

The Many Facets of Wunderlich Syndrome: A Multidetector Computed Tomography based Review

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A B S T R A C T

Introduction: Wunderlich syndrome (WS) is a rare potentially lethal condition characterized by acute spontaneous non-traumatic subcapsular and perirenal haemorrhage. Classically presents with acute flank pain, flank mass and hypovolemic shock. Multidetector computed tomography (MDCT) is the modality of choice for evaluating WS. The etiologies of WS are widespread with renal neoplasms and vascular pathologies comprising most of the cases. This original research article provides an account on the various etiologies and the role of MDCT in evaluating them.

Material and methods: This was a retrospective study over a period of 2 years in patients who underwent computed tomography of the abdomen. 92 patients with renal subcapsular hematoma were detected and analysed for their respective causes.

Results: On correlation with clinical history of trauma and iatrogenic causes, 7 cases of spontaneous non-traumatic renal subcapsular haemorrhage were identified from the 92 cases in this study. With the aid of MDCT the cause for haemorrhage in each of these patients were elucidated.

Conclusion: Computed tomography plays a pivotal role in the diagnosis of patients with Wunderlich syndrome. The typical imaging findings of the various causes of WS and the knowledge of this entity is required for prompt diagnosis and management.

Keywords: Wunderlich Syndrome; Subcapsular Haemorrhage; Kidney; CT;

INTRODUCTION

Wunderlich syndrome (WS) is a rare entity that involves spontaneous non-traumatic haemorrhage within the subcapsular and perirenal spaces of the kidney. This is a potentially life-threatening emergency condition. Although the first glimpse of this condition as observed by Bonet dates back to 1700, it was first described by Wunderlich in 1856 as 'Spontaneous renal capsule apoplexy.' The term 'Wunderlich syndrome' was later coined by Coenen in 1910.^{1,2} Clinically this condition presents with acute flank pain, palpable flank mass and hypovolemic shock together known as 'Lenk's triad'.³ Historically, renal neoplasms followed by vascular diseases were the most common causes of WS. Although ultrasound imaging (US) is the preliminary modality used in assessing patients with flank pain, multidetector computer tomography (MDCT) is the imaging modality of choice in WS. Magnetic resonance imaging (MRI) and renal angiography are the other modalities useful in identifying the cause of WS. This article furnishes the various causes of WS and illustrates few of the rare causes and their characteristic

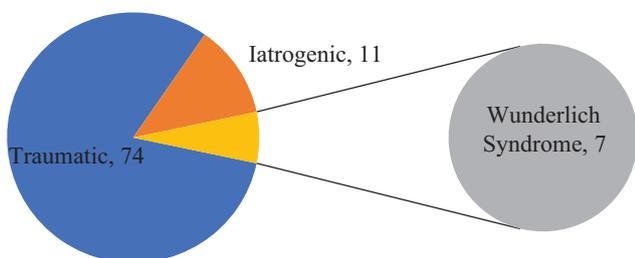
imaging findings as observed on MDCT.

MATERIAL AND METHODS

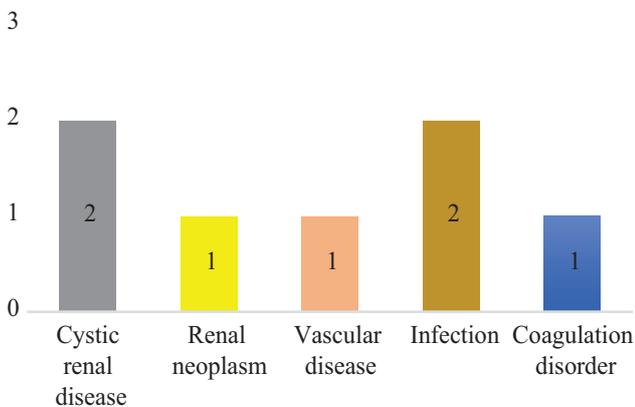
This was a retrospective study done on rare causes of Wunderlich syndrome and their typical imaging findings as observed in our institution over a period of 2 years from April 2016 to April 2018. A GE 64 slice VCT machine was used for imaging of the abdomen, which acquires data from the dome of the diaphragm to the pubic symphysis. The imaging protocol consists of a routine non-contrast study followed by contrast enhanced study on arterial, venous and delayed phases if required with a slice thickness of 5 mm. The images are acquired on axial plane and reformatted into coronal and sagittal planes with 0.625 mm thickness. Low osmolar contrast agent Omnipaque, 350 mg Iodine/ml with saline chase of 30 ml, was infused at the rate to 4 to 4.5 ml/seconds. Automated bolus tracking technique was performed, and images were acquired in arterial, venous and delayed phases at 18 to 22 seconds, 55 to 65 seconds and 12 to 15 minutes respectively. The non-contrast study was used for detection of hyperdense subcapsular/perinephric hematoma within the

Neoplasms	Vascular	Infection
Benign Angiomyolipoma Lipoma Fibroma Oncocytoma Adenoma Malignant Renal cell carcinoma Transitional cell carcinoma Metastases Sarcoma	Arterial Polyarteritis Nodosa Renal artery true/false aneurysms Renal artery arteriosclerosis Wegener granulomatosis Venous Renal arteriovenous malformations Renal arteriovenous fistulas Renal vein thrombosis Portal hypertension	Abscess Tuberculosis Pyelonephritis Acute Emphysematous Xanthogranulomatous
Renal cystic diseases	Haematological	Miscellaneous
Simple/complex cyst Haemorrhagic cyst Acquired cystic renal disease Autosomal dominant Polycystic Kidney disease	Coagulation disorders Blood dyscrasias Anticoagulant therapy	Idiopathic Drug-induced End-stage renal disease Post partum status

Table-1: Various etiologies of wunderlich syndrome



Graph-1: Distribution of causes of subcapsular renal haemorrhage



Graph-2: Distribution of causes of wunderlich syndrome

kidney. The arterial phases were used for vascular assessment, venous for characterization of space occupying lesions and delayed for assessment of the renal pelvis and ureters. Informed consent was obtained from all individual participants included in the study. Consent was obtained for publishing the case and the radiological images. No information has been included in the article that would reveal the identities of the patients.

RESULTS

This retrospective study was done for 2 years and around 92 cases of renal subcapsular haemorrhage were detected. This includes 74 cases of traumatic, 11 cases of iatrogenic and 7 cases of spontaneous non-traumatic renal subcapsular

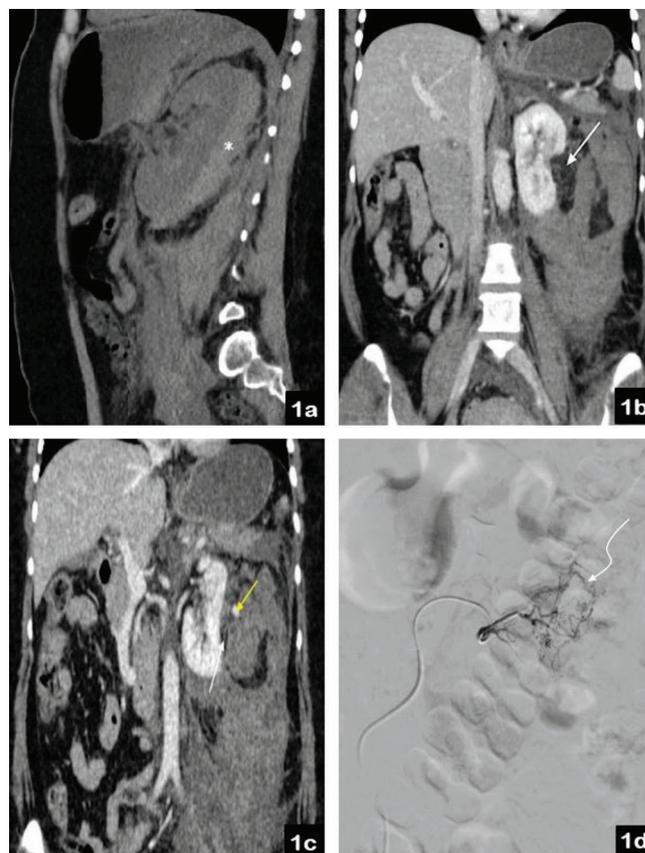


Figure-1: AML
 A 48 year old female with acute left flank pain and hypotension diagnosed with Wunderlich syndrome - hyperdense subcapsular haemorrhage (Asterisk) in sagittal non contrast (a) CT image secondary to rupture of an exophytic fat density left renal angiomyolipoma (straight arrow) with an active site of bleed (yellow straight arrow) – contrast blush on coronal venous (b) and (c) phase CT images. Pre-operative confirmatory catheter renal angiogram showing hypervascular mass (Curved arrow) with dense early arterial network in the left kidney consistent with an angiomyolipoma.

haemorrhage (graph 1). Among the seven patients with Wunderlich syndrome, two

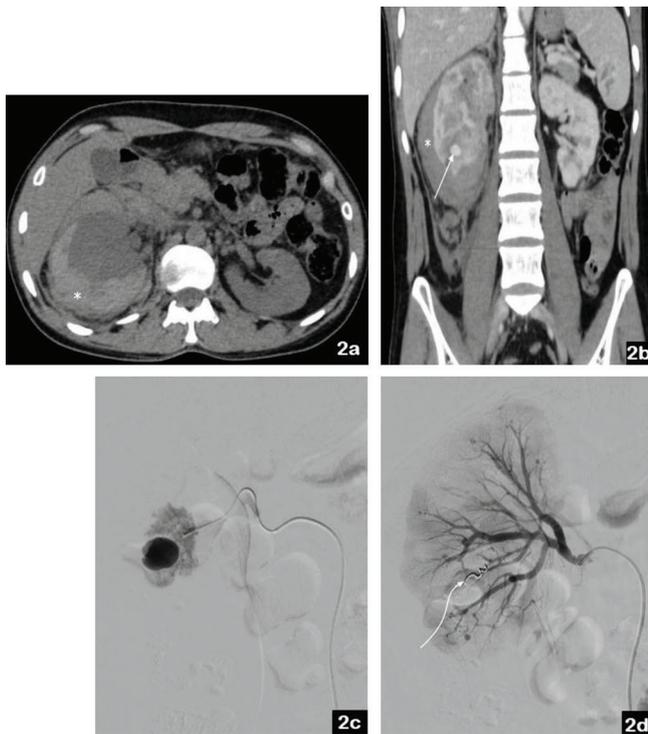


Figure-2: PAN

A 25 year old male with severe abdominal pain with Wunderlich syndrome - hyperdense subcapsular haemorrhage (Asterisk) in axial non-contrast (a) CT image with an active site of bleed (straight arrow) – contrast blush on coronal vein (b) CT image. Catheter renal angiogram (c) showing contrast blush at the active bleed site with post embolization coil (Curved arrow) in the right kidney with multiple intrarenal microaneurysms (d) consistent with the diagnosis of polyarteritis nodosa

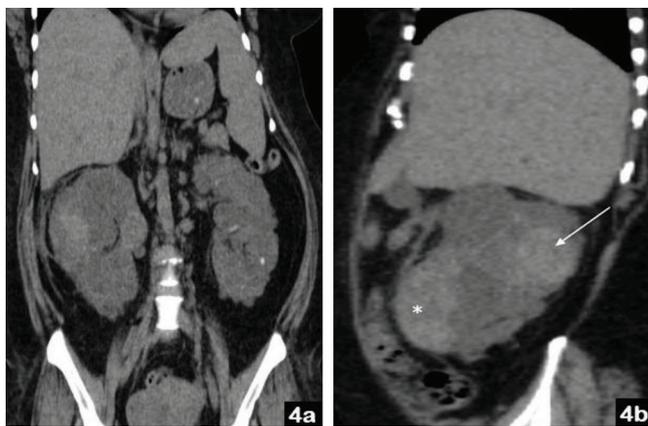


Figure-4: ADPKD

A 52 year old female, a known case of Autosomal Dominant Polycystic Kidney Disease (a) and chronic renal failure with sudden onset abdomen pain displays Wunderlich syndrome as a result of rupture of a haemorrhagic cyst (Straight arrow) on sagittal (b) non-contrast CT image with hyperdense subcapsular hematoma (Asterisk).

were cystic renal diseases – complex renal cyst and autosomal dominant polycystic kidney disease, two were infections – emphysematous and xanthogranulomatous pyelonephritis and one each of angiomyolipoma, vasculitis – polyarteritis nodosa and haemophilia A respectively (graph 2).

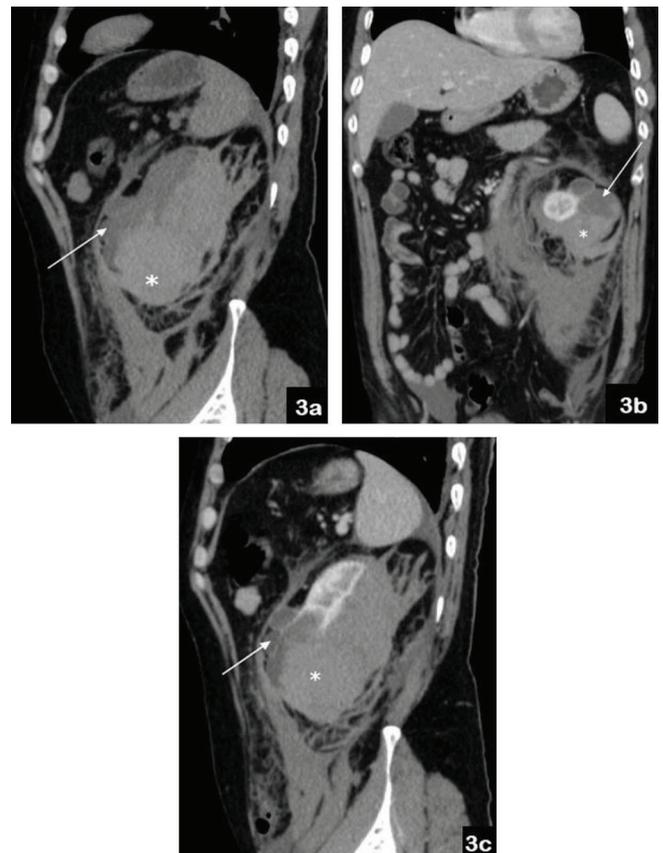


Figure-3: Complex renal cyst

A 46 year old male with sudden dull aching left flank pain shows Wunderlich syndrome exhibiting typical hyperdense subcapsular hematoma (Asterisk) in sagittal non-contrast (a) CT image, Coronal (b) and sagittal (c) venous phase CT images shows a complex renal cyst (Straight arrow) with discontinuity along the inferior margin suggestive of rupture.



Figure-5: Haemophilia A

A 36 year old male, a known case of haemophilia A came with acute onset of right flank pain diagnosed with Wunderlich syndrome showing hyperdense subcapsular renal hematoma involving the right kidney (Asterisk) in both axial (a) and coronal (b) non contrast CT images.

DISCUSSION

Wunderlich syndrome (WS) is characterized by acute onset of spontaneous haemorrhage confined to the subcapsular and perirenal spaces of the kidney with no previous history of trauma.⁴ It was first described by Carl Reinhold August

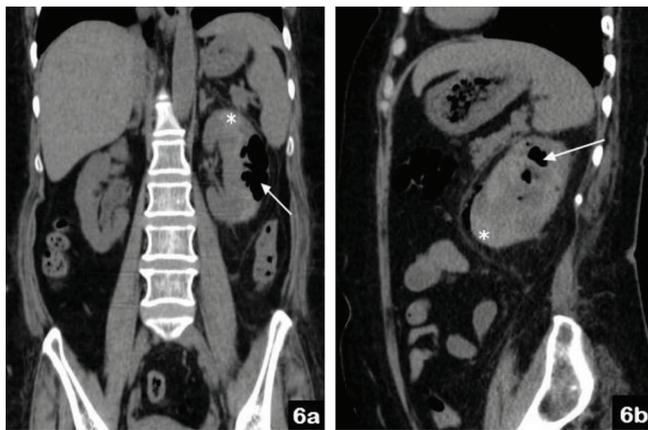


Figure-6: Emphysematous pyelonephritis

A 62 year old female with fever and lower abdominal pain shows hyperdense renal subcapsular hematoma (Asterisk) in both coronal (a) and sagittal (b) non-contrast CT images with multiple intraparenchymal air pockets (Straight arrow) - Wunderlich syndrome secondary to emphysematous pyelonephritis.

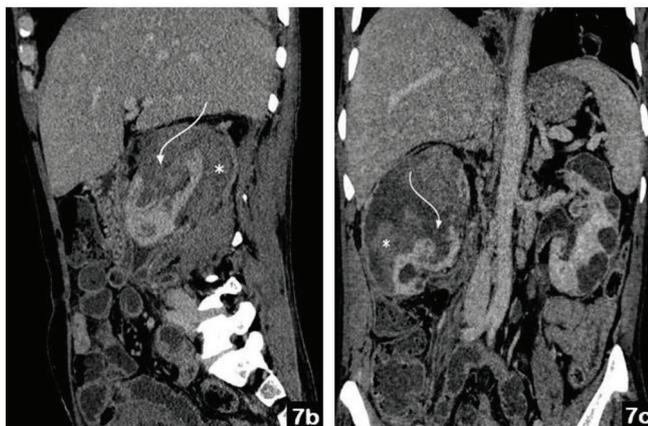


Figure-7: Xanthogranulomatous pyelonephritis

A 60 year old male with fever and diffuse abdominal pain more on the right lumbar region shows Wunderlich syndrome – hyperdense renal subcapsular hematoma (Asterisk) in non-contrast axial (a) CT image as a result of renal parenchymal disruption (Curved arrow) in sagittal (b) and coronal (c) venous phase CT images in a patient with obstructive uropathy secondary to bilateral Xanthogranulomatous pyelonephritis.

Wunderlich, a German physician in 1856.¹ Upto 450 cases of spontaneous perirenal haemorrhage has been published in literature till 2000 and a further 266 cases more since 2000.⁵ There is a slight male preponderance in cases of WS with male to female ratio of 6:5 with few females being affected in pregnancy.^{5,6} Clinically it is characterized by Lenk's triad, which include acute flank pain, palpable mass

and hypovolemic shock. They can also present with gross or microscopic hematuria. Symptomatically 83% presented with acute flank or abdominal pain, 19% had hematuria and 11% with features of hypovolemic shock.⁶ A multi-modality approach is usually the norm in cases of WS. US, MDCT and MRI all play a crucial role in diagnosing the hemorrhage and its cause. Renal angiography is useful in identifying active bleeds and aids in the diagnosis of vasculitis.⁷ Among these US may be the initial modality to detect the perinephric haemorrhage, but cross-sectional imaging like MDCT and MRI are 100% sensitive in detecting hematoma.⁸ MDCT is superior to other imaging modalities in its sensitivity and specificity to detect subcapsular and perirenal haemorrhage and its etiology.⁴⁻⁸

Wunderlich syndrome although rare has a plethora of causes for its occurrence. The various etiologies of WS include renal neoplasms, vascular diseases, infection, cystic renal diseases, haematological diseases, idiopathic and other rare causes (Table 1). In literature approximately 5 to 10% of all cases of WS are idiopathic, which refers to the absence of any underlying pathology within the kidney.^{4,6}

The most common cause of WS is renal neoplasms constituting approximately 60 to 65%.^{4,6,9} They are further classified into benign and malignant etiologies. Angiomyolipoma is the most common neoplasm and renal cell carcinoma is the most common malignant etiology comprising of approximately 30 to 35% cases of WS.^{4,7} Other neoplasms that rarely cause spontaneous perinephric haemorrhage include metastases, sarcoma, fibroma, adenoma, oncocytoma and transitional cell carcinoma.

Renal vascular diseases form the second most common cause of WS. They account for approximately 20 to 30% of all cases with polyarteritis nodosa being the most common.^{6,10} They are further classified as arterial and venous etiologies. Arterial causes include polyarteritis nodosa and renal artery aneurysms, while venous causes include renal vein thrombosis, renal arteriovenous malformations, fistulas and portal hypertension.¹⁰

Renal infections are a rare cause of WS that occurs as a result of complications of these infections. Infections include renal abscess, acute pyelonephritis, emphysematous pyelonephritis and Xanthogranulomatous pyelonephritis (XGP) and account for 5 to 10% of spontaneous perinephric haemorrhage. The risk of haemorrhage is compounded in a patient with diabetes mellitus.¹¹

The propensity for a ruptured renal cyst to cause perinephric haemorrhage is relatively uncommon as the cysts generally rupture into the pelvicalyceal system.¹² Yet isolated cases of ruptured cyst leading to perinephric haemorrhage have been established in literature. The causes of renal cystic diseases leading to WS include acquired renal cystic disease, rupture of simple or haemorrhagic cysts and autosomal dominant polycystic kidney disease.

Others rare causes of WS include haematological disorders like haemophilia and blood dyscrasias, anticoagulation therapy and post-puerperal status.

Angiomyolipoma

Angiomyolipoma (AML) is a benign neoplasm of mesenchymal origin. It consists of dysmorphic blood vessels,

mature adipose tissue and smooth muscle tissue, the so called triphasic tumor.¹³ The incidence of AML as the etiology of WS is approximately 35 to 40%.^{6,10} The majority of AML's occurs sporadically with a strong female predilection and the remaining is associated with phakomatoses, especially tuberous sclerosis and rarely with Von Hippel-Lindau syndrome. The CT features of AML include a well defined heterogeneous lesion with varying degrees of macroscopic fat, hypervascular soft tissue components and intralesional aneurysms.¹⁴ AML are notoriously prone for spontaneous rupture and perinephric haemorrhage that is directly proportional to the large size of the lesion (> 4 cm) and larger diameter of the intralesional aneurysms (> 5 mm).¹⁵ In cases of WS due to ruptured AML, the appearance of the lesion may vary but the sensitivity of CT in detection of the lesion and haemorrhage is still 100% [Figure 1]. The treatment for patients with WS secondary to AML rupture includes therapeutic embolization and surgery. Renal catheter angiography with embolization helps prevent the tumor growth by occluding the aneurysms, trans arterial chemo embolization causes necrosis of the solid components [Figure 1 (d)] thus eliminating the need for radical surgery.¹⁵ Surgery either partial or complete nephrectomy is indicated in cases with uncontrolled bleeding after embolization.

Polyarteritis nodosa

Polyarteritis nodosa (PAN) is a systemic vasculitis of small to medium arteries, predominantly involving the renal arteries which shows multifocal areas of necrosis within.¹⁶ WS is a rare complication of PAN secondary to ruptured aneurysms accounting for approximately 12%.¹⁰ The CT features of PAN includes diffuse enlargement of the kidneys with loss of corticomedullary distinction, multiple wedge-shaped parenchymal infarcts and multiple microaneurysms. Identification of microaneurysms is necessary to differentiate PAN from acute pyelonephritis.¹⁷ In addition to renal microaneurysms and parenchymal changes, presence of subcapsular and/or perinephric haemorrhage is seen in cases of WS [Figure 2]. Renal catheter angiography is required for confirmation of PAN [Figure 2 (d)]. Treatment for PAN includes conservative management, arterial embolization and surgery. In cases of WS, renal catheter angiography along with arterial embolization is the preferred choice of treatment. However, as PAN is progressive condition with frequent relapses, nephron sparing surgery is indicated on a long-term basis.

Renal cystic diseases

Renal cysts are usually asymptomatic and are seen as incidental lesions on imaging. On CT they appear as well defined thin walled non-enhancing lesions of water attenuation. On contrast CT Bosniak classification of renal cystic lesions is used to provide the risk of malignancy and appropriate management. Cyst can be simple, complex or haemorrhagic. Features of a complex cyst include enhancing internal septations, solid components and calcifications with a varied appearance. Haemorrhagic cysts appear hyperdense on nonenhanced CT. Haemorrhage within a cyst occurs as a result of rupture of the sclerotic arteries on the cyst wall.¹⁸ Although rare, WS secondary to rupture of simple/complex

and/or haemorrhagic cysts have been reported in literature.¹⁹ The reasons for cyst rupture include infection or hemorrhage within the cyst and larger size of the cyst. In cases of WS characteristics of the cyst with focal wall discontinuity and perinephric hematoma is seen [Figure 3]. On few occasions, large perinephric and subcapsular hematomas may obscure the ruptured cyst and hence follow-up CT imaging is essential for diagnosis of the etiology with complete obliteration of the cyst and resolution of the hematoma. Rare cases of WS in Autosomal dominant polycystic kidney disease secondary to cyst rupture have also been reported. On CT along with the features of multiple simple/complex and/or haemorrhagic cysts in both kidneys, perinephric hematoma is also seen in WS [Figure 4]. The treatment of WS secondary to ruptured cysts is primarily conservative management, although large and infected residual cysts warrant other managements.

Coagulation disorders – Haemophilia A

Coagulation disorders are heterogeneous group of disorders associated with blood clotting or abnormal bleeding conditions. Coagulation disorders as an etiology of WS is extremely rare with isolated case reports in literature. Haemophilia A which is the absence or deficiency of coagulation factor VIII is the commonest of the coagulation disorders. The hall mark of haemophilia is spontaneous haemorrhage commonly seen in abdomen and soft tissues.²⁰ On CT, the characteristic subcapsular haematoma is seen in cases of Wunderlich syndrome secondary to haemophilia A [Figure 5]. In cases of haemophilia A, the appropriate clinical history is essential to not term it as an idiopathic cause of WS. Treatment depends on the severity and type of manifestations and to replace the clotting factor.

Emphysematous pyelonephritis

Emphysematous pyelonephritis is a lethal acute necrotizing infection of the kidney constituting collection of gas within or around the renal parenchyma. Classically presents with acute flank pain and fever. Diabetes mellitus augments the incidence of this condition. The modality of choice for evaluating emphysematous pyelonephritis is CT and the typical findings include enlarged kidney with parenchymal destruction and pockets/ linear streaks of gas within the parenchyma. Fluid collections, gas-fluid levels and abscess formations are commonly seen.²¹ The incidence of WS in emphysematous pyelonephritis is rare with isolated cases reported in literature.²² In addition to the above-mentioned findings of emphysematous pyelonephritis on CT, a hyperdense subcapsular hematoma is seen in cases of WS [Figure 6]. Treatment depends on the type and severity of involvement ranging from conservative antibiotic therapy to total nephrectomy.

Xanthogranulomatous pyelonephritis

Xanthogranulomatous pyelonephritis is a chronic granulomatous infection of the kidney characterized by destruction and replacement of the renal parenchyma with lipid-laden macrophages as small collections. It is a form of obstructive uropathy with the presence of renal calculi leading to non-functional kidney. Symptoms are vague with fever and abdomen pain being the common complaints. The incidence of bilateral XGP is extremely rare²³ and has a focal

and diffuse form. The typical CT features of XGP include an enlarged non-functioning kidney with a contracted renal pelvis, expanded renal calices and large calculi within the renal pelvis. However atypical features include atrophy of the renal parenchyma and 10% of the cases show absence of renal calculi.²⁴ The incidence of WS in XGP is relatively rare with few documented in literature. We have a unique case of atypical bilateral XGP with hyperdense subcapsular hematoma in one of the kidneys [Figure 7]. Nephrectomy is the only treatment for XGP.

CONCLUSION

Wunderlich syndrome is an acute emergency with a broad spectrum of etiologies. CT plays a pivotal role in identifying the cause in correlation with the clinical history. The awareness of such a rare entity is imminent for all the clinicians and imaging plays a important role in deciding the further course of management.

Abbreviations

WS – Wunderlich Syndrome, US - Ultrasound, MDCT – Multidetector Computed Tomography, CT - Computed Tomography, MRI – Magnetic Resonance Imaging, VCT – Volumetric Computed Tomography, AML - Angiomyolipoma, XGP - Xanthogranulomatous pyelonephritis, PAN – Polyarteritis Nodosa, ADPKD – Autosomal Dominant Polycystic Kidney Disease

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