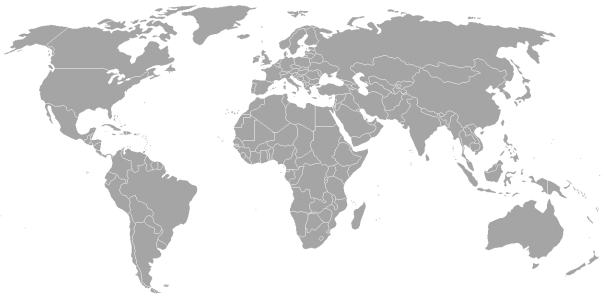

# *Sneddon's Syndrome*

## *Unusual Features and Associations*

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**ABSTRACT**

*A 43-year-old Caucasian female, with known 46XY chromosome pure gonadal agenesis and systemic hypertension, presented with upper motor neuron weakness of the right face and upper limb. She was also noted to have livedo reticularis and advanced finger clubbing. Left-sided cerebral infarction was confirmed on brain computed tomography (CT) and, following further investigations, a diagnosis of Sneddon's s syndrome (SS) was made. Three years later, she went on to develop adenocarcinoma of the right lung, which sadly claimed her life within 4 months. To our knowledge, this is the first reported case of SS in association with finger clubbing and pure gonadal agenesis.*

**Key words:** *Sneddon's syndrome, pure gonadal agenesis, finger clubbing, adenocarcinoma*

**Sheddon's Sendromu**
Nadir Özellikleri ve İlişkileri

*Sistemik hipertansiyon ve bilinen 46XY kromozom saf gonadal agenezisi olan kırk üç yaşında beyaz kadın hasta üst ekstremite ve sağ yüzde üst motor nöron güçsüzlüğü ile başvurdu. Hastanın aynı zamanda belirgin livedo retikülarisi ve ileri derece çomak parmağı mevcuttu. Bilgisayarlı beyin tomografisinde sol taraflı serebral infarkt tespit edildi ve ileri araştırmalar sonrasında Sheddon's sendromu (SS) tanısı kondu. Üç yıl sonra, hastada 4 ay içinde hayatının sonlanmasına neden olan sağ akciğer adenokarsinomu gelişti. Bildiğimize göre bu vaka çomak parmak ve saf gonadal agenezi ile birliktelik gösteren ilk SS idi.*

**Anahtar kelimeler:** *Sheddon's sendromu, saf gonadal agenizi, çomak parmak, adenokarsinom*

## INTRODUCTION

Sneddon's syndrome (SS) is a rare disease of unknown aetiology, characterised by ischaemic cerebrovascular accident and generalised idiopathic livedo reticularis. It is more common in females between the third and fifth decade, with an estimated incidence of four cases per million per year. It has a mortality rate of 9.5% over 6.2 years, likely secondary to recurrent stroke and vascular dementia (1). Systemic hypertension, headaches, venous thrombosis, and valvulopathy have also been mentioned as possible clinical manifestations (1-3).

It has been found that around 59% of cases are positive for antiphospholipid antibody. However, the link between SS and antiphospholipid antibody syndrome remains the subject of much debate. Diagnosis consists of cerebral imaging, laboratory studies, including autoantibody screening, and skin biopsy (2). The mainstay of treatment is with anticoagulant agents (3).

## CASE

A 43-year-old Caucasian female presented with sudden onset right facial and upper limb weakness. She had a past medical history of 46XY chromosome pure gonadal agenesis, for which she was on long-term hormone replacement therapy (HRT), well-controlled systemic hypertension, and was also a smoker. On examination, she was found to have peri-orbital xanthemata, plethoric facies, widespread livedo reticularis, and newly reported finger clubbing (drum stick appearance). Upper motor neuron weakness of the seventh cranial nerve and the right upper limb were also observed. Carotid Doppler revealed left internal carotid occlusion, whilst brain CT scan demonstrated a left-sided cerebral infarct in the parieto-occipital region. Trans-thoracic and later trans-oesophageal contrast echocardiography showed no evidence of cardiac or pulmonary shunting, whilst pulmonary function tests were consistent with mild obstructive airways disease. Thrombophilia and autoantibody screening, including anti-phospholipid antibody and anti-thrombin III, were negative. Skin biopsy of the livedo reticularis showed patchy mild perivascular inflammation in the dermis only and was non-specific. She went on to have two further transient ischaemic attacks and presented again three years later with a history of cough and weight loss. A CT scan of the thorax showed a right hilar mass with regional lymphadenopathy. Right bronchial biopsy confirmed pulmonary adenocarcinoma; CT staging T4-N3-M1. She was planned for palliative radiotherapy and chemotherapy, and later sadly died of her metastatic disease.

## DISCUSSION

We present the first recorded case of SS in a 43-year-old female in association with pure gonadal agenesis and advanced finger clubbing. The association of SS with pure gonadal agenesis has not been previously documented in the literature. In addition, her finger clubbing at initial presentation with cerebrovascular accident (CVA) is another very interesting sign and, despite her diagnosis of pulmonary adenocarcinoma three years later, we believe that this sign may be a new feature of SS. It is important to consider the possibility that the clubbing in this case was instead a very early sign of her pulmonary adenocarcinoma, which was diagnosed after three years of her initial presentation with SS. However, only 29% of pulmonary adenocarcinoma is associated with digital clubbing (4), and the earliest recorded manifestation of this sign preceding adenocarcinoma in the literature is 18 months (5). Taking this evidence into account, the aetiology of this patient's finger clubbing remains far from certain and the association with SS is worth strong consideration. One also cannot rule out the possibility that long term HRT in this patient, who is genotypically male, may have increased their risk of developing stroke in the presence of SS, as a recent meta analysis noted a significant increase in the risk of ischaemic-type stroke with HRT (6). It has also been quoted that SS is more common amongst smokers and females taking oral contraceptives (7).

Pulmonary involvement is an uncommon complication of SS and the association with lung adenocarcinoma in this case is unclear. Occam's razor dictates that it is likely to be secondary to smoking and the combination here with SS may be purely coincidental. Conversely, chronic inflammation may be a plausible hypothesis (8-10), which may offer some explanation for the rare association of all these uncommon disorders. However, our current understanding of the aetiology of SS denotes an idiopathic or non-inflammatory disease process (11). As a result of this case, it may be necessary to revisit the aetiology and genetics of SS.





In concluding, it is our view that this case does present a collection of uncommon disorders and potentially new clinical features affecting the same patient, and is thus worthy of note within the pantheon of case reports of SS.

### *REFERENCES*


1. *Zelda B, Sepp N, Stockhammer G, et al. Sneddon's Syndrome. A long-term follow-up of 21 patients. Arch Dermatol 1993;129:437-7.*
2. *Bolayir E, Yilmaz A, Kugu N, Erdogan H, Akyol M, Akyuz A. Sneddon's Syndrome: Clinical and Labarotory Analysis of 10 Cases. Acta Med Okayama 2004;58:59-65.*
3. *Aladdin Y, Hamadeh M, Butcher K. The Sneddon Syndrome. Arch Neurol 2008;65:834-5.*
4. *Sridhar KS, Lobo CF, Altman RD. Digital clubbing and lung cancer. Chest 1998;114:1535-7.*
5. *Faller BA, Atkinson JP. New-Onset Clubbing Associated with Lung Cancer. N Engl J Med 2008;359(13):e15.*
6. *Bath P, Gray L. Association between hormone replacement therapy and stroke: a metaanalysis. BMJ 2005;330:342-5.*
7. *Karagulle A, Karadag D, Erden A, Erden I. Sneddon's syndrome: MR imaging findings. Eur Radiol 2002;12:144-6.*
8. *Coussens LM, Werb Z. Inflammation and cancer. Nature 2002;420(6917):860-7.*
9. *Coull BM. Inflammation and Stroke: Introduction. Stroke 2007;38:631.*
10. *Coggins KG, Coffman TM, Koller BH. The Hippocratic finger points the blame at PGE. Nature Genetics 2008;40:691-2.*
11. *Schellong SM, Weissenborn K, Niedermeyer J, Wollenhaupt J, Sosada M, Ehrenheim C, Lubach D. Classification of Sneddon's syndrome. Vasa 1997;26(3):215-21.*

***Figure 5***. *Both of inner and outer lumens are associated with the branches*

***Figure 6***. *Both of inner and outer lumens are associated with the branches*