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Multifocal Cerebral Abscesses Complicating Total Anomalous Pulmonary Venous Return in an 8 Year Old Boy: A Case Report and Literature Review

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Abstract: *Total anomalous pulmonary venous return(TAPVR) is a rare cyanotic congenital cardiac defect (CCHD) characterisedby the absence of direct communication between the pulmonary veins and the left atrium (LA), resulting in the pulmonary veins draining abnormally into the systemic venous circulation or into the right atrium (RA). The pathophysiology of TAPVR predisposes to the development of cerebral abscess; however, documented cases of TAPVR complicated by cerebral abscess are not commonly encountered. Both TAPVR and cerebral abscess are associated with high mortality rates, emphasising the need for early diagnosis and prompt and appropriate interventions. This is the case report of an 8 year old boy with an uncorrected TAPVR managed for multifocal cerebral abscesses with good outcome.*

Key words:*total anomalous pulmonary venous return, multifocal, cerebral abscess, cranial CT*

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I. Introduction

Total anomalous pulmonary venous return (TAPVR) is a rare cyanotic congenital heart defect (CCHD)characterized by the absence of direct communication between the pulmonary veins and the left atrium (LA), instead draining abnormally into the systemic venous circulation or into the right atrium (RA).[1]Consequently, there is total mixing of deoxygenated systemic venous blood and oxygenated pulmonary venous blood, before or within the RA with ensuing cyanosis.[1]

Patients with CCHD are predisposed to developing neurological complications as a consequence of several mechanisms which include the acute global hypoxia of cyanotic spells to focal ischaemia due to arterial thrombosis, paradoxical embolisation and cardioembolisation.[2] Chronic hypoxia, the resultant polycythaemia and hyperviscosity, and the passage of bacteraemic blood across right to left shunts foster a suitable environment for infection and abscess formation.[2]Although these conditions are present in TAPVR, cerebral abscess appears to be an infrequent complication in patients with TAPVR,[3,4]from the relatively few reports available.

This case report documents an uncommon complication in an equally uncommon heart defect, as seen in an 8 year old boy with TAPVR complicated by multifocal cerebral abscesses.

II. Case Report

An 8 year old boy presented to the emergency paediatric unit with a week's history of headache, and a day's history of vomiting and convulsions. The headache wasof insidious onset, was generalized and throbbing, increased in severity to interfere with sleep, with associated photophobia. There was short-lived relief following administration of ibuprofen. Six days later, he had 2 bouts of vomiting, which were postprandial, non-projectile, and not bile-stained or bloody. A few hours later, he had a single episode of generalized tonic-clonic convulsions which lasted for about 5 minutes, and aborted spontaneously.There was postictal sleep, but no urinary or faecal incontinence.There was no fever, excessive weight gain or loss; however, poor appetite was observed from the onset of symptoms. He received antimalarial medications and oral antibiotics, however, he presented to the hospital when symptoms worsened.

Prior to this presentation, he had been in regular attendance at the paediatric cardiology clinicfor supracardiactotal anomalous pulmonary venous return (TAPVR) withatrialseptal defect (ASD) and severe pulmonary artery hypertension (PAH); diagnosed with transthoracic echocardiography 5 years ago, when he presented at 3 years of age with recurrent cough and fast breathing, poor weight gain and darkdiscolouration of the lips from the age of 4 months. He was commenced on oral antifailure medications (digoxin, frusemide and spironolactone) and a pulmonary antihypertensive (sildenafil); follow up visits had been regular.At diagnosis,

his parents were advised on the need for immediate cardiac catheterization and subsequent surgery if operable, outside the country.However, they were of low socio-economic status and had been unable to secure the required funds.

On examination, he was conscious, irritable, and in painful distress, with central cyanosis, pulse oxygen saturation (SpO_2)was 90% on room air, andhad grade III digital clubbing. He was afebrile (temperature 36.4^0 Celsius), was not dehydrated, and not pale. He was moderately malnourished, weight for height Z-score (WHZ) was between -2 and -3 standard deviations (SD). Neurological examination revealed neck stiffness, and Kernig's and Brudzinski's signs. Cardiovascular examination revealed a precordial bulge with a left parasternal heave, fixed splitting of the 2nd heart sound, accentuated pulmonary component of the 2nd heart sound, and a grade 3 of 6 ejection systolic murmur audible at the 2nd left intercostal space.

A complete blood count (CBC) showed normal haematocrit of 33%, leucocytosisandneutrophilia; erythrocyte sedimentation rate (ESR) was elevated. Blood culture andabscess aspirate were sterile. Tuberculin skin test (TST) and human immunodeficiency virus (HIV) antibody screening were both negative. Random blood glucose was normal. Serum electrolytes revealed mild metabolic acidosis. Contrast-enhanced cranial computed tomography (CT) showed multiplering enhancing lesions in the left fronto-parietal and occipital regions measuring 6.2 x 4.1cm and 3.1 x 2.7cm, respectively, andperilesionaloedema. There was marked pressure effect as evidenced by contralateral shift of the midline,near total obliteration of the anterior horn and body of the lateral ventricle, as well as compression of the 3rd ventricle and the left posterior horn of the lateral ventricle (figure 1).

Diagnosis was TAPVR complicated by multifocalcerebralabscesses. Empirical parenteral antibiotic therapy was instituted: ceftriaxone 100mg/kg/day q12h, metronidazole 7.5mg/kg/dose q8h, and vancomycin20mg/kg/dose q8h, which the patient received for 4 weeks. Emergency right frontal burr hole and drainageof the left fronto-parietal abscess was performed, 70mLs of frankpus was aspirated using a Dandy cannula. The left occipital abscess was not drained as it appeared to be in the stage of late cerebritis with a thin capsule, and could respond to antibiotic therapy.His post-operative recovery was satisfactory,the headachesubsided, and there were no neurological deficits. Repeat cranial CT to reassess the occipital abscess could not be carried out due to severe financial difficulties, which also impacted on the duration of parenteral antibiotic therapy of 4 weeks. He was discharged on oral antibiotics for 2 weeks, andinitial follow up visits were uneventful.

Three weeks after discharge, the patient presented to the paediatriccardiology clinic with 2 days' history of severe headache, early morning projectile vomiting, high grade fever that was associated with chills and rigors, neck stiffness, and irritability. There was no history of seizures. Neurological examination revealed neck stiffness, and positive Kernig's and Brudzinski's signs, there were no motor abnormalities. Cranial CT showed persistence and increase in size of the left occipital lesion with features consistent with a cerebral abscess (figure 2). Parenteral ceftriaxone, metronidazole, and vancomycin were instituted, left occipital burr hole and abscess aspiration was performed, with 12mLs of frank pus aspirated.The post-operative period was uneventful and he had no neurological deficits.He received parenteral antibiotic therapy for 4 weeks, and was discharged on oral antibiotics for 2 weeks. Aerobic, anaerobic, and fungal cultures of the aspirate did not yield any isolates. He has been discharged from neurosurgical follow up, and has continued with cardiology follow up visits. Financial difficulties that have hindered timely access to cardiac surgery have persisted.

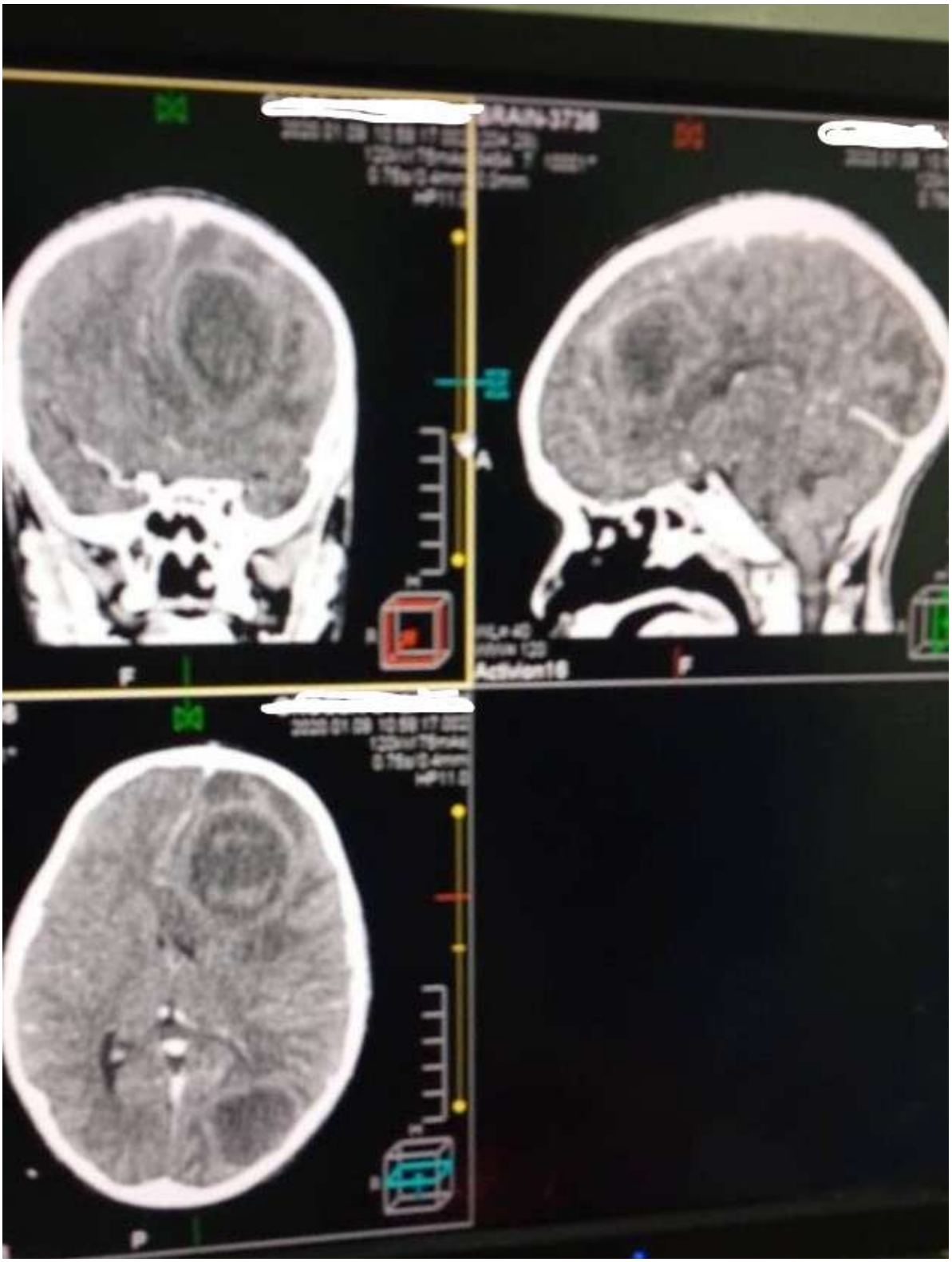

Figure 1: Contrast-enhanced cranial CT (coronal, sagittal and axial sections) showing multiple hypodense lesions of varying sizes with thin uniform ring-like enhancement and perilesionaloedema in the left fronto-parietal and occipitalregions.

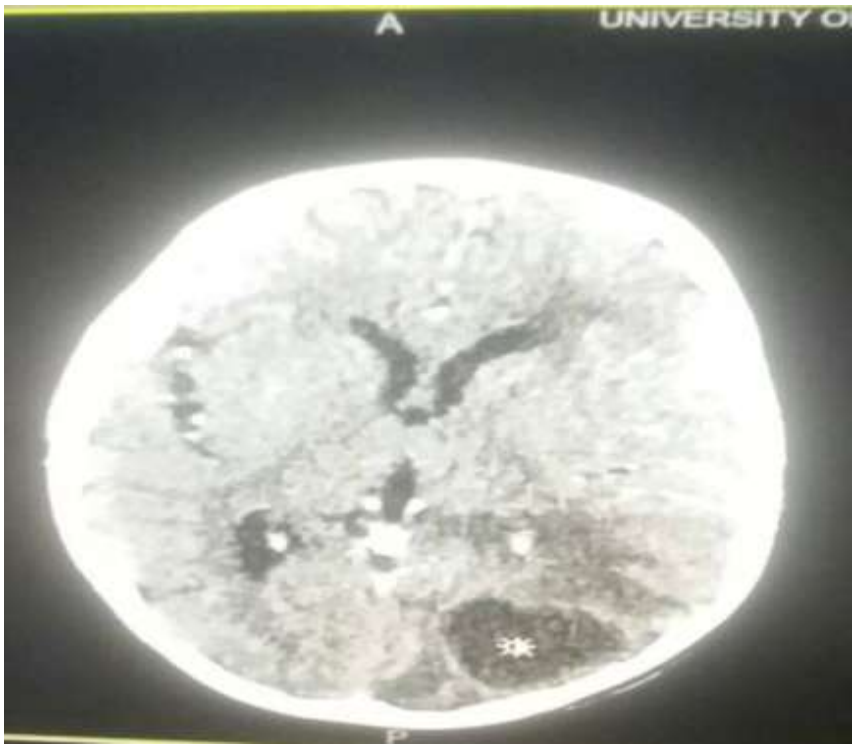

Figure 2: : Contrast-enhanced cranial CT (axial section) showing a hypodense lesion with thin uniform ring-like enhancement and perilesionaloedema in the left occipital region.

III. Discussion

Cerebral abscess is a serious neurological condition accounting for approximately 8% of intracranial space-occupying lesions in developing countries.[5] It is associated with high morbidity and mortality, with mortality rate ashigh as24%.[6,7]It affectschildren of all ages, however, it is most common in children between 4 and 8 years.[8]Several predisposing factors have been identified and include congenital heart disease (CHD) with a right to left shunt, meningitis, suppurative otitis media, mastoiditis, sinusitis, orbital cellulitis, soft tissue infections of the face and scalp, penetrating skull injury, comminuted skull fracture, intracranial surgery including insertion of ventriculo-peritoneal shunts, dermal sinuses and immunocompromised states.[9-12]

Patients with CCHD account for 25-46% of all cases of cerebral abscess.[3,4,12]Between 2 and 12 years of age, patients with CCHD have an increased risk of developing cerebral abscess,[13]and our patient presented within this range as an 8 year old. Pathogenic processes responsible for abscess formation include chronic hypoxia predisposing to anaerobic infection, polycythaemia and hyperviscosity causingsluggish blood flow in cerebral microcirculationfacilitating the formation of microthrombi and focal encephalomalacia, and also causing alterationsin blood-brain barrier permeability. The passage of possibly infected blood from systemic venous circulation across right to left shuntsthereby bypassing the phagocytic-driven filtration process in the pulmonary circulation is another factor.[2,3,13]

TAPVR is a raredefect occurring in 1% of patients with CHD[1]and in 4% withCCHD.[14]The absence of direct communication between the pulmonary veins and the left atrium (LA), results in the pulmonary veins draining into the systemic venous circulation or into the right atrium (RA).[1] Complete mixing of deoxygenated systemic venous blood and oxygenated pulmonary venous blood occurs before or within the RA causing cyanosis.[1] An atrial septal defect (ASD) or patent foramen ovale (PFO) provides the obligate interatrial connection that is essential for survival.[1] Four types of TAPVR have been described, based on the site of drainage of the pulmonary veins: supracardiac seen in 50% of patients, cardiac in 20%, infracardiac in 20%, and mixed type in 10%.[1] Clinical presentation depends on the presence or absence of obstruction to the pulmonary venous return, and extent ofinteratrial blood flow.[1] Pulmonary venous obstruction occurs in majority of patients with the intracardiac type, and less frequently in the supracardiac and cardiac types. Pulmonary hypertension develops early in such patients, and clinical deterioration can be rapid.[1]Majority of patients with uncorrected infracardiac TAPVR will die within 2 months, while two-thirds of those without pulmonary venous obstruction will die by 1 year of age.[1]

In TAPVR, the pathologic process that facilitates the development of cerebral abscesses in CCHD with right-to-left shunts is present, more so as survival depends on the presence of a large unrestricted right-to-left shunt.It is to be expected that this should increase the risk of abscess formation in TAPVR. Interestingly, the

occurrence of cerebral abscesses in TAPVR has largely been limited to isolated case reports,[4,15]while larger studies on TAPVR and CHD did not report cerebral abscess as a complication of TAPVR.[3,16-18]Some authors have postulated that the impact of bacteraemic deoxygenated blood from the systemic venous circulation being diluted with oxygenated blood from the pulmonary circulation which has been filtered from pathogens could provide some explanation for the apparently lower incidence of cerebral abscess among patients with TAPVR; however, there is no data to support this hypothesis.[4]

Cerebral abscess presents with nonspecific features in the early stages, and includes low grade fever, headache, and lethargy. As the disease progresses, nausea, vomiting, severe headache, photophobia, seizures, papilloedema, focal neurological signs, and coma may develop. Meningeal signs may also be prominent as seen in our patient. Rupture of the abscess into the ventricles may occur with overwhelming shock and death ensuing.[3,4,6,8]A number of these features were present in our patient.

Peripheral white blood cell (WBC) count and ESR may be normal or elevated;haematocrit is usually within normal,although in CCHD polycythaemiamay be present. Our patient had normal haematocrit, leucocytosis, and elevated ESR. Mild metabolic acidosis documented in our patient is in keeping with serum biochemistry of patients with CCHD, serum sodium was within normal, makingthe possibility of syndrome of inappropriate ADH secretion (SIADH) as a complication of cerebral abscess unlikely.[3]

Streptococcus is the most common causative organism in cerebral abscess,anaerobes and gram negative aerobic bacilli have also been isolated.[3,6,8] In children with CCHD, *Streptococcus milleri*is increasingly being implicated as the most common organism isolated in aspirates.[3,8]It is not unusual for aspirates to be sterile,[3,4] and blood cultures may infrequently yield a causative organism.[3]Fungal organisms*(Aspergillus, Candida)* are more common in immunosuppressed patients.[8]In our patient, aspirate and blood cultures (aerobic, anaerobic, and fungal) were sterile. In a child suspected to have cerebral abscess, lumbar puncture for cerebrospinal fluid (CSF) examination should not be performed as it may cause herniation of the cerebellar tonsils, and is seldom of additional benefit.[8]

Imaging studies are the mainstay of diagnosis and have contributed significantly to the reduction in mortality from almost 50% to <25%.[7,8]Cranial CT with contrast,magnetic resonance imaging (MRI), and radioisotope brain scan are extremely reliable methods of demonstrating cerebritis and abscess formation.[8] The CT findings of cerebritis are characterized by a parenchymal low-density lesion, and MRI T2 weighted images indicate increased signal intensity.[8] An abscess cavity shows a ring-enhancing lesion by contrast CT, and the MRI also demonstrates an abscess capsule with gadolinium administration.[8]Midline shift, and cerebral edema may be obvious, and are common in children with CCHD.[3] Cerebral abscess presents as solitary lesions in the majority, but are multiple in 30% of cases and may involve more than 1 lobe.[8]Lesions affect both cerebral hemispheres evenly, distributed between the frontal, parietal, and temporal lobes in about 80% of cases;the occipital lobe, cerebellum, and brainstem account for the remainder.[3,8]Cranial CT findings in our patient were consistent with these features, revealing multifocal abscesses in the frontal, parietal and occipital lobes of the left cerebral hemisphere, as well as evidence of midline shift.

Treatment modalities include medical therapy with parenteral antibiotics andsurgical drainage, which is indicated if there areabscesses larger than 2 cm in diameter, features of increased intracranial pressure and/or neurological deficits, gas is present in the abscess, multiloculated lesions, posterior fossa abscesses, or if fungi are isolated.[3,8]Empirical parenteral antibiotic therapy is initiated before results of bacteriology are obtained. A combination of a 3rd generation cephalosporin, metronidazole, and vancomycin is recommended, although in CCHD,vancomycin may be omitted;duration of therapy is 4-6 weeks.[8]Surgical treatment options include burr hole and aspiration and where recurrent re-accumulation occurs, excision is required.[3]Multiloculated abscesses may require frequent aspirations.[3]

Timely diagnosis and prompt treatment is essential in ensuring good outcomes. Poor prognosis is associated with presentation in infancy,delayed presentation, coma, cerebral oedema, multiple abscesses, and poor immunologic status. Approximately 50% of patients may suffer long-term sequelae including hemiparesis, seizures, hydrocephalus, cranial nerve deficits, and behavioural and learning disabilities.[3,8]

IV. Conclusion

Cerebral abscess is an infrequent although expected complication of TAPVR that should be considered in the differential diagnosisofa child with TAPVR presenting with neurological symptoms. Uncorrected TAPVR and cerebral abscess are characterized by high mortality rates. Prompt diagnosis and treatment is essential in ensuring favourable outcomes in these patients.

Patient's consent
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Conflicts of interest

There are no conflicts of interest.

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