO_4 rapidly disintegrates in the airway it may not be detected via bronchoscopy. An endobronchial biopsy specimen may show iron deposits up to a year after aspiration [11,15]. Bronchial washings may also reveal reactive epithelial cells and histiocytes with both intracellular and extracellular, refractile, crystalline material positive for Prussian-blue iron stain [16]. Given the risk of severe aspiration-related airway injury it would be worthwhile to avoid Ferrous sulfate and use alternative iron preparations, especially in patients at risk of aspiration and swallowing disorders.

We performed an extensive literature search in PubMed, EMBASE, and Scopus using the keywords iron or iron sulfate and aspiration. We were able to retrieve 45 cases reported in the literature from 1975 to December 2022. Excerpts from the articles are summarized in Table 2. Among the reported cases age range was 22 months–92 years with a mean age of 68.44 (IQR 16.34). Clinical features at presentation include cough, shortness of breath and wheezing. 14 patients of the reported case had hemoptysis at the initial presentation [4,16–21]. Two cases were reported to present with fatal hemoptysis due to hemorrhage originating from the airway [19,21]. Abnormalities detected on plain radiographs of the chest are limited and mostly include suggestive findings including post-obstructive atelectasis and consolidation. Cases reported after 2010 have reported abnormalities in computed tomography (CT) of the chest including detection of foreign bodies, post obstructive atelectasis, consolidation, and airway stenosis. This can be attributed to wider availability and use of high-resolution CT [3,12,22–30]. It further suggests higher diagnostic yield of CT chest compared to chest x-ray in setting of clinical suspicion. Bronchoscopy is the quintessential part of the overall clinical management as it is both diagnostic and therapeutic. Since the degree of injury is determined by the duration of contact with caustic byproducts of Ferrous sulfate, early bronchoscopy can help with aspiration of degraded iron pill minimizing the contact time. Bronchoscopic aspiration of the pill content is reported in eleven cases [1,4,12,16,17,19,20,23,27–29,31,32]. Other therapeutic measures during the acute phase includes bronchial lavage. Cytology specimen from the bronchial washing are reported to have necro-inflammatory exudates involving extracellular golden-brown fibrils [16,28]. Most commonly reported long term sequelae include fibrotic response and resultant bronchial stenosis, noted as granulation tissue and fibrosis on histopathology [11,12,20]. Use of systemic corticosteroids is well reported in the literature to prevent fibrotic response and resultant airway stenosis [1,12,18,27,28,33,34]. Saeed et al. have reported the use of intralesional steroids at a stenotic segment [35]. Johnson et al. have reported debridement with the use of cryoprobe in one of the two cases [23]. They have also reported local administration of methylprednisone and topical administration of mitomycin-C [23]. Use of topical mitomycin-C combined with bronchoplasty has been previously reported by Lee et al. [11].

Herein our patient was treated with early bronchoscopy. A part of the degraded pill was aspirated using a bronchoscope which suggests that there was a minimization of the duration of contact. Extensive debridement was performed with bronchoalveolar lavage using normal saline. Cryoprobe debridement could not be performed due to logistical constraints. Post-procedurally high PEEP ventilation was used to minimize airway collapse. Systemic corticosteroid was administered to curtail the inflammatory response. In the follow-up bronchoscopies at 48 hours and four weeks there was no evidence of airway stenosis. Follow-up PFT showed mild restrictive ventilatory defect along with reduced DLCO in the setting of reduced VA. This can be attributed to parenchymal loss from intense inflammatory response.

4. Conclusion

Iron pill aspiration syndrome can result in life-threatening caustic and inflammatory injury of the airway with potential long-term sequelae. Clinicians should be aware of this clinical conundrum and should have a high index of suspicion. Further, considering the caustic properties of Ferrous sulfate injury it would be worthwhile to avoid it and use alternative iron preparations, especially in patients at risk of aspiration and swallowing disorders.

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Written informed consent

Obtained.

Ethical approval

Abiding with the ethical principles.

IRB approval

Waived.

Contribution

YRS conceived the concept and wrote the entire manuscript. PB, DS, KS, IW, DS, TMAK, NK, RTS revised the manuscript contributed to its scientific content.

Table 2

Summary of case reports of iron pill aspiration syndrome reported in literature from 1975 to December 2022.

Author-Year	Age	Clinical Presentation	Bronchoscopy	Imaging
Marco et al., 2022 [31]	22 months	Sudden onset of dry cough after foreign body aspiration.	Foreign body retrieved using a bronchoscope. Inflammatory response was noted in the initial bronchoscopy. Later developed bronchial stenosis which was treated with sequential balloon bronchoplasty.	Chest x-ray 6 mm foreign body in the right bronchus intermedius
Sarda et al., 2022 [22]	81	Cough and Wheezing	Flexible bronchoscopy performed later revealed mucosal irregularities with orange-red pigmentation with bronchial stenosis in the right middle lobe and a tight bronchial stenosis at the superior segment of the left lower lobe.	Tree in bud opacity on CT chest.
Saeed et al., 2021 [35]	50	Presented months after aspiration of iron pill with wheezing and dyspnea on exertion	Bronchoscopy revealed complete obstruction of the right lower lobe (RLL) bronchus with thick mucoid secretions coated in iron and granulation tissue. Follow up bronchoscopy a few weeks later showed similar finding. Cultures obtained grew cryptococcus neoformans. Patient was she was treated with oral Fluconazole for 1 year. Stenotic segment was later treated with intralesional steroid. Stenosis partly improved after administration of intra-lesional steroid.	Normal chest x-ray
Kohli et al., 2020 [36]	57	Persistent cough and hemoptysis	Mucosal inflammation, granulation tissue, and stenotic segments	–
Johnson et al., 2019 [23]	Two cases Case 1: 62 Case 2: 69	Acutely aspirated Iron tablet while traveling in a car Presented with chronic cough, had a history of aspiration one month prior to presentation.	At bronchoscopy, it was noted metallic, disintegrated iron pill was found in the bronchus intermedius and in the right lower lobe. Cryoprobe, 12mm endobronchial basket, and forceps were used to completely remove the metallic material from the airway wall. After inspection of the airway, methylprednisolone (Depo-Medrol) injection and topical Mitomycin C was applied. Initial bronchoscopy noted inflamed, discolored mucosa throughout the right lower lobe. Biopsy was indicative of prior pill aspiration. In addition to airway clearance, Solumedrol and Topical Mitomycin C were applied.	CT chest: 10 mm foreign body in the CT chest: right lower lobe bronchus Right lower lobe obstruction
Tihabono et al., 2018 [37]	80	Cough chest pain, fever, and wheezing	Nodular mucosal changes at the carina, and bronchial segment between the right middle and lower lobe bronchus	–
Thapa et al., 2018 [38]	57	Persistent cough for six weeks	Intense inflammatory response with granulation tissue. Bronchial stenosis at multiple segments, referred for endobronchial intervention	–
Keshishyan et al., 2018 [24]	70	Presented three months after aspiration with cough and dyspnea	Initial bronchoscopy revealed an endobronchial lesion in the bronchus intermedius (BI). Endobronchial biopsies and washings were non-revealing. Positron emission tomography (PET) scan revealed a focal area of wall thickness and mild hypermetabolic uptake involving the right BI. A repeat biopsy was non-revealing. Findings likely represented inflammatory scarring. Eventually underwent balloon dilatation.	CT chest narrowing of the bronchus intermedius
Chu et al., 2018 [3]	61	Presented four week following aspiration of iron pill	Necrosis and stenosis of distal right bronchus intermedius	CT chest showed ground glass infiltrates in the right lower lobe
Okamoto et al., 2017 [25]	91	Presented with dyspnea and cough	Hemorrhagic friable mucosa in the left mainstem bronchus. Near complete stenosis was removing the inflammatory debris	CT chest near complete occlusion of left mainstem bronchus.
Abusief et al. (2017) [26]	44	Severe cough and wheezing	Inflammation and stenosis localized at the bronchus intermedius	8 mm foreign body localized at the bronchus intermedius on CT chest
Henriques et al., 2017 [39]	91	Presented with fever, cough, and chest pain.	Bronchoscopy performed after one week revealed friable necrotic airway mucosa	Chest x-ray: consolidation of right middle and lower lobes
Lim et al., 2016 [27]	91	One week of cough, sputum expectoration and dyspnea	Bronchial mucosa was yellow brown and friable to touch	Chest x-ray: atelectasis and consolidation of the right lung. CT scan: radio-dense contents in the right bronchus.

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Table 2 (continued)

Author-Year	Age	Clinical Presentation	Bronchoscopy	Imaging
Somalaraju et al., 2016 [32]	80	Progressive cough and dyspnea for five days	Bronchial mucosa surrounding the pill was pigmented	Chest x-ray suspicious for aspiration into the right middle lobe.
Caterino et al., 2015 [12]	Four cases	Aspiration during pregnancy, cough, dyspnea, and chest discomfort	Severe stenosis of the bronchial lumen in the bronchoscopy performed after pregnancy	CT chest, pulmonary consolidation
	Case 1: 36			
	Case 2: 40	Cough, chest discomfort, and dyspnea following aspiration	Ulceration and necrosis of bronchus intermedius, stenosis noted in bronchoscopy performed after one month.	
	Case 3: 70	–	Patient was evaluated three months after initial aspiration, tablet was visible without major mucosal changes	–
	Case 4: 92	Persistent dry cough and stridor	Circumferential granuloma occluding the bronchial lumen	–
Kwak et al., 2015 [28]		Prior history of aspiration. Presented with cough along with brown sputum expectoration.	Nodular appearing mucosa friable to touch	Near complete atelectasis of left lower lobe on chest x-ray and CT chest.
Venci et al., 2014 [40]	53	Presented with history of dyspnea four months after the aspiration event.	Severe bronchial stenosis four months after the aspiration event.	Normal chest x-ray and CT chest
Jimenez Rodriguez et al., 2013 [14]	66	Aspiration noticed by patient; pill expectorated with coughing four days later	Stenosis of Left mainstem bronchus at follow up bronchoscopy performed six months later	CT chest was normal
Cimino-Mathews, 2013 [16]	84	–	Friable mucosa with poplar lesions	Normal chest x-ray
Delgado-Sanchez et al., 2012 [4]	64	Cough and hemoptysis immediately following aspiration	Friable ulcerated mucosa with easy bleeding.	Normal chest CT scan
Maw et al., 2012 [33]	84	Presented 4 h after aspiration with coughing and expectoration of brown sputum.	Inflammation along with brown tablet remnants. Follow up bronchoscopy at two months revealed granulation tissue	Normal chest x-ray
Grosu et al., 2012 [29]	68	Patient was asymptomatic, incidentally detected foreign body on PET CT for breast cancer.	Brown necrotic material retrieved on bronchoscopy.	Foreign body incidentally detected on PET CT
Takahashi et al., 2010 [30]	84	Fever and Dyspnea	Foreign body removed during bronchoscopy	Foreign body noted on CT scan.
Zeno and Duffy, 2009 [41]	72	–	Foreign body noted during bronchoscopy. Severe stenosis one year later	Not reported
Raos et al., 2004 [42]	Two pediatric cases	Case 1 required pneumonectomy, Case 2 required stenting and laser dilatation.	Not reported	Not reported
Kim et al., 2003 [17]	Three cases	Hemoptysis	Edematous friable bronchial mucosa with areas of necrosis	Chest X-ray: Partial left lower lobe collapse
	Case 1: 76			
	Case 2: 66	Patient had background history of lymphoma, presented with fever and cough	Bronchial lumen obstructed by a foreign body along with stricture formation	Chest X-ray: Right lower lobe consolidation
	Case 3: 64	Fever, cough	Ulceration and sloughing of bronchial mucosa	Chest X-ray: Right lower lobe consolidation
Clarke and Kim, 2002 [18]	75	Chest discomfort and hemoptysis	Friable, edematous bronchial mucosa	Chest X-ray: Left lower lobe collapse.
Lee et al., 2002 [11]	69	Chocking, coughing, and wheezing.	Bronchoscopy performed two months after aspiration. Extensive inflammation with greenish brown necrotic material in the left mainstem bronchus. Left main stem bronchus stenosis at three months after aspiration	Chest X-ray normal

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Table 2 (continued)

Author-Year	Age	Clinical Presentation	Bronchoscopy	Imaging
Hernandez and Martinez, 1997 [34]	77	Dysphagia, foreign body sensation and cough	Friable necrotic mucosa. Pill was visualized during bronchoscopy and was retrieved. An ulcer was visualized after extraction of the aspirated pill. Changes were persistent at revision bronchoscopy at six weeks.	Chest X-ray in Left mainstem bronchus.
Babatasi et al., 1996 [19]	Reported two cases.	Presented with hemoptysis 9 days after aspiration.	Necrotic mucosa	Chest X-ray: Right lower lobe collapse
	Case 1: 59			
	Case 2: 54	Presented with cough along with voluminous hemoptysis	Polypoidal mass like material covered with necrotic tissue. Could not be retrieved with bronchoscopy	Patchy opacification of Left middle and lower zones.
Lamaze et al., 1994 [1]	83	Presented with chest pain along with cough in the absence of history of aspiration.	Inflammation and stenosis of bronchial wall	Normal chest. X-ray
Godden et al., 1991 [20]	84	Presented with cough and hemoptysis for four weeks	Bronchial mucosa lined with greenish brown material	Patchy opacification of right and left mid and lower lung zones.
Evrard et al., 1990 [21]	x	Presented with 10 days of hemoptysis after Iron pill aspiration. Treated with therapeutic bronchial lavage with sodium bicarbonate.	Circumferential erosion of the bronchial mucosa	Not reported
Tarkka et al., 1988 [43]	60	Presented with choking, wheezing,.	Severe bronchial stenosis noted three months after aspiration	Normal chest x-ray
Mizuki et al., 1989 [44]	44	Iron pill aspiration noticed. Patient presented with wheezing and shortness of breath. Moderate partial stenosis of the bronchus noticed later. Bronchoscopic removal of the pill in the acute phase.	Not available	Not available
Hirschler-Schulte et al., 1981 [45]		Abstract not available in the online repository		
Melilo et al. [5], 1975		Abstract not available in the online repository		

Agreement

All the authors have independently read the content of the submitted manuscript and are agreement with the submission.

Declaration of competing interest

No conflict of interest

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