CASE REPORT

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Mediastinal Plexiform Neurofibroma Presenting as Asthma in a Patient with Neurofibromatosis Type 1: A Case Report

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ABSTRACT

Plexiform neurofibroma (PN) is a pathognomonic feature of neurofibromatosis type 1 (NF1). When the clinical manifestations of NF1 are unrecognized and PN develops in deep anatomical locations, diagnosis may be delayed until the tumor is large enough to compress adjacent structures. We report a case of PN in which delayed recognition of NF1 led to years of misdiagnosis. A 27-year-old female with a history of poorly controlled asthma and a bizarre, lobulated opacity on chest X-ray had experienced respiratory symptoms since her early twenties, initially diagnosed with asthma at age 22. Despite multiple courses of antibiotics, bronchodilators, and steroids, her symptoms persisted. Computed tomography (CT) revealed a lobulated mass encasing the bronchial tree and pulmonary vessels, consistent with PN. The combination of a positive family history and a thorough physical examination is a cornerstone in the diagnostic process, ultimately establishing the diagnosis of NF1. This case underscores the crucial importance of a comprehensive clinical examination in the early recognition of PN and NF1.

Keywords: : Café au lait spots; Plexiform neurofibroma; Neurofibromatosis type 1; Case report; Asthma.

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INTRODUCTION

Neurofibromatosis type 1 (NF1) is an autosomal dominant disorder. It is caused by a mutation in the NF1 gene on chromosome 17q11.2 that is characterized by the formation of multiple benign nerve sheath tumors, such as plexiform neurofibroma (PN) associated with skin pigmentations, malformations of the bone, and formation of numeroustumors in the central and peripheral nervous systems [1]. It results from an NF1 gene mutation responsible for the formation of numerous benign nerve sheath tumors. PN is the characteristic tumor that develops in the context of NF1 and is considered pathognomonic for the condition [2]. The epidemiology and clinical characteristics of PN vary with the age of the patients and, most importantly, with the site of the lesions. Cutaneous lesions usually presented early as a disfiguring cutaneous mass, while those involving the internal organs, such as the gastrointestinal, urinary tracts, and respiratory tract, usually had a silent course till a mass effect was exerted on the surrounding body organ [3]. Mediastinal PN primarily involves the sympathetic chain and involves the posterior mediastinum. A protean of presentations had been described, including radicular chest pain, shortness of breath, and cough [4]. Diagnosis is usually suggested on imaging, including computed tomography (CT) scan and magnetic resonance imaging (MRI); however, on endobronchial lesions, both imaging modalities could be negative, and the diagnosis is suggested only by biopsy through a bronchoscopy [5].

It is sometimes challenging to distinguish mediastinal neu-

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rofibroma from other mediastinal tumors, such as lymphoma, schwannoma, and malignant peripheral nerve sheath tumors, owing to similar imaging characteristics. Therefore, further work-up is required, and occasionally, histopathological confirmation is needed [6]. We present an uncommon manifestation of PN in a patient with NF1, characterized by respiratory symptoms attributable to a peri-bronchial PN. This case poses a diagnostic challenge, as the failure to recognize the clinical stigmata of NF1 complicates the identification of the underlying pathology.

CASE PRESENTATION

A 27-year-old Iraqi female presented to the outpatient respiratory clinic of Al-Karama Hospital, Baghdad, Iraq, with a history of poorly controlled asthma and a bizarre, lobulated opacity on multiple chest X-rays (CXR). She had been experiencing respiratory complaints, including dry cough and shortness of breath, since her early twenties. At 22 years of age, she was diagnosed with asthma and prescribed daily controller medications, but her symptoms persisted. The patient's physical examination revealed numerous small brownish freckles widely distributed across the chest, abdomen, and back, along with multiple larger brownish lesions. The patient presented to the outpatient respiratory clinic of Al-Karama Hospital, Baghdad, Iraq, predominantly located on the thighs. In addition, multiple subcutaneous firm palpable, not tender nodules were seen involving the scalp, forehead, forearms, and thighs (Figure 1). These cutaneous lesions first appeared in childhood and have progressively increased in size and number with age.

Multiple previous CXRs during presumed asthma exacerbations showed lobulated outline branching opacities involving the right lung radiated from the right hilum extending to the upper, middle, and lower zones, with the first CXR done in 2020 when the lesion diagnosed as consolidation and antibiotics were given (cephalosporin injection and azithromycin oral tablets), although the symptoms not significantly resolved. The patient continues to seek medical advice, and subsequent chest radiographs, taken in 2024 and 2025, revealed the same pulmonary lesion in the exact location and distribution (as noted in Figure 2).

Contrast-enhanced CT of the chest is requested for further evaluation, which shows a well-defined lobulated outline elongated sausage-shaped hypo dense mass involving the subcarinal region extending to the hilar region and surrounding the upper, middle, and lower lobe bronchi linearly encasing the pulmonary vessels, causing a mass effect in the underlying bronchi inform of narrowing resulting in lung hyperinflation. These masses showed mild enhancement post-contrast administration (Figure 3-A and B). The sections within the upper abdomen show a few mildly enhancing elongated masses involving the neural foramina bilaterally in keeping with neurofibromas (Figure 3-C).

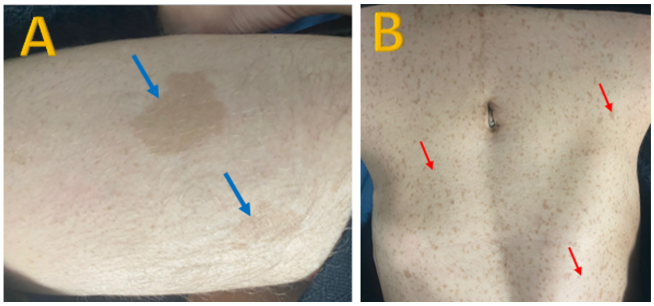

Figure 1. A) The upper right thigh shows two well-demarcated, irregularly shaped, smooth surfaces with a light brown cafe au lait spot (blue arrows). B) Anterior abdomen shows clusters of small, rounded freckles distributed over the abdomen, flank, and pelvic skin (red arrows).

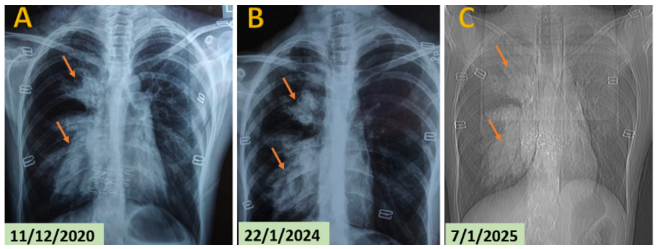

Figure 2. Posterior-anterior chest X-ray A) on 2020, B) on 2024, C) on 2025: Shows a lobulated outline of elongated branching opacities arising from the right hilum extending to the upper, mid, and lower zones (orange arrows).

The lung window of the scan showed signs of hyperinflation, and mild interstitial findings indicated some subpleural reticulations involving the apical segments of both upper lobes and subpleural bullae and blebs (Figure 4).

Ultrasound of the palpable skin lesions showed elongated hypoechoic masses with no significant internal vascularity in keeping with subcutaneous neurofibromas (Figure 5). The fundoscopic examination was normal. A cervical spine MRI shows multiple bilateral neurofibromas involving the cervical neural foramina. Brain MRI was normal. Her family's history showed that several of her relatives had similar skin pigmentation and subcutaneous neurofibromas. The patient met the criteria for neurofibromatosis 1 (having a first-degree relative with NF1, more than two neurofibromas, and more than six

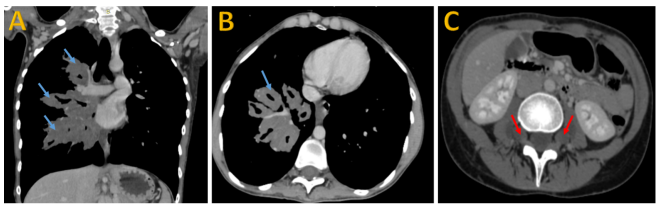

Figure 3. Contrast-enhanced computed tomography scan of the chest and upper abdomen–mediastinal window :(A) coronal section, (B and C) axial sections. A and B show extensive, confluent lobulated outline low- density masses (17HU) (blue arrows) extending from the carina region, right hilum and extending along the right bronchial tree encasing the pulmonary vessels, showing mild enhancement post contrast administration (40 HU)., lobulated, low-density masses (17HU) (blue arrows) extending from the carina region, right hilum, and e right bronchial tree encasin,g the pulmonary vessels, shows shwhich showhancement post conpost-contrast C) show hypo-enhancing hypo-dense masses involving the intervertebral foramen bilaterally extending medially to the psoas muscles (red arrows).

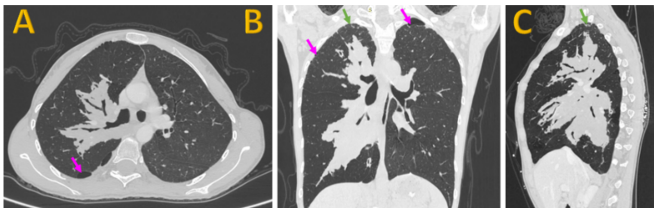

Figure 4. Contrast-enhanced computed tomography scan of the chest (lung window) shows hyperinflation and mild subpleural reticulation predominantly involving the apical segment of the right upper lobe (green arrows) and subpleural bullae (pink arrows).

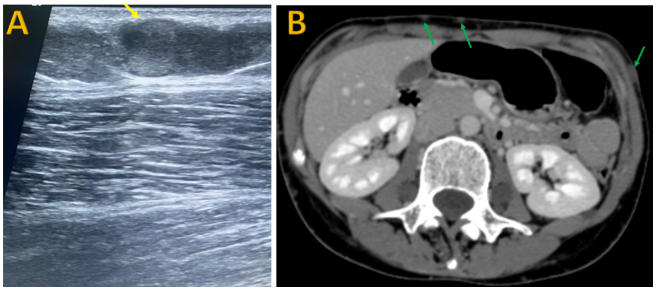

Figure 5. The ultrasound of the forehead shows a well-defined, lobulated, outlined, elongated hypoechoic mass lesion involving the subcutaneous tissue (yellow arrow). B) axial contrast-enhanced computed tomography scan section at the upper abdomen shows a few small subcutaneous enhancing fibromas (green arrows).

café au lait spots (Figure 1), so the pulmonary lesion was diagnosed as PN involving the pulmonary plexus. Chest radiograph in 2025 reveals the same mass lesion without change in size. Financial limitations prevented her from undergoing the recommended genetic testing.

Following a thorough assessment and review of the chest CT scan images, radiology reports, and the patient's clinical examination by a multidisciplinary team, the thoracic surgeon opted against surgical intervention. The decision was based on the patient's fulfilment of diagnostic criteria for NF1, along with the presence of a large, branching chest mass that encased the pulmonary arteries and enveloped the bronchial tree, rendering surgery highly complex and hazardous. Over the past six months, the patient has been managed with conservative and symptomatic therapy, accompanied by regular follow-up visits to the respiratory clinic. During this period, no complications or exacerbations were reported.

Informed consent was obtained from the patient for publishing her clinical data and accompanying images.

DISCUSSION

PN has been rarely reported as an isolated lesion, more commonly associated with systemic NF1 [7]. It arises in about one-third of NF1 cases with no ethnic, racial, or sex predilection [8]. Most reports indicate that PN is present in early childhood or even at birth; however, when it arises in deep organs, it may not be detected early, as in the current case, it was not diagnosed until her third decade of life [6].

The accurate diagnosis of PN is of critical importance due to its inherent potential for malignant transformation [9]. Unfortunately, it may pose a significant diagnostic challenge when it develops within internal organs, as it may remain undiagnosed for years or even decades, only becoming apparent once it exerts a mass effect on adjacent structures [4].

In the current case, the patients had other stigmata of NF1, but the condition escaped diagnosis. The respiratory symptoms were initially misattributed to asthma, and the persistent pulmonary shadow observed on CXR was repeatedly interpreted as a chest infection. The clothing style commonly worn by Mediterranean women, characterised by long sleeves and the hijab, could explain the missing cutaneous manifestation of NF1, which subsequently impedes the suspension of peri-bronchial PN [10]. Having a high degree of suspicion is fundamental for PN diagnosis, as the condition has a non-specific presentation. Previously reported non-cutaneous PN cases included the gastrointestinal tract, which presented as abdominal pain [11, 12]. Spinal nerve compression sequelae, mass effect, paresthesia, numbness, and pain can all be symptoms of deep lesions [13].

Confirmed cases of PN may present years after the initial diagnosis of respiratory symptoms. Irion et al. reported a PN case diagnosed at 15 years old age, and presented at 65 years with worsening dyspnea, chronic cough, and recurrent chest infections. Imaging revealed bilateral emphysematous bullae and multiple PN lesions in the larynx and tracheobronchial trees, which were subsequently resected via bronchoscopy [2]. The mediastinal PN had been presented with chest pain, dysnea or shortness of breath, or may be incidentally found on imaging The mediastinal PN had been presented with chest pain, dysnea, or shortness of breath, or may be an incidental finding on imaging [4, 13]. To our knowledge, four cases have been reported to have mediastinal PN. Chalmers et al. reported 2 cases; the first case was a 2-year-old boy who presented with a recurrent chest infection and stridor. Examination confirmed a supraclavicular mass and café-au-lait spots. Imaging studies showed a middle mediastinal mass extending from the lung apices to the diaphragm with narrowing of the trachea and left bronchus; additionally, there was subluxation of the C2 vertebrae. The second case was a 10-year-old boy who suffered from a cyanotic choking attack post-febrile illness; he had a positive family history and café-au-lait spots. Imaging showed a widened posterior mediastinum with a normal lung field [1]. Pivnick et al. reported a 1.5-year-old baby boy with a positive family history and nasal PN. During a randomly performed CT scan, an incidental asymptomatic mediastinal mass was discovered, extending from the subclavian area to the aorta and pulmonary artery, with associated narrowing of the left bronchus [14]. The fourth case was a 21-year-old asymptomatic male who was routinely scanned, and the CXR showed a widened mediastinum. A CT scan showed extension up to the lower neck and down to the subdiaphragmatic area; the case was followed for 2 years and showed no symptoms or progression [15]. The fifth case, which is the current case, the patient presented with a longstanding cough and shortness of breath, which suggests the diagnosis of asthma as the PN exerts a mass effect on the bronchial tree. The mass extending from the mediastinum, encasing the bronchial tree, has not changed its shape during the 5 years of follow-up. In addition, the patient has innumerable subcutaneous neurofibromas, multiple cafés au lait macules, axillary, groin, and diffuse skin freckles, and a first-degree relative's history of NF1; all these have led to the diagnosis of NF type 1.

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When the patient is symptomatic and treatment is mandatory, a multidisciplinary team should be consulted when deciding between surgical and medical management; if there is no substantial morbidity and the PN can be removed, surgery is usually the best option. Regretfully, this is unfeasible in most situations because PN is invested with the nerve [14]. The first FDA-approved treatment for inoperable PN in patients with NF1 is selumetinib, an MEK inhibitor approved for symptomatic inoperable cases in the pediatric group. It has shown optimistic results [3]. However, its use is hindered by high cost and limited global bioavailability, as in the current case.

It is advisable to follow the patient, as malignant peripheral nerve tumors may develop in 8%-12% of PN cases [7]. A whole-body MRI screening is recommended, but the patient's family declined it due to financial constraints. Physicians should remain vigilant for warning signs, including rapid growth and worsening pain or progressive neurological weakness.

CONCLUSION

This case describes an exceptionally delayed diagnosis of deep-seated PN in a female patient with previously undiagnosed NF1. For seven years, the condition was misdiagnosed and managed as bronchial asthma, representing an unusually prolonged clinical course in which key radiological findings were repeatedly misinterpreted. The definitive diagnosis was established through the recognition of a positive family history and multiple cutaneous café-au-lait spots, underscoring the critical importance of a thorough clinical examination and consideration of the genetic context. key learning points emerge from this mediastinal PN case. Numbered list First, atypical asthma, particularly when accompanied by persistent pulmonary imaging abnormalities, should prompt consideration of alternative diagnoses, including intrathoracic PN. Second, the failure to recognize NF1, especially in settings where clothing practices conceal the skin, may delay diagnosis and expose patients to unnecessary treatments. Finally, given the risk of malignant transformation and the inoperability of large, infiltrative PN underscores the necessity of early recognition and the value of long-term multidisciplinary management.

Availability of Data and Materials. All relevant data have been published.

ETHICAL DECLARATIONS

Acknowledgments

None.

Ethics Approval and Consent to Participate

Written approval was gained from the Ethical Approval Committee of Al-Kindy medical College (Reference number 203, April 2025). Informed consent was obtained from the patient for the publication of the case and its images.

Consent for Publication

Informed consent was obtained from the patient for the publication of the case and its images.

Availability of Data and Material

Not applicable.

Competing Interests

The authors declare that there is no conflict of interest.

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Authors' Contributions

All of the listed authors agreed on the final manuscript version for publication and made substantial, direct, and intellectual contributions to the work.

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