# PARANEOPLASTIC HYPOGLYCEMIA SECONDARY TO A SOLITARY FIBROUS TUMOR: A CASE OF DOEGE-POTTER SYNDROME

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**Abstract**

Paraneoplastic syndromes result from tumor-secreted hormones or immune cross-reactivity, with paraneoplastic hypoglycemia—specifically non-islet cell tumor hypoglycemia (NICTH) induced by "big" insulin-like growth factor-2 (IGF-2)—representing a rare but critical clinical entity. We report the case of a 63-year-old woman presenting with acute confusion and dysarthria. Initial evaluation revealed profound hypoglycemia (33 mg/dL), which was managed with intravenous glucose, leading to rapid clinical recovery. Biochemical analysis during the episode showed appropriately suppressed insulin (0.30 μIU/mL) and C-peptide (0.21 ng/mL) levels, along with normal cortisol, suggesting an extrapancreatic source. Radiographic imaging via chest X-ray and CT scan identified a 14.8 cm heterogeneously enhancing mass in the left lower lung. Histopathological examination and positive CD34 staining confirmed a solitary fibrous tumor. The constellation of a solitary fibrous tumor and IGF-2-mediated hypoglycemia confirmed a diagnosis of Doege-Potter Syndrome. This case highlights the importance of considering non-islet cell tumor hypoglycemia in patients presenting with refractory low blood glucose and a localized mass.

**Keywords:** paraneoplastic hypoglycemia, non-islet cell tumor hypoglycemia, solitary fibrous tumor, Doege-Potter Syndrome, insulin-like growth factor-2

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## Introduction

Paraneoplastic syndromes encompass a diverse group of clinical disorders caused by systemic effects of a malignancy, occurring independently of local tumor invasion or metastasis. These syndromes are typically mediated by the ectopic production of hormones, peptides, or cytokines, or via immune-mediated cross-reactivity. Among these, paraneoplastic hypoglycemia is a rare but life-threatening metabolic complication. While most clinicians first consider insulinoma or iatrogenic causes when faced with fasting hypoglycemia, non-islet cell tumor hypoglycemia (NICTH) remains a critical differential diagnosis, particularly in patients with large mesenchymal or epithelial tumors.[1]

The most common mechanism underlying NICTH is the overproduction of an incompletely processed form of insulin-like growth factor-2, often referred to as "big" IGF-2.[2] Unlike mature IGF-2, this high-molecular-weight precursor does not readily bind to its carrier proteins (IGFBP-3 and acid-labile subunit), resulting in an increased fraction of free IGF-2 that can cross the capillary membrane and activate insulin receptors. Thus, it increases peripheral glucose utilization and suppresses hepatic glucose output, clinically mimicking hyperinsulinism despite suppressed endogenous insulin and C-peptide levels.

Doege-Potter Syndrome (DPS) is a specific and exceedingly rare subset of NICTH caused by a solitary fibrous tumor (SFT). First described independently by Doege and Potter in 1930[3], this syndrome is associated with large, typically slow-growing mesenchymal tumors most often found in the pleura, though they can arise anywhere. Given the rarity of SFTs and the fact that less than 5% of these tumors result in symptomatic hypoglycemia, DPS is frequently misdiagnosed during initial presentation.[4]

In this report, we describe a case of a 63-year-old female presenting with severe neuroglycopenic symptoms. The diagnostic workup revealed a massive pulmonary solitary fibrous tumor and biochemical evidence of NICTH, ultimately confirming a diagnosis of Doege-Potter Syndrome. This case emphasizes the clinical challenge of managing refractory hypoglycemia in the setting of large thoracic masses.

## Case report

A 63-year-old female with a medical history of hypertension and dyslipidemia, managed with amlodipine (5 mg/day) and simvastatin (20 mg/day), was referred to the Internal Medicine Department for the evaluation of refractory hypoglycemia. The patient's family reported a one-week history of progressive acute confusion and dysarthria. Prior to the onset of these neurological symptoms, she had been physically fit and independent. Physical examination upon admission revealed a patient in a confused state, with neuroglycopenic symptoms that fluctuated in correlation with her glycemic status. Thoracic examination was notable for dullness to percussion and diminished breath sounds over the left lower lung field; the remainder of the physical examination, including abdominal and cardiovascular assessments, was unremarkable.

During a symptomatic episode of neuroglycopenia, laboratory investigations confirmed profound hypoglycemia with a capillary blood glucose of 33 mg/dL. The patient improved rapidly after intravenous dextrose, fulfilling Whipple's triad.[5] A comprehensive biochemical workup was performed during the hypoglycemic state to determine the etiology. Results showed markedly suppressed serum insulin (0.30 μIU/mL; reference: 1.9–23) and C-peptide (0.21 ng/mL; reference: 0.98–4.32). Serum cortisol levels were within the normal range, effectively ruling out primary adrenal insufficiency as a contributing factor. The combination of low blood glucose with suppressed insulin and C-peptide levels strongly suggested a non-islet cell tumor hypoglycemia (NICTH) mechanism. **Table 1** shows the laboratory data at admission.

Radiographic evaluation was initiated to identify a potential extrapancreatic source of the hypoglycemia. A chest X-ray revealed a massive opacity occupying the lower half of the left hemithorax (**Figure 1**). Subsequent computed tomography (CT) of the chest identified a large, well-circumscribed, heterogeneously enhancing mass in the left lower lung, measuring approx-

**Table 1.** Laboratory data

| Variable | At admission | Reference range |
|---|---|---|
| Hemoglobin (g/dL) | 10.9 | 12 - 14 |
| White blood cell count (cell/uL) | 10390 | 4060 - 10600 |
| Platelet count (cell/uL) | 303000 | 173000 - 383000 |
| Blood urea nitrogen (BUN) (mg/dL) | 4 | 8 – 20 |
| Creatinine (Cr) (mg/dL) | 0.60 | 0.55 – 1.02 |
| Albumin (g/dL) | 3.6 | 3.5 – 5.2 |
| Total bilirubin (TB) (mg/dL) | 0.99 | 0.3 – 1.20 |
| ALT (U/L) | 8 | < 35 |
| AST (U/L) | 22 | < 35 |
| Blood sugar level (mg%) | ***33*** | 70 - 200 |
| Morning cortisol level (µg/dL) | 12.47 | 6.7 – 22.6 |
| Insulin (µIU/mL) | ***0.33*** | 1.9 - 23 |
| C-peptide (ng/mL) | ***0.21*** | 0.98 – 4.31 |
| Serum ketone (mmol/L) | 0.03 | 0.02 – 0.27 |

ALT (SGPT), alanine aminotransferase; AST, aspartate aminotransferase

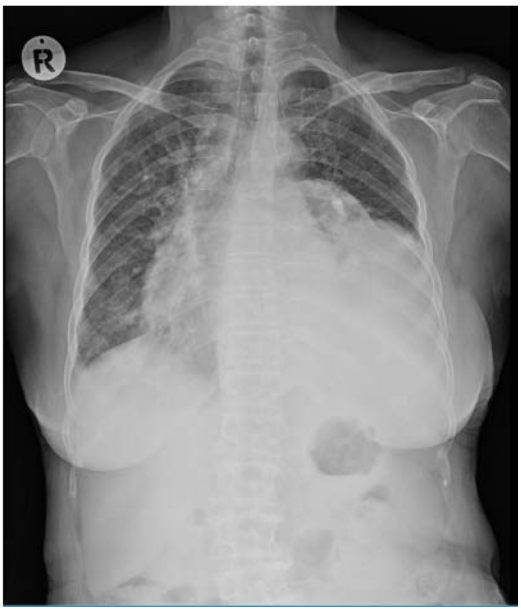



**Figure 1.** Chest x-ray images showed a heterogeneous well-circumscribed mass at the left lower lung, of which the silhouette lay on the left heart border with an obtuse angle. The estimated diameter from the chest X-ray was 15 cm.

imately 14.8 cm in its largest diameter (**Figure 2A, 2B**). No distant metastasis or significant mediastinal lymphadenopathy was seen. Given the size and location of the lesion, an image-guided core needle biopsy was performed.

Histopathological analysis of the biopsy specimen revealed a proliferation of spindle cells arranged in a "patternless" architecture within a collagenous stroma (**Figure 3A**). Immunohistochemical staining was strongly and diffusely positive for CD34 (**Figure 3B**), while negative for other markers such as AE1/AE3, CD117, desmin, or S100. These findings confirmed the diagnosis of a solitary fibrous tumor (SFT). Based on the clinical constellation of a large thoracic SFT and IGF-2-mediated paraneoplastic

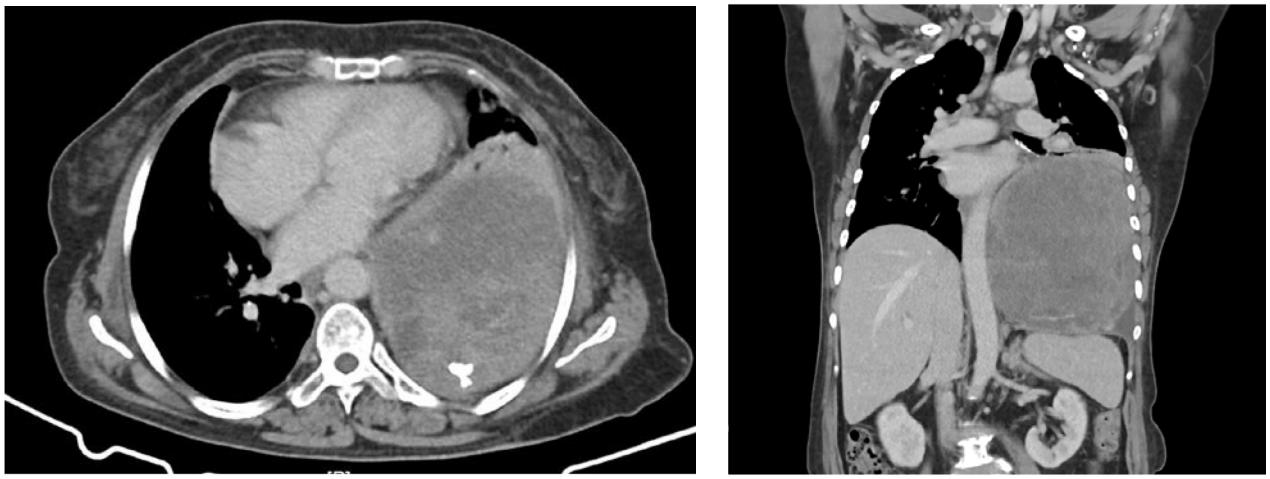


**Figure 2.** CT chest with the whole abdomen shows a heterogeneously enhancing mass with internal calcification in the left lower lung measuring about 13.5 x 12.3 x 14.8 cm, with a small amount of left pleural effusion.

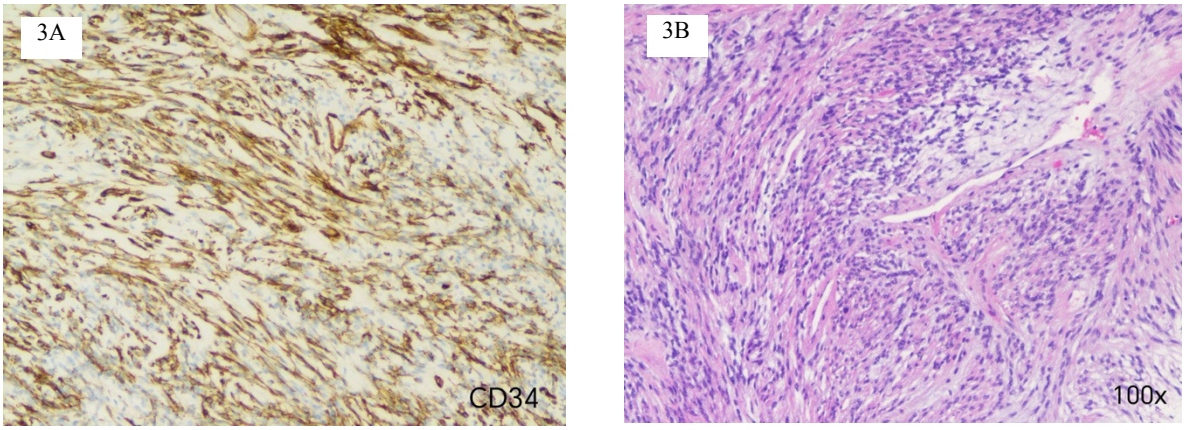



**Figure 3.** Histopathological examination (H&E stain, original magnification x100) showing spindle cell tumor arranged in patternless, short fascicles and hemangiopericytic patterns set in loose fibrocollaenous and myxoid stroma containing a few dilated and branching vessels (A) and Immunohistochemical stain (100x) showing diffuse and robust CD34 expression (B).

hypoglycemia, the patient was diagnosed with Doege-Potter Syndrome.

To initially manage the refractory hypoglycemia, the patient required 8 grams per hour of intravenous glucose. Dexamethasone (8 mg/day) was subsequently initiated, allowing successful weaning and discontinuation of the glucose infusion. The case was presented at a multidisciplinary tumor board conference to determine the optimal management for the massive solitary fibrous tumor. Surgical oncology evaluation deemed the 14.8 cm mass unresectable due to its extensive local involvement. Furthermore, standard systemic options for unresectable or metastatic SFT—including targeted therapies such as the combination of temozolomide and bevacizumab or sunitinib—were not feasible due to the patient's financial constraints. Cytotoxic chemotherapy with agents such as doxorubicin was also deferred, as the patient's poor performance status (ECOG 3) following the prolonged hypoglycemic episodes made her an unsuitable candidate for aggressive systemic treatment. Given these limitations, palliative radiotherapy was selected as the most appropriate therapeutic option. This strategy aimed to achieve local tumor control and potentially reduce the paraneoplastic "big" IGF-2 production to alleviate the refractory hypoglycemia. The patient continued a maintenance dose of dexamethasone (4 mg/day) to

maintain euglycemia as she transitioned to oncological care.

## Discussion

Doege-Potter Syndrome (DPS) represents a rare and challenging clinical manifestation of solitary fibrous tumors (SFT), characterized by non-islet cell tumor hypoglycemia (NICTH). This paraneoplastic phenomenon occurs in less than 5% of SFT cases (4) and typically involves large tumors exceeding 10 cm in diameter. The 14.8 cm thoracic mass identified in our patient aligns with the clinical profile of previously reported DPS cases, where tumor size correlates with the likelihood of metabolic disturbances. The pathophysiology of DPS is primarily driven by the ectopic secretion of "big" insulin-like growth factor-2 (IGF-2). This incompletely processed, high-molecular-weight precursor cannot form stable complexes with its acid-labile subunit and binding proteins. Consequently, "big" IGF-2 readily crosses the capillary endothelium to activate insulin receptors, increasing peripheral glucose uptake and suppressing hepatic gluconeogenesis. Clinically, this manifests as fasting hypoglycemia with a distinct biochemical signature: low plasma glucose with suppressed insulin, C-peptide, and proinsulin levels. Our patient's labs—showing a glucose level of 33 mg/dL with near-absent insulin and C-peptide—were classic for this mechanism.

Diagnostically, SFTs present a histological challenge. The "patternless" arrangement of spindle cells and "hemangiopericytoma-like" vascular patterns seen in this patient's biopsy are characteristic. However, because spindle cell morphology can overlap with other mesenchymal tumors, immunohistochemistry is essential. Strong, diffuse CD34 expression is a hallmark of SFT, as demonstrated in our case. While STAT6 has emerged as a more specific modern marker, the robust CD34 positivity combined with the clinical presentation of DPS was sufficient for a definitive diagnosis.[6] It is important to acknowledge as a diagnostic limitation that STAT6 immunohistochemistry was not performed in this case due to local resource constraints and test availability. However, given the patient's financial limitations and the classic clinicopathological correlation, this did not preclude clinical management.

Management of DPS is two-fold: stabilization of hypoglycemia and treatment of the primary tumor. Complete surgical resection remains the only definitive cure for both the tumor and the associated hypoglycemia. However, when a tumor is deemed unresectable—as in this case due to extensive local involvement and the patient's poor performance status (ECOG 3)—management becomes complex. While targeted therapies like bevacizumab-temozolomide or sunitinib are recommended for advanced SFT[7], socioeconomic barriers often limit their accessibility in resource-constrained settings. In such scenarios, glucocorticoids serve as a vital bridging therapy. As seen in our patient, dexamethasone was highly effective in weaning the requirements for intravenous glucose. Glucocorticoids not only stimulate gluconeogenesis but also reduce the production of "big" IGF-2 and improve its clearance.[8, 9] Palliative radiotherapy, chosen here for its potential for local control and reduction of paraneoplastic output[10], represents a pragmatic approach when surgery and expensive targeted agents are not viable. This case underscores the need for individualized, multidisciplinary treatment strategies that account for both clinical severity and socioeconomic realities in managing rare paraneoplastic syndromes.

## Conclusion

Doege-Potter Syndrome is a rare but critical differential diagnosis for refractory hypoglycemia in patients with large thoracic masses. Early recognition of the biochemical profile of NICTH can expedite diagnosis. While surgery is the gold standard, this case illustrates that a combination of glucocorticoids and radiotherapy can provide essential metabolic and oncological stabilization in unresectable cases where standard systemic therapies are inaccessible.

## Informed consent

The patient provided written informed consent for the publication of this case report and associated images.

**Ethics approval**

This research did not require ethical approval, as the IRB committee does not mandate approval for reporting individual cases or case series.

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