A 55-Day-Old Female Infant infected with COVID 19: presenting with pneumonia, liver injury, and heart damage

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Abstract

Previous studies on the pneumonia outbreak caused by the 2019 novel coronavirus disease (COVID-19) were mainly based on information from adult populations. Limited data are available for children with COVID-19, especially for infected infants. We report a 55-day-old case with COVID-19 confirmed in China and describe the identification, diagnosis, clinical course, and treatment of the patient, including the disease progression from day 7 to day 11 of illness. This case highlights that children with COVID-19 can also present with multiple organ damage and rapid disease changes. When managing such patients, frequent and careful clinical monitoring is essential.

Keywords. COVID-19 pneumonia; liver injury; heart damage.

Data about infants infected with novel coronavirus disease (COVID-19) are scarce. Herein, we report a 55-day-old case who presented with COVID-19 pneumonia. The exposure, symptoms, laboratory indicators and hospitalization were described in detail.

Keywords. COVID-19 pneumonia; liver injury; heart damage.

A 55-day-old otherwise healthy female infant of mixed feeding became ill with rhinorrhoea and a dry cough from January 28, 2020.She was admitted to our hospital on February 2, 2020. Before the onset of symptoms,she had been taken to Lu'an, Hubei Province by her parents for a family party between January 16 and January 24. At that party,the infant's uncle and aunt,Wuhan residents, presented as cough and fever.Then the child's parents were diagnosed as coronavirus disease 2019 (COVID-19) on January 31,2020 based on their symptoms, chest imaging, and viral RNA in pharyngeal swabs. The nasopharyngeal swab obtained from the infant also tested positive for severe acute respiratory syndrome coronavirus (SARS-CoV-2) on real-time reverse transcription–polymerase-chain-reaction (RT-PCR) assay.

On admission, the physical examination showed that vital signs were within normal ranges except for pharyngeal hyperemia. A chest computed tomographic (CT) scan was reported as showing patchy shadows and ground glass opacity in the right lung (Figure 1A). Laboratory results reflected there were alterations in hepatic function measures and mildly abnormal myocardial zymogram(Table1). Lymphocyte count,platelet count, CD8+ T lymphocyte count and serum IgM level were all mildly elevated.Other laboratory examinations including hemoglobin,D-dimer, activated partial thromboplastin time, prothrombin time, C-reactive protein, erythrocyte sedimentation rate,and renal function in this patient showed no abnormalities. Both Rotavirus in stool and Cytomegalovirus DNA in blood were negative.Based on the definite contact history and the above test results,the infant was diagnosed as COVID-19 (ordinary type).She was isolated and treated empirically with the inhaled interferon α-1b(15μg,bid), amoxicillin potassium clavulanate(30mg/kg, Q8H,ivgtt), reduced glutathione, ursodeoxycholic aci and traditional Chinese medicine lotus qingwen.

On days 2 through 6 of hospitalization (days 7 through 11 of illness), the patient became sicker, presenting as a frequently productive cough accompanied by occasional tachycardia(150-170 beats per minute). Decreased arterial oxygen partial pressures (lowest PaO2, 56 mmHg) with elevated lactic acid while breathing ambient air were found in the morming of hospital day 4(Figure 2). She received sputum suctioning. Meanwhile,oxygen was supplied through a nasal cannula immediately,and ambroxol was administrated to eliminate phlegm. Because there was a trend of aggravation in the disease grade,a second chest CT scan was performed in the evening of hospital day 4 (illness day 9) ,which showed evidence of progressive pneumonia(Figure 1B). These radiographic findings coincided with a progress in respiratory status. Abnormal myocardial zymogram on admission and increased troponin I(0.025μg per liter) on hospital day 4 indicated myocardia injury, so intravenous sodium creatine phosphate was added to protect her heart. During this period,the baby still had a good appetite, without diarrhea,oliguria or shock. On day 11 of the patient's illness, a stool specimen was collected for the first time to detect the viral RNA and the PCR result showed positive.

On days 7 through 12 of hospitalization (days 12 through 17 of illness), the patient's clinical condition gradually improved and the respiratory symptoms disappeared on hospital day 11.Supplemental oxygen was discontinued, and her oxygen saturation values were 94 to 100% while breathing ambient air. The heart rate fluctuated between 120 and 140 beats per minute. The laboratory examinations on hospital day 10 showed elevated myocardial zymogram and abnormal liver function both recovered. On hospital day 11 (illness day 16), a third chest CT scan showed patchy shadows and ground glass opacity were obviously absorbed (Figure 1C). In view of the patient's clinical manifestations and other laboratory findings,the citrobacter freundii in two sputum cultures was considered as a colonized bacteria of the respiratory tract, not being treated. Three pharyngeal swabs obtained from

hospital day 10 to hospital day 13 were found to be negative for SARS-CoV-2 on RT-PCR assays.Amoxicillin potassium clavulanate was discontinued on hospital day 11, and interferon α-1b was discontinued on the following day. According to the latest interim guidance of the COVID-19 diagnosis and treatment in China, the patient met the discharge criteria.However, we found that her anal swabs collected on hospital day 11 and 13 were still positive for SARS-CoV-2 RNA. Thus, the patient remained hospitalized. From February 16,she was transferred to another hospital for continued isolation and observation. In the process of manuscript revision,we have learned that she was still asymptomatic during this period,and the anal swab collected on February 28 was negative for this viral RNA.

About her mother, we have learned that this viral RNA had been detected in the mother's stool sample on February 4 (illness day 8) and anal swab on February 7(illness day 11),although she also had no abdominal symptoms.In addition,three consecutive tests of SARS-CoV-2 RNA in breastmilks of the monther were negative between February 2 to February 4. The mother's urine specimen collected on February 6 was negative for SARS-CoV-2.

Discussion

The SARS-CoV-2 infection can lead to acute resolved or fatal pneumonia. Currently, the main source of infection is COVID-19 patients. The route of human-to-human transmission of SARS-CoV-2 is mainly through respiratory droplets and contacts. The faecal–oral route and maternal-infant transmission have not been confirmed or ruled out. Although the number of cases has increased rapidly, information on the clinical characteristics of affected pediatric patients is rare. We have learnt that middle east respiratory syndrome-coronavirus(MERS-

CoV) in children is less frequent and seems to be associated with less mortality unless the patient has underlying comorbidities[1,2]. This impression in children with MERS-CoV was also reported during the severe acute respiratory syndrome coronavirus (SARS-CoV) infections in pediatric patients, where symptoms were milder, few hospitalizations, and resulted in no death[3,4]. Possible explanations include low exposure, presence of asymptomatic or mildly symptomatic patients, the immature immune system and the presence of yet to be identifed factors. SARS-CoV-2 strains are less genetically similar to SARS-CoV (with 79% identity) and MERS-CoV (about 50%)[5], so regarding the infection of SARS-CoV-2 in children,there are still many gaps in our understanding, including route of transmission,susceptibility,clinical course of patients, the disease pathogenesis, pharmacological therapies, prognosis and so on.

MinWei et al reported nine infants diagnosed with COVID-19,including one baby at age of 1 month 26 days.However, there was no detailed information about the patients' examination and treatment in this letter[6]. Our report illustrated the full clinical course of the infected infant.The patient had traveled to Hubei, China, and had the sick contacts during her stay in Hubei. Although signs and symptoms caused by SARS-CoV-2 infection at the prodromal phase was atypical and nonspecific, the chest CT scan showed bilateral patchy shadows, in line with the atypical pneumonia.Acute liver injury and cardiac damage were also observed in this patient. Due to the difficulty of specimen collecting and the risk of cross infection when going out for examination,other etiological tests of cardiac and hepatic abnormalities except for rotavirus and cytomegalovirus detection were not performed. Given the patient's definite contact history of COVID-19, positive SARS-CoV-2 RNA,and good response to treatment, the two injuries were thought to relate with COVID-19. Elevated $CD8^+$ cell count in peripheral blood and increased serum IgM level on admission might indicate that both cellular immune and humoral immune in acute infection have been activated to

produce cytotoxic T lymphocyte and antibodies to kill and neutralize the virus. Huang C et al found that SARS-CoV-2 infection appears to be initially associated with an increased T helper 2 cell response, which might reflect a physiological reaction to suppress overt inflammatory responses[7].

Our case patient initially presented with mild dry cough and no fevers.However,from day 7 of her illness, her symptoms were gradually getting worse,especially on day 9 of her illness, coinciding with results of the second chest CT scan. The timing of our patient's progression is consistent with that reported in adults[8,9]. Due to the lack of effective verbal communication with infants, more frequent and careful clinical monitorings should be performed to find disease progression. When the patient's status was worsening, symptomatic support was strengthened.Corticosteroids were not used in this patient,because her clinical condition was not completely out of control and there is still no conclusive evidence of net benefit in the treatment of respiratory infection due to several viruses including SARS-CoV and MERS-CoV[10,11].Therefore, the timely and appropriate symptomatic support treatment and patients' own immune system may be the best means to combat the SARS-CoV-2 in pediatric patients.

We have noticed that three consecutive tests of SARS-CoV-2 RNA in the breastmilk of the infant's monther were negative.Whether the virus could not enter the milk due to some barrier and whether a confirmed case could continue to provide her breastmilk for baby deserve further study.In addition,The SARS-CoV-2 RNAs have been detected in the stool specimens or anal swabs of both the patient and her mother, indicating a potential alternative route of fecal-oral transmission, even in patients without gastrointestinal symptoms. But the clinical significance of this detection of viral RNA outside the respiratory tract is unknown at this stage.Faecal RNA appeared later than that of pharyngeal swab in the mother,which might indicate that the virus is swallowed into the digestive tract during the process of its

elimination from the respiratory tract.Moreover,we also observed that it takes longer for a faecal SARS-CoV-2 RNA to turn negative than which of pharyngeal specimen in the infant. This phenomenon might indicate that the digestive tracts clear the virus more slowly than the respiratory tracts. Whether the patient isolation should not be terminated until SARS-CoV-2 RNA in the stool turns negative is worth exploring.Just like the other two studies[9,12],we found no evidence of viral shedding in urine of the patient's monther. However, improved systematic serial collection and testing of an increased number of urine samples is warranted to exclude this route of transmission.Finally, our understanding of COVID-19 is changing on a daily basis,and with continuous efforts from all sides, we hope and believe that this abominable disease can be controlled soon.

(1A) CT images on admission (illness day 6): Multiple patchy shadows and ground glass opacity in the upper and lower lobes of the right lung(red arrow).

(1B) CT images on hospital day 4 (illness day 9): Compared with day 6 of illness, the lesion progressed and the range widened(yellow arrow), accompanied with small consolidation shadow and a few stripe shadows(red arrow).

(1C) CT images on on hospital day 11 (illness day 16): Compared with day 9 of illness, the inflammation of the right lung was obviously absorbed. Small patchy shadows with increased density and a few strip-like shadows were still observed in the upper lobe of the right lung(red arrow).

Figure 1: Chest CT images of a 55-Day-Old Female Infant With COVID-19

Note:the scanning condition was low dose CT with 80kV tube voltage and 23-26mAs tube current (automatic).

Table 1.Laboratory indicators on admission and the changes after treatment

Figure 2.Disease course of the infected infant and important information about her parents

Notes

Acknowledgment. We thank this infant and her parents involved in the study. We acknowledge all health-care workers involved in the diagnosis and treatment of patients with COVID-19 in Guizhou Provincial People's Hospital.

Role of the Funder/Sponsor. None.

Potential conflicts of interest. All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript

have been disclosed.

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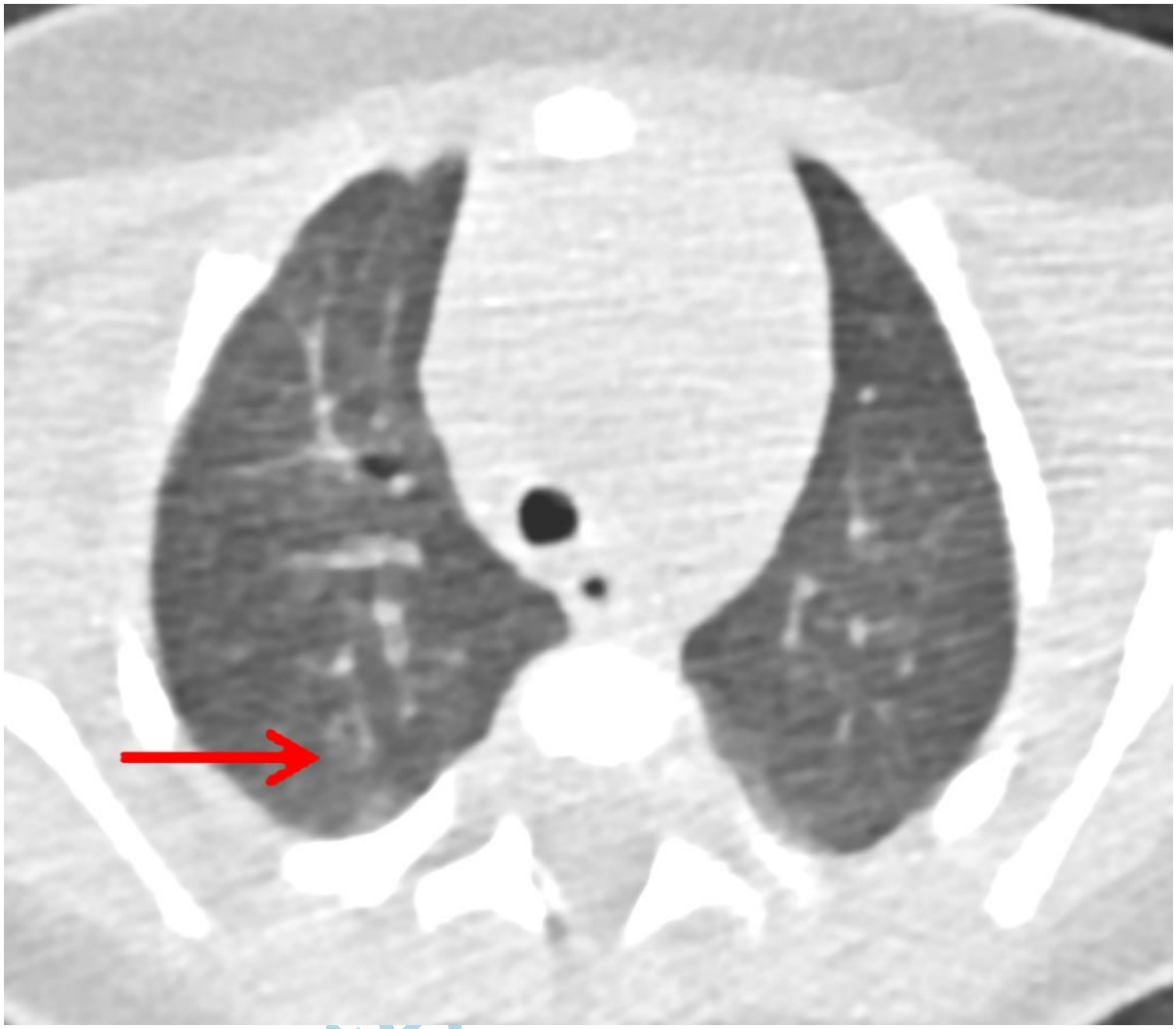
Measure	Reference Range	Illness Day 6 Hospital Day1	Illness Day9, Hospital Day4	Illness Day15, Hospital Day10
White-cell count ($\times 10^9$/L)	6-18	7.96	10.04	9.46
Lymphocyte count ($\times 10^9$/L)	1.1-3.2	5.22#	6.59#	6.25#
Neutrophil count ($\times 10^9$/L)	1.8-6.3	1.87	2.44	2.01
Platelet count ($\times 10^9$/L)	125-350	406#	449#	604#
Hemoglobin (g/l)	95-145	112	91*	101
Erythrocyte sedimentation rate (mm/h)	0-20	7	2	-
C-reactive protein (mg/L)	0-5	0.56	0.63	0.32
Procalcitonin(ng/ml)	0-0.046	0.15#	0.11#	-
Alanine aminotransferase (U/L)	7-40	84#	49#	33
Aspartate aminotransferase (Ul/L)	13-35	100#	47#	35
Total bilirubin (μmol/L)	3.4-20.5	33.7#	20.1#	10.9
Direct bilirubin (μmol/L)	0-8.6	25.2#	16.6#	7
Total bile acid (μmol/L)	0-10	154.4#	89.8#	46.4#
Creatine kinase isoenzyme (U/L)	0-25	46#	-	25
α-hydroxybutyrate dehydrogenase (U/L)	44-148	237#	-	143
Troponin I (μg/L)	0-0.0156	-	0.025#	-
Creatinine(μmol/L)	15-45	20	19	21
Blood urea nitrogen(mmol/L)	1.8-6	3.61	2.09	2.15
Serum Immunoglobulin M (g/L)	0.06-0.21	0.66#	-	-
$CD8^+$ T cell count (cell/μl)	400-1700	2208#	-	-
D-dimer(μg/ml)	0-1.5	0.54	-	-
Activated partial thromboplastin time(sec)	21.1-36.5	30.6	-	-
Prothrombin time(sec)	9.2-12.2	9.7	-	-
Rotavirus in stool	Negative	Negative		
Cytomegalovirus DNA in blood	Negative	Negative		

The value in the patient was above normal.

*The value in the patient was below normal.

Figure 1A-1



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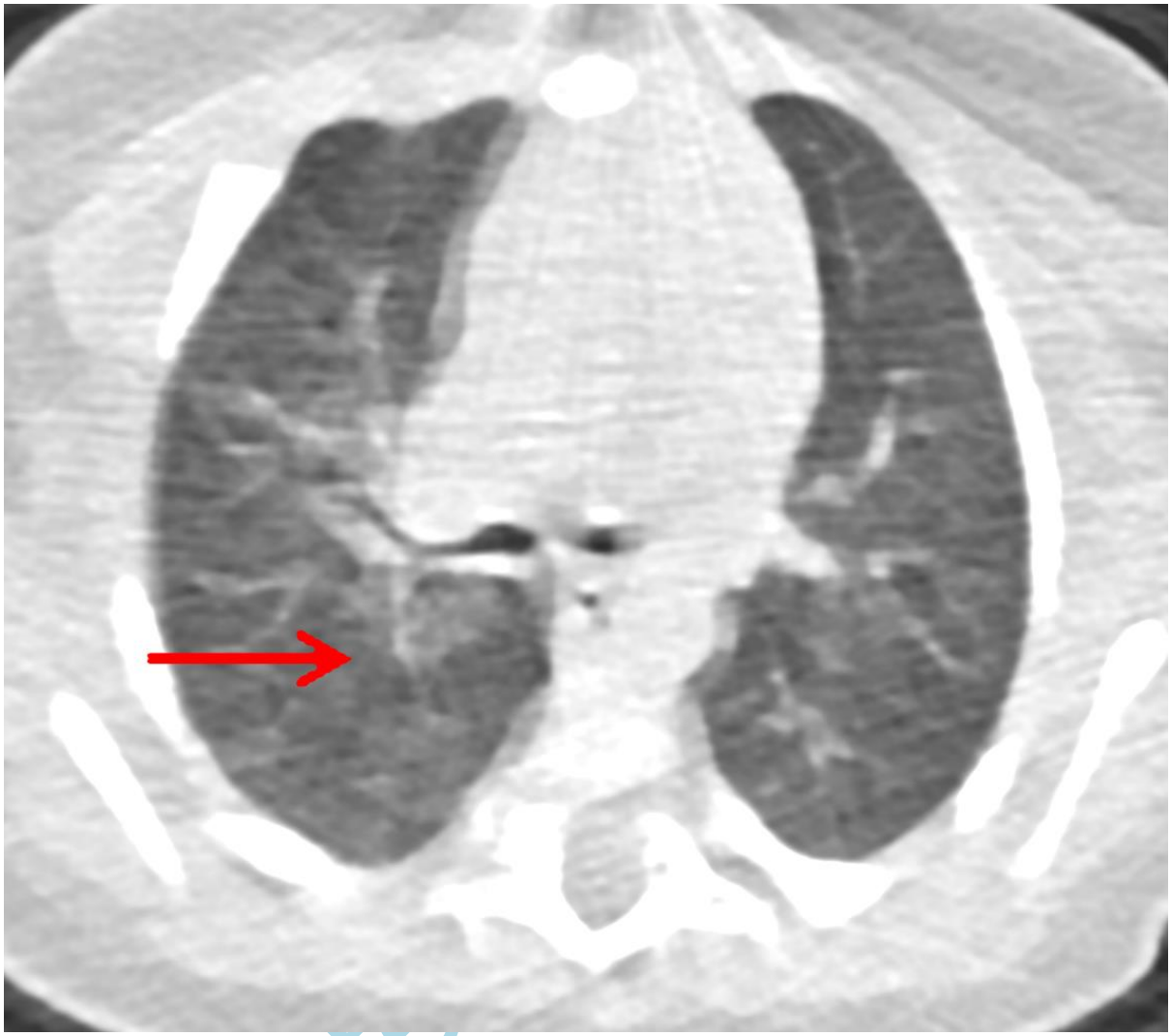

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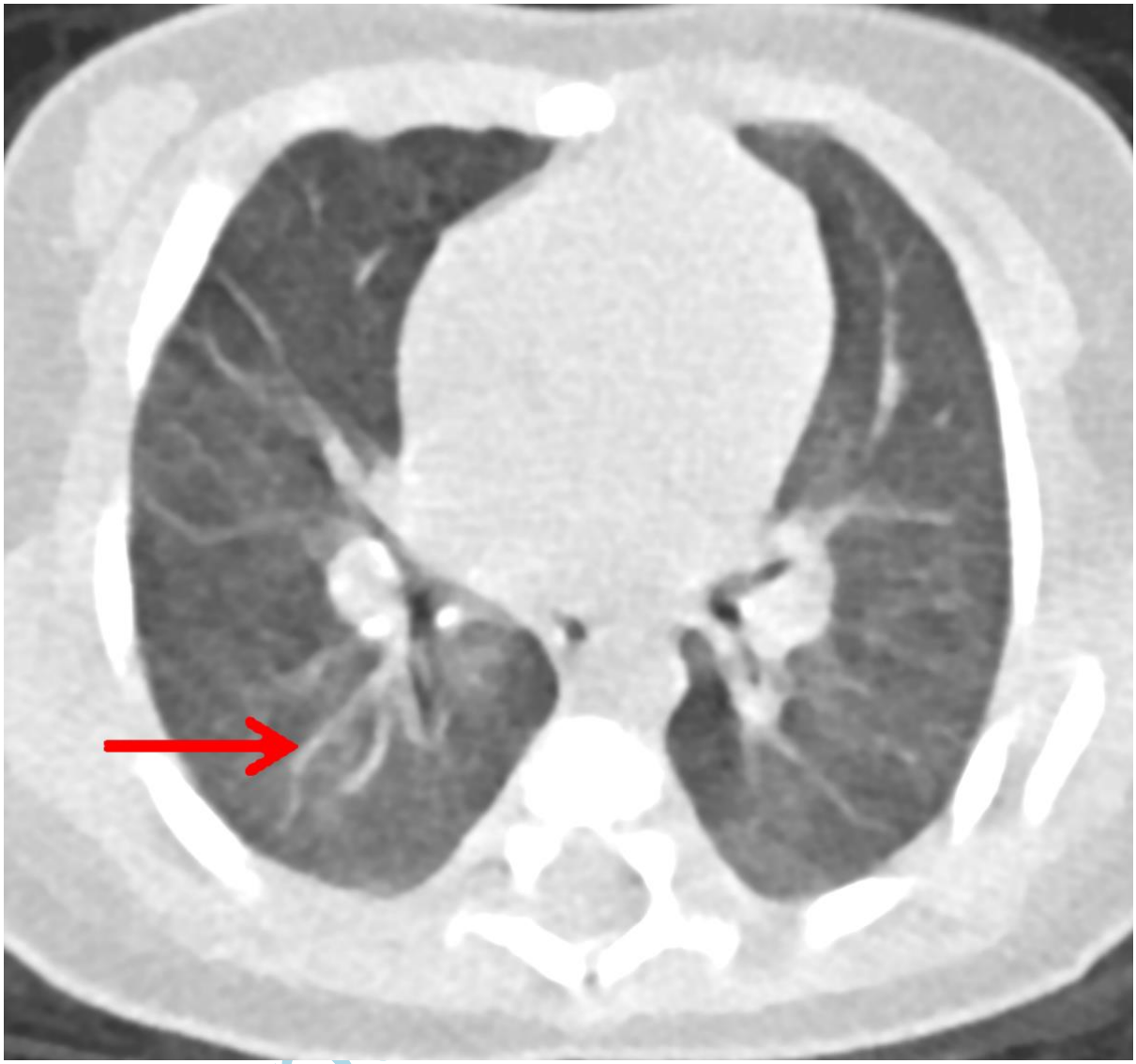

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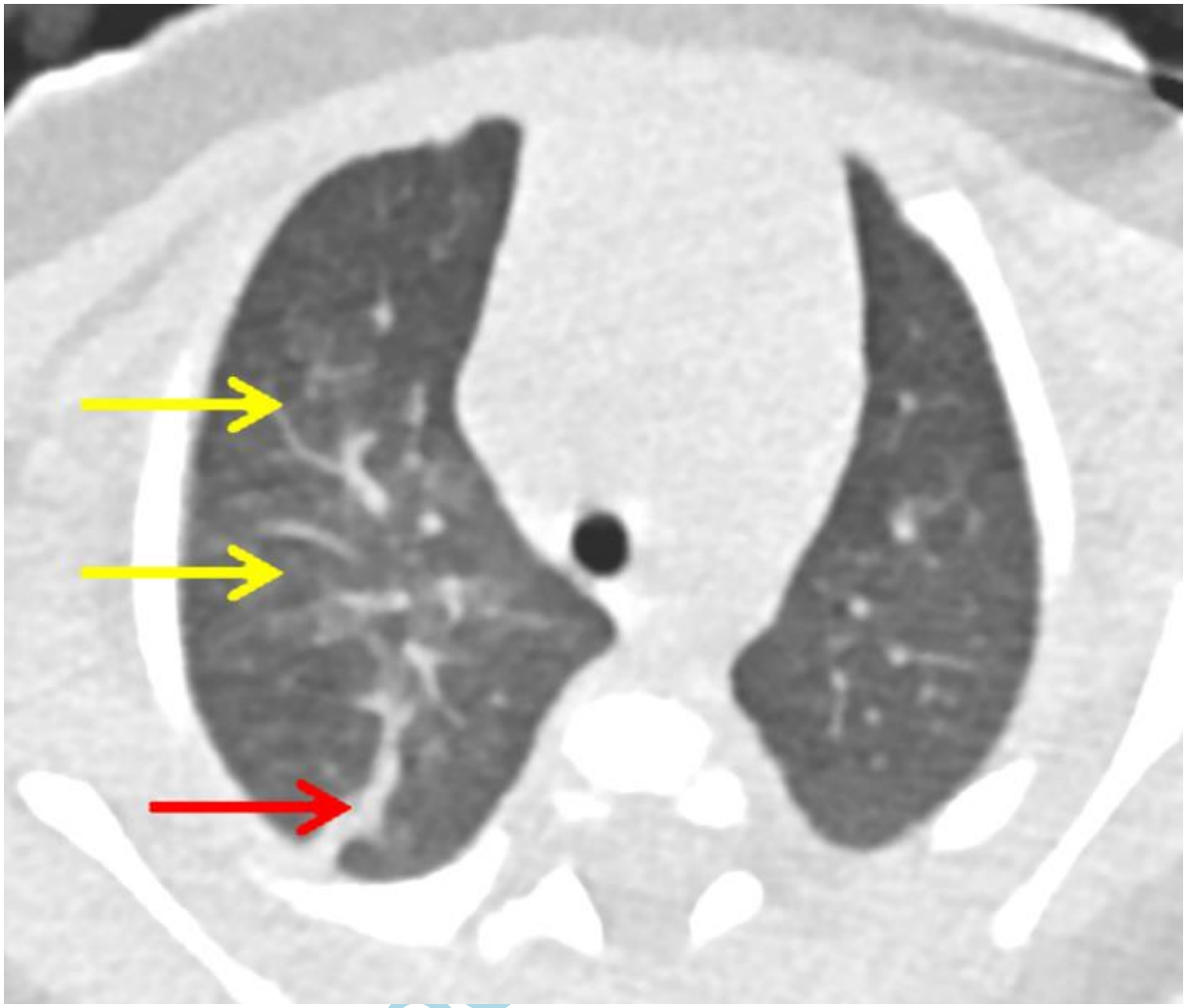

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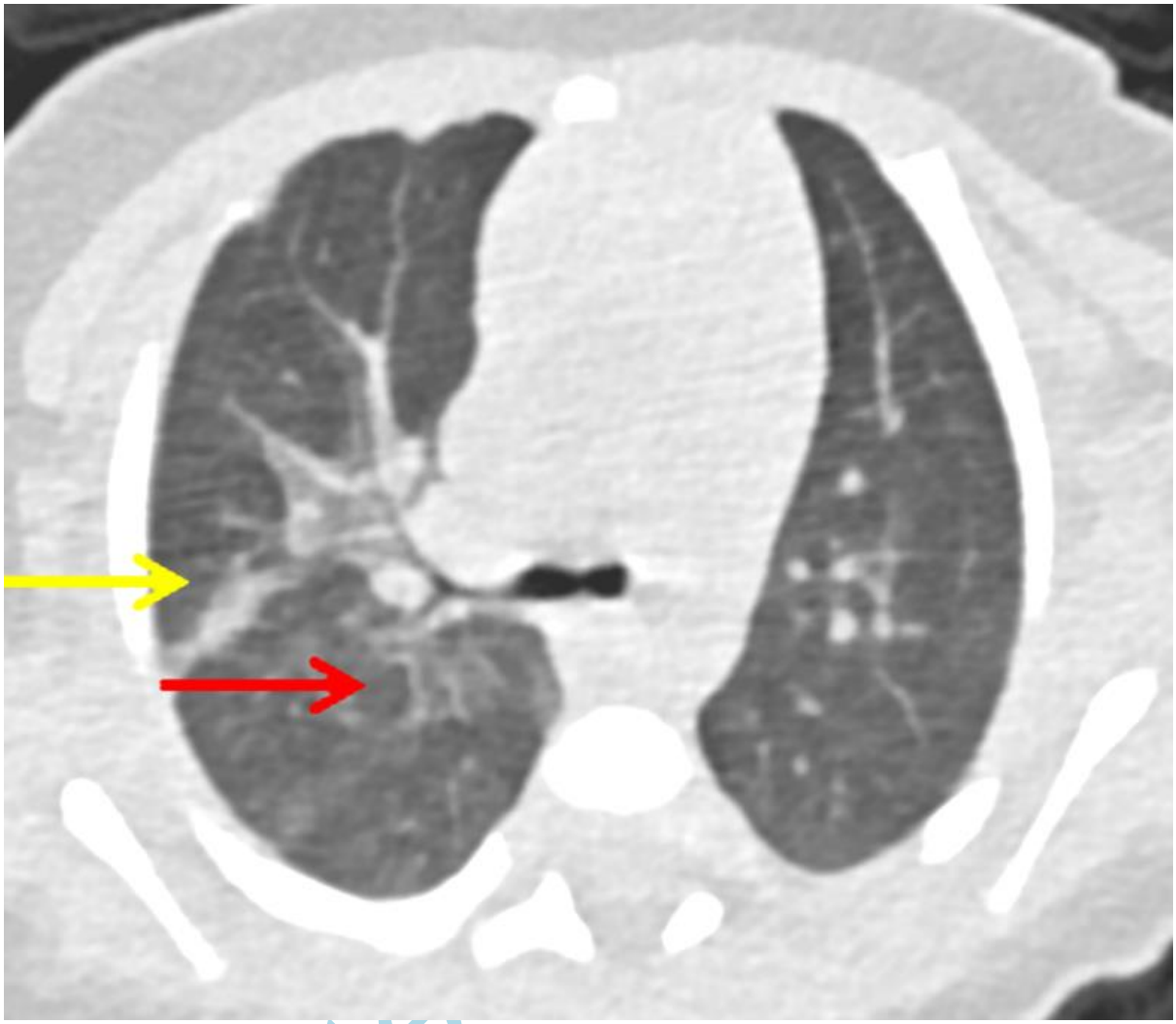

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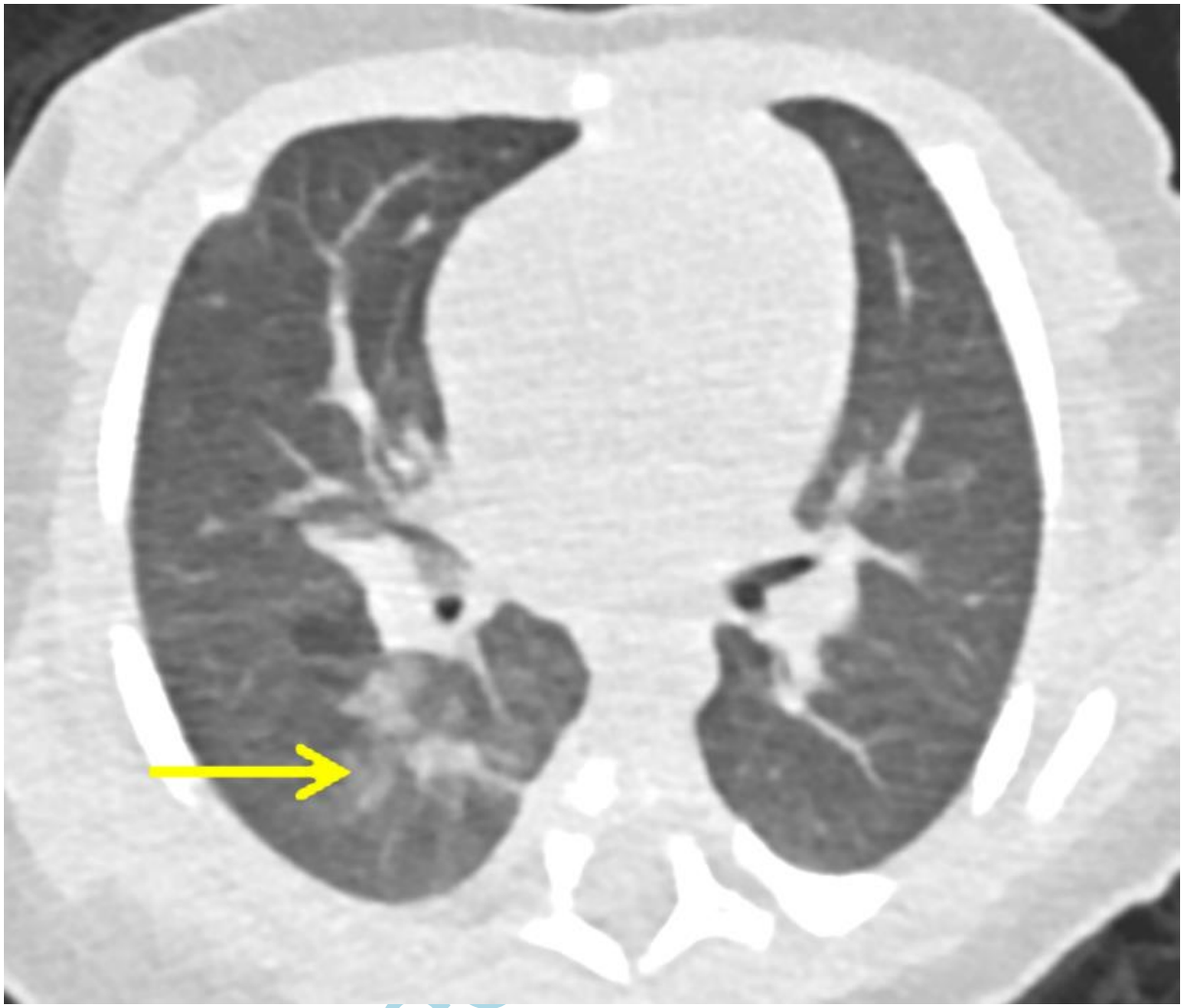

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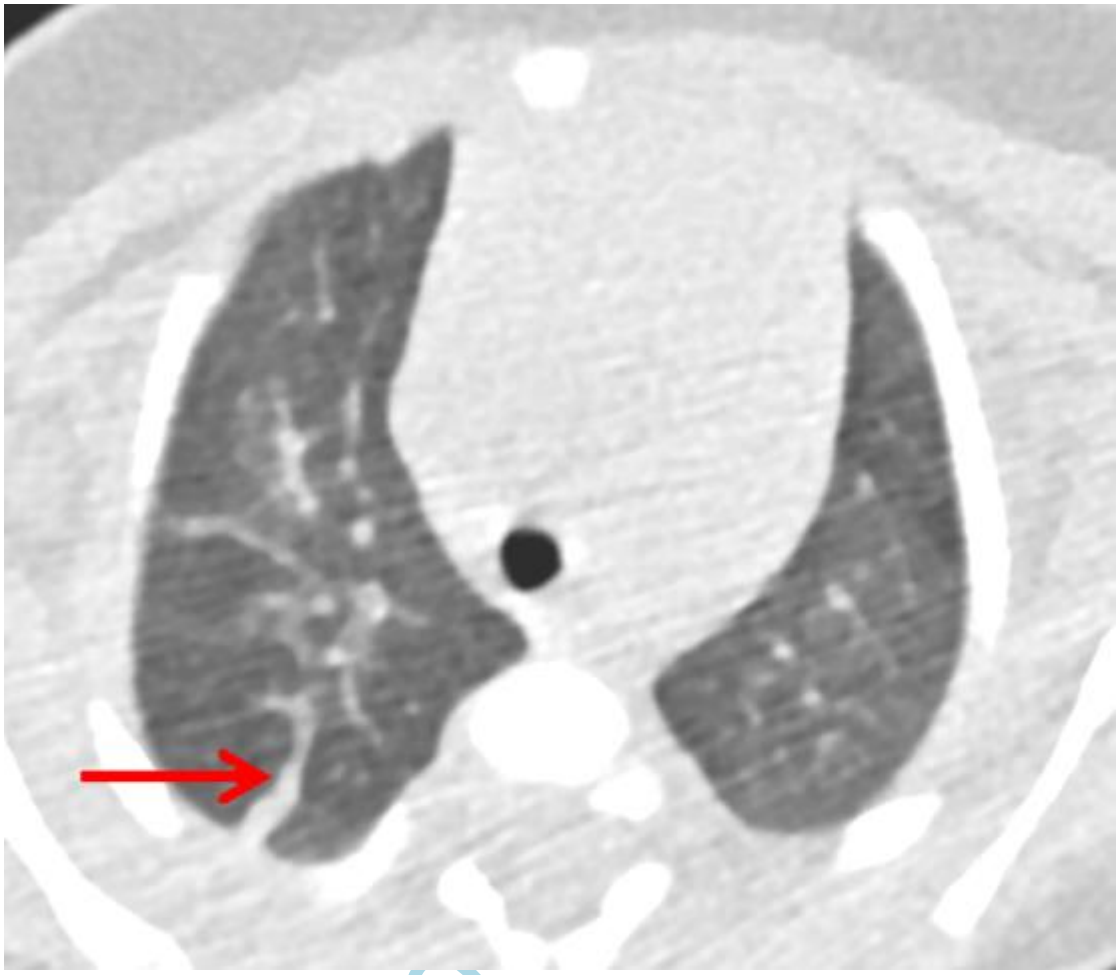

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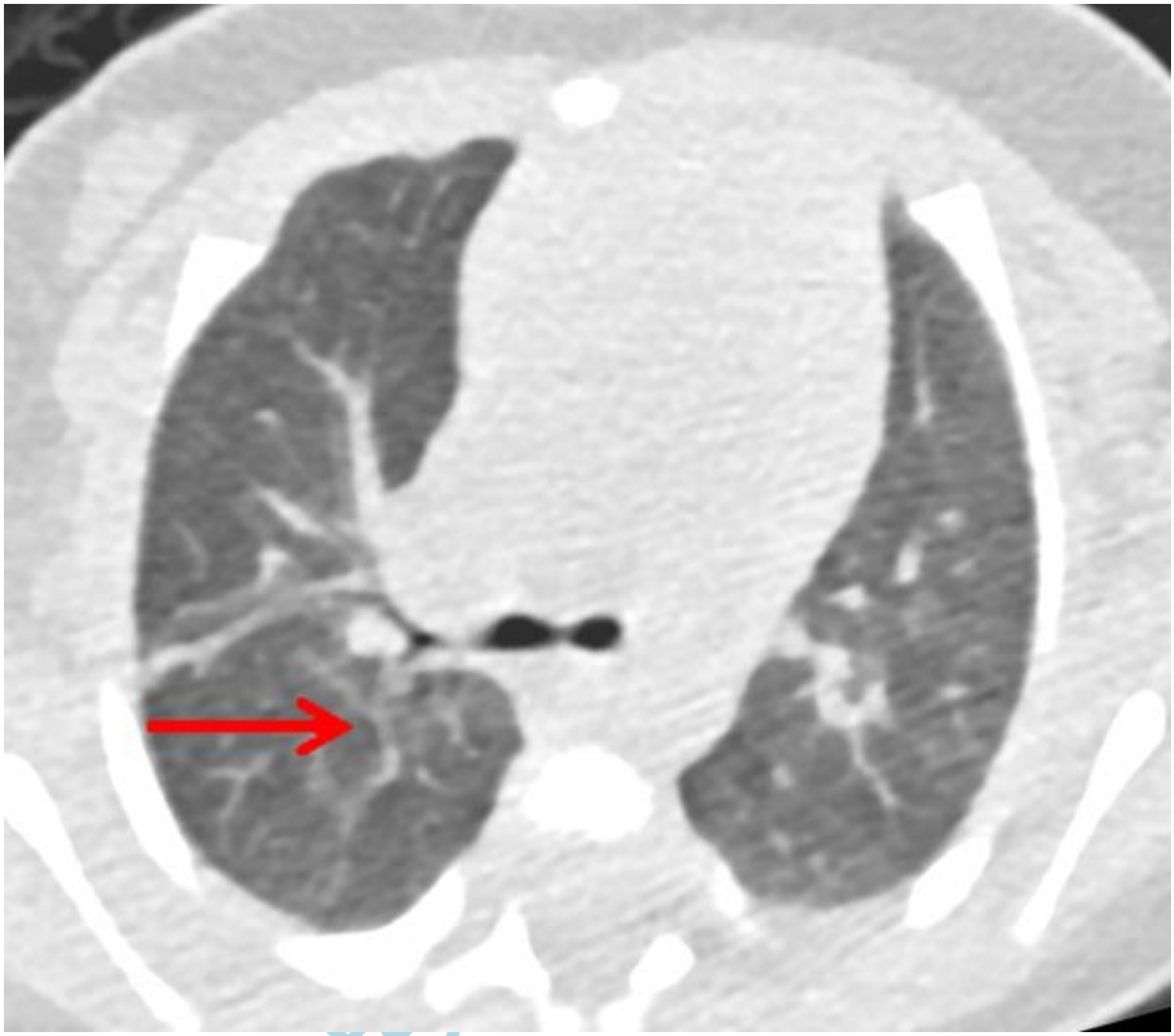

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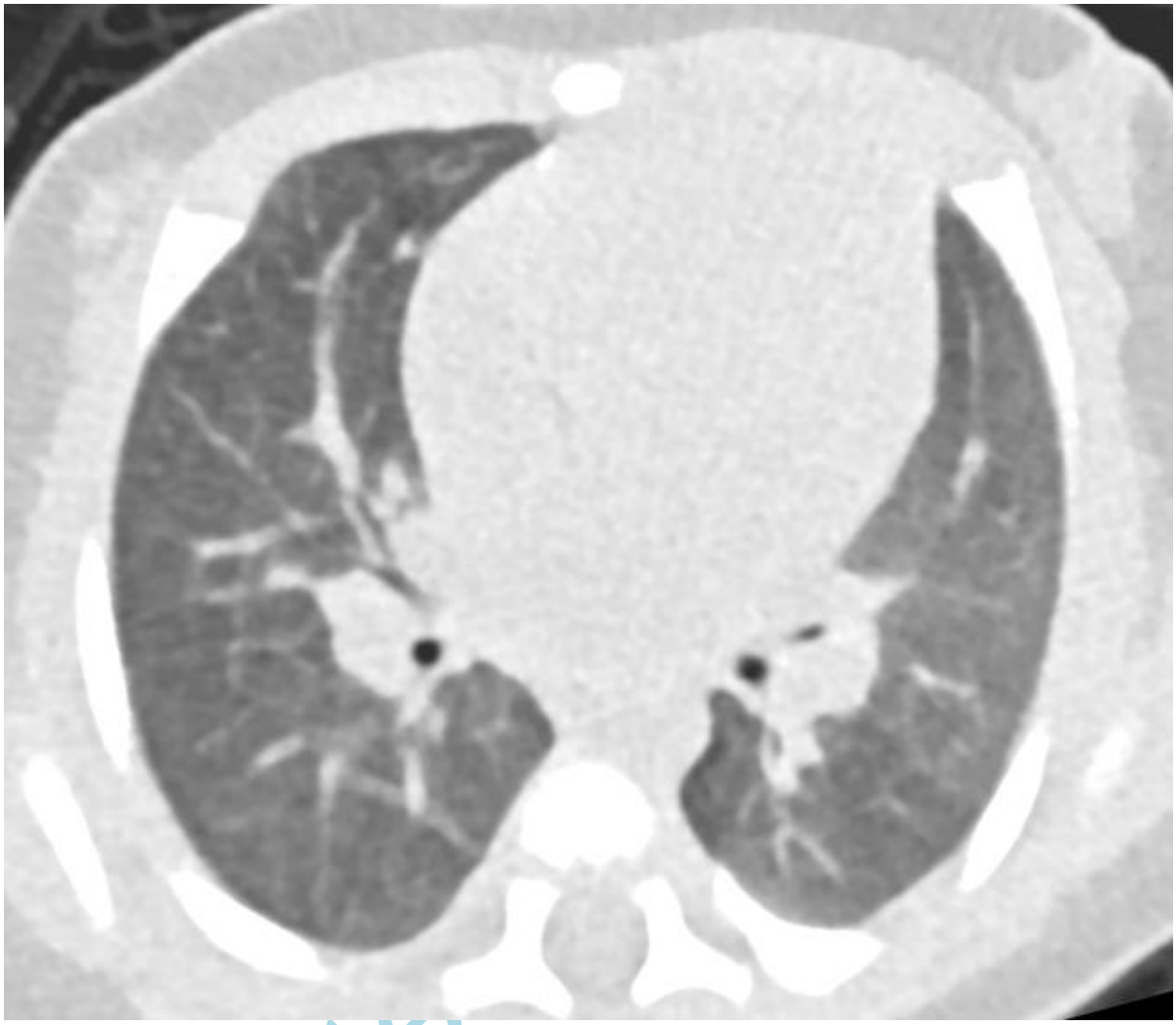

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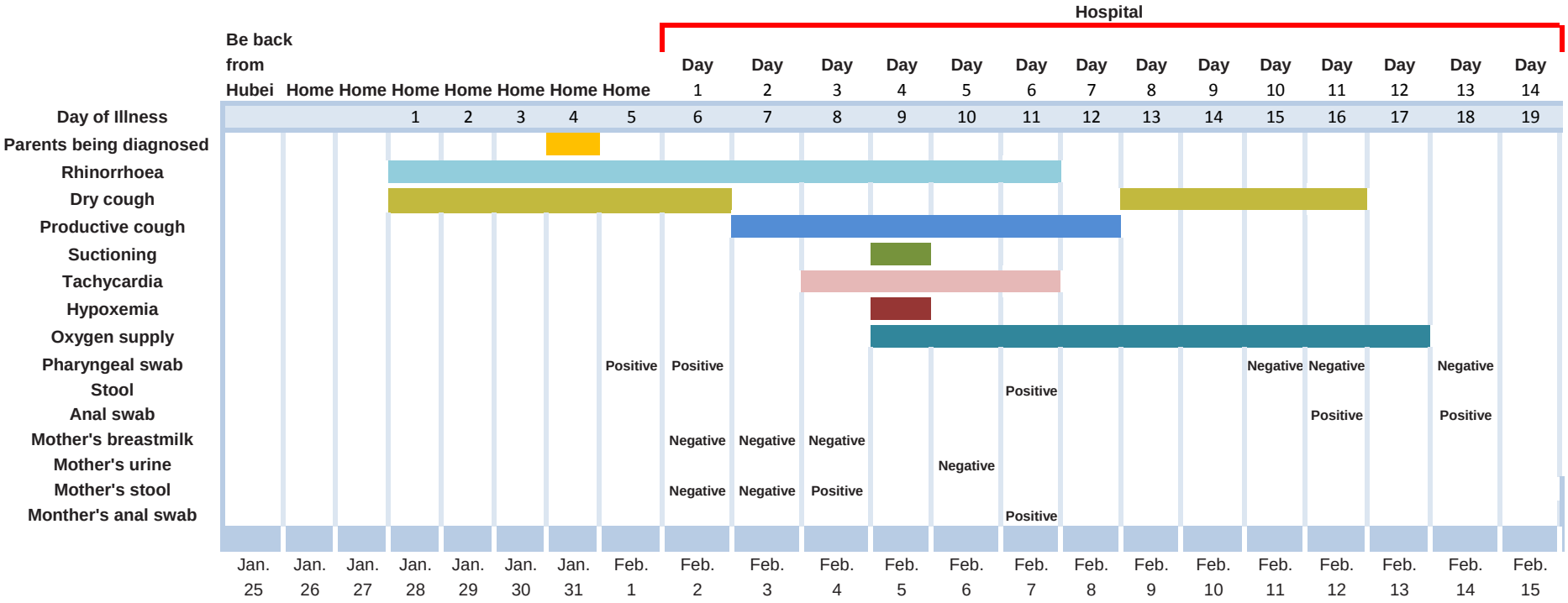

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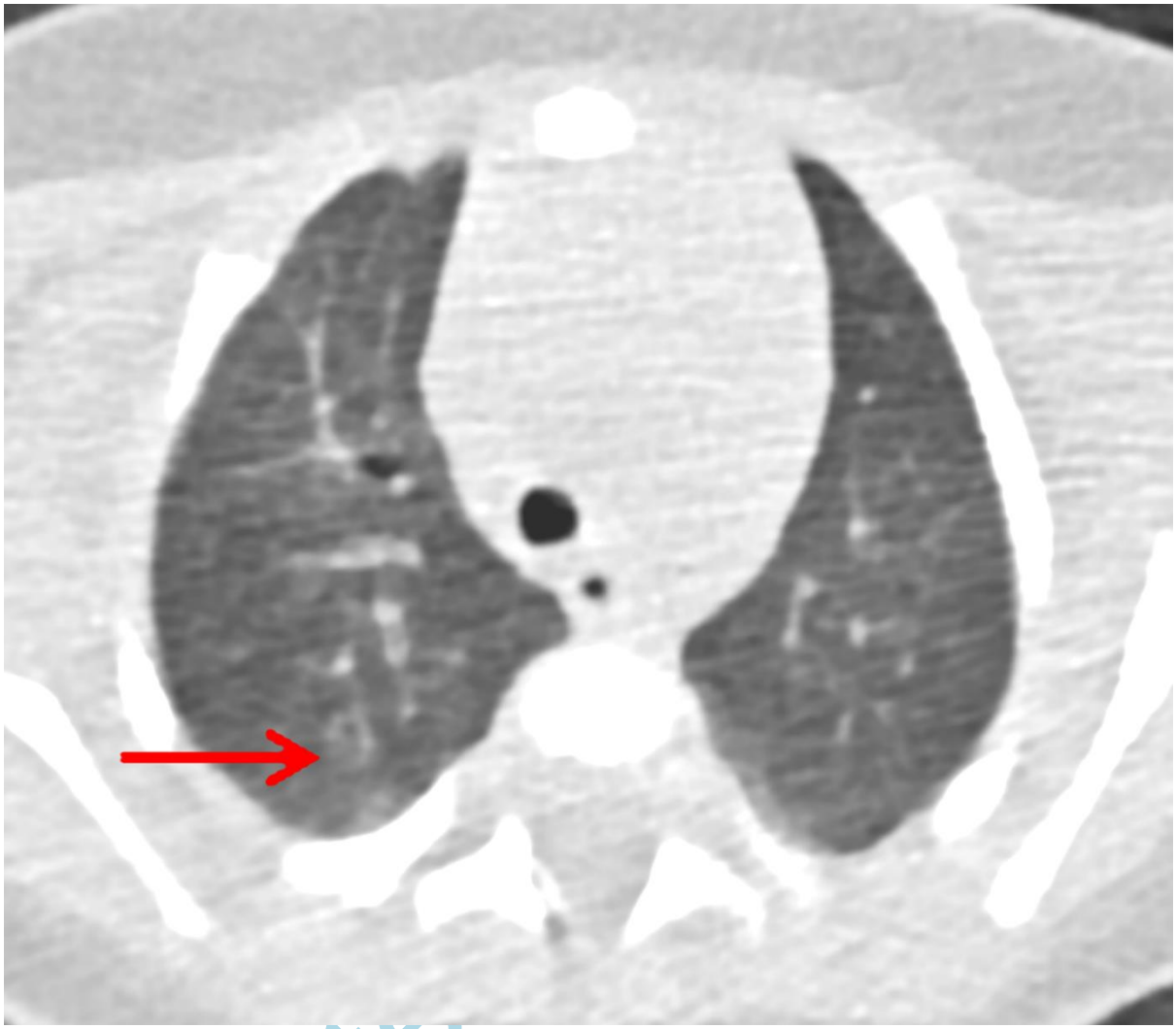

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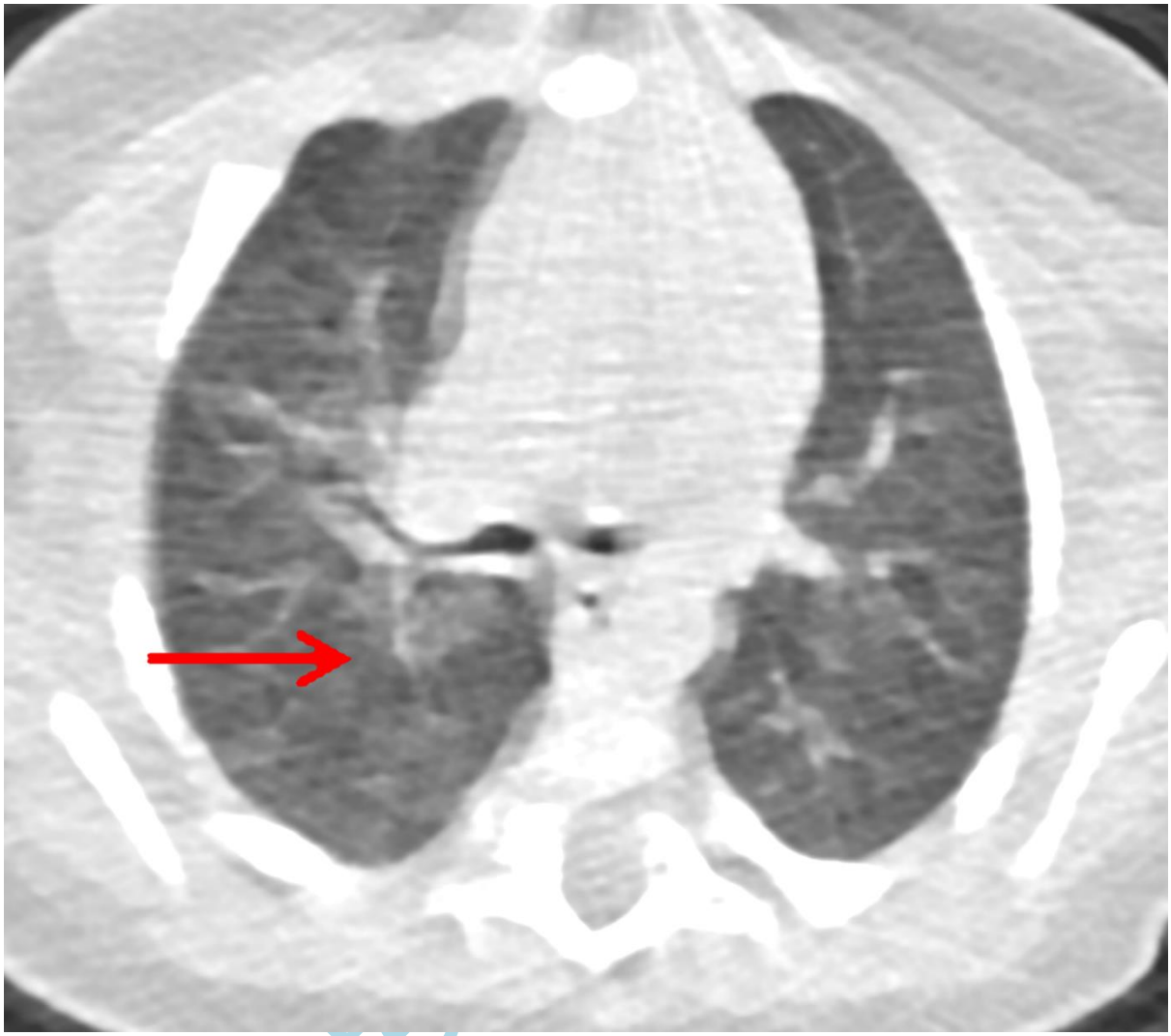

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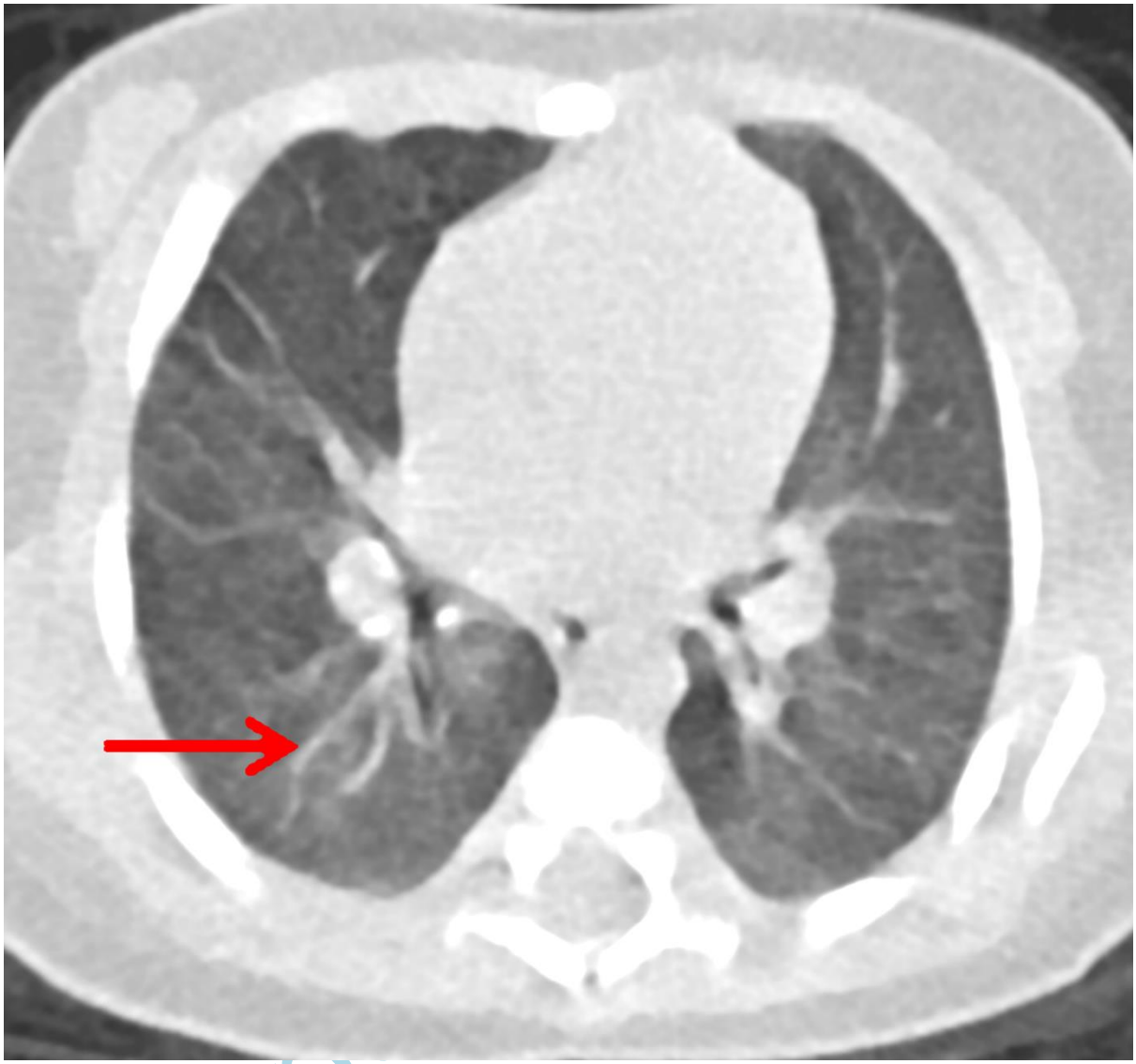

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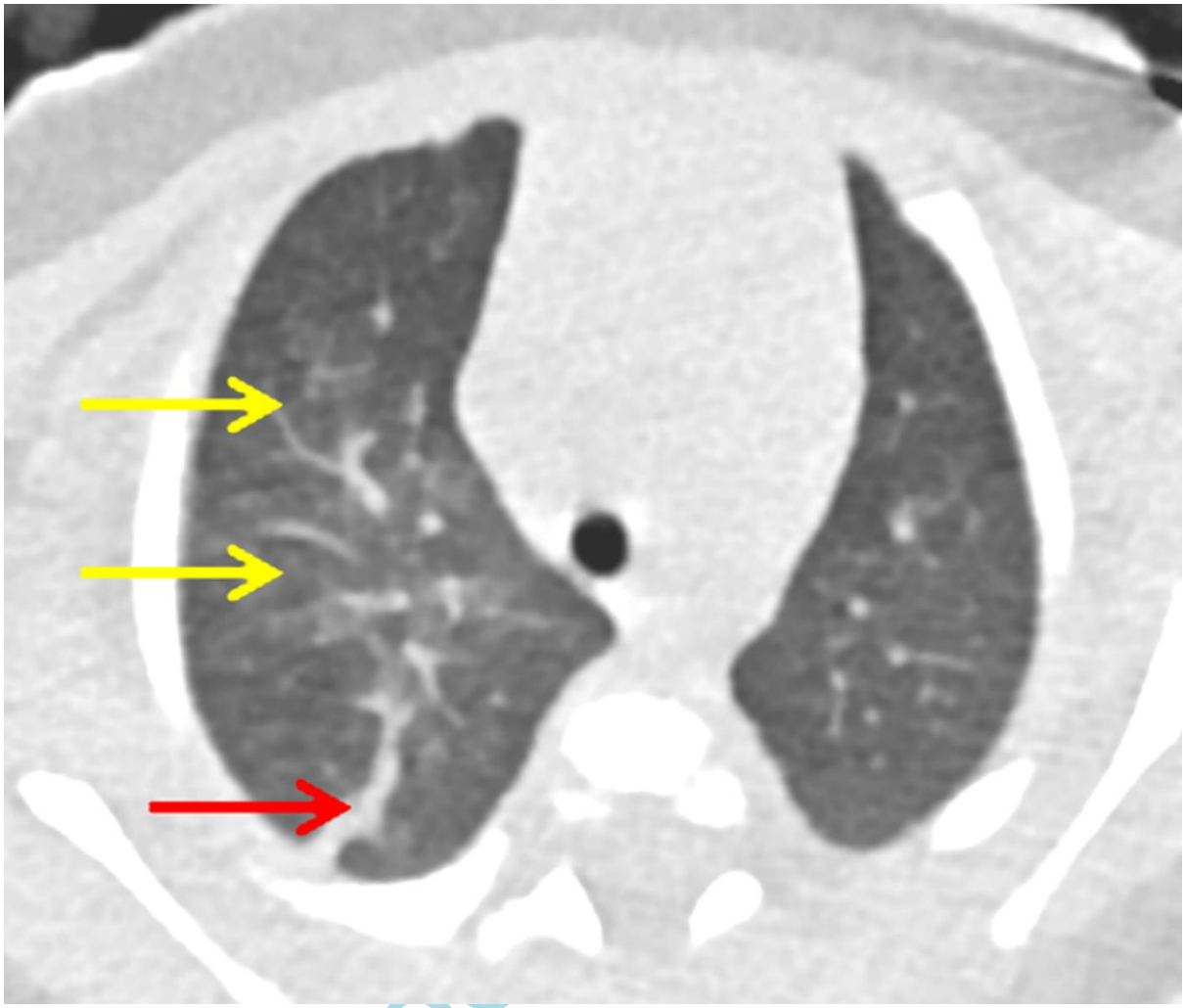

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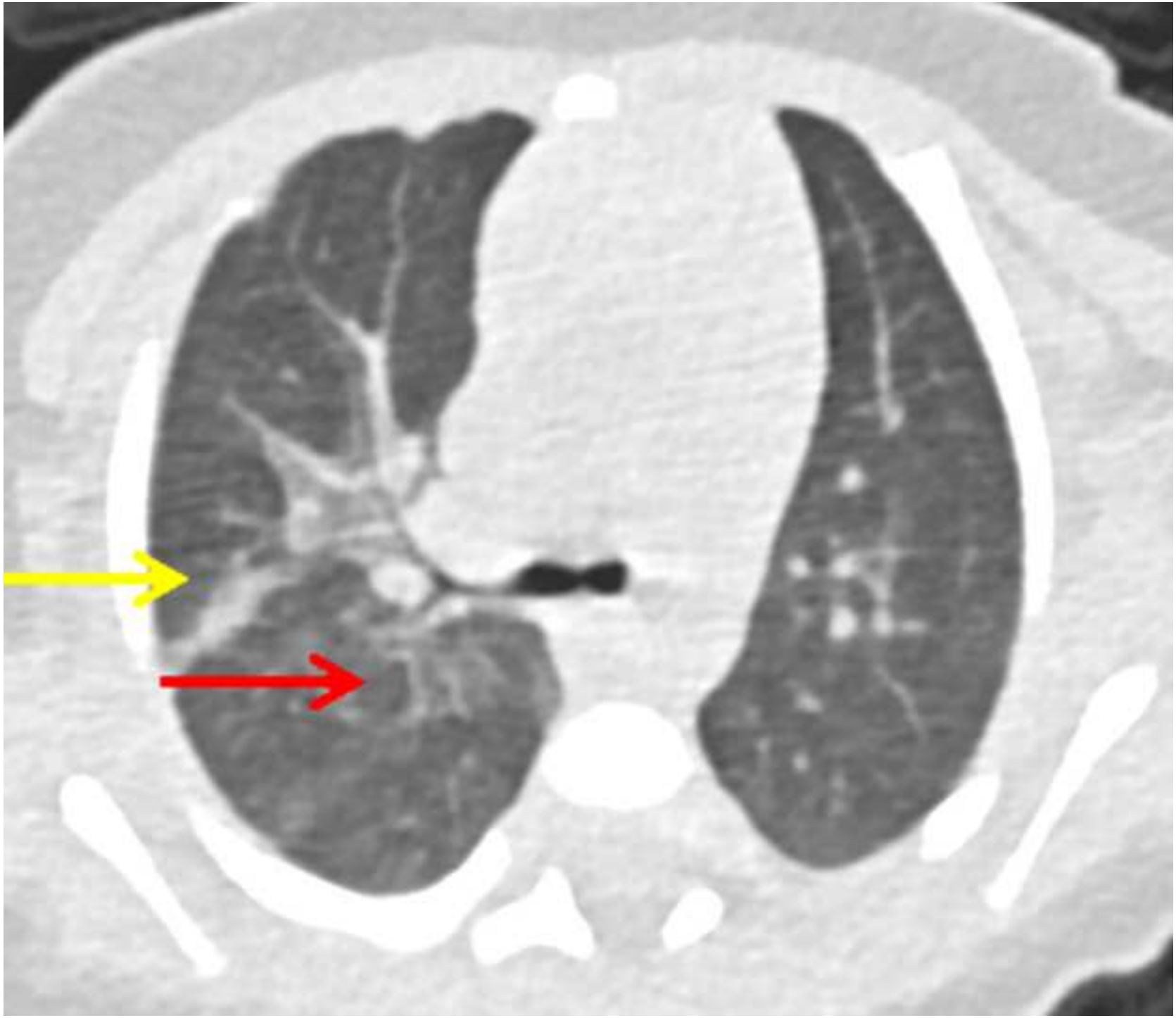

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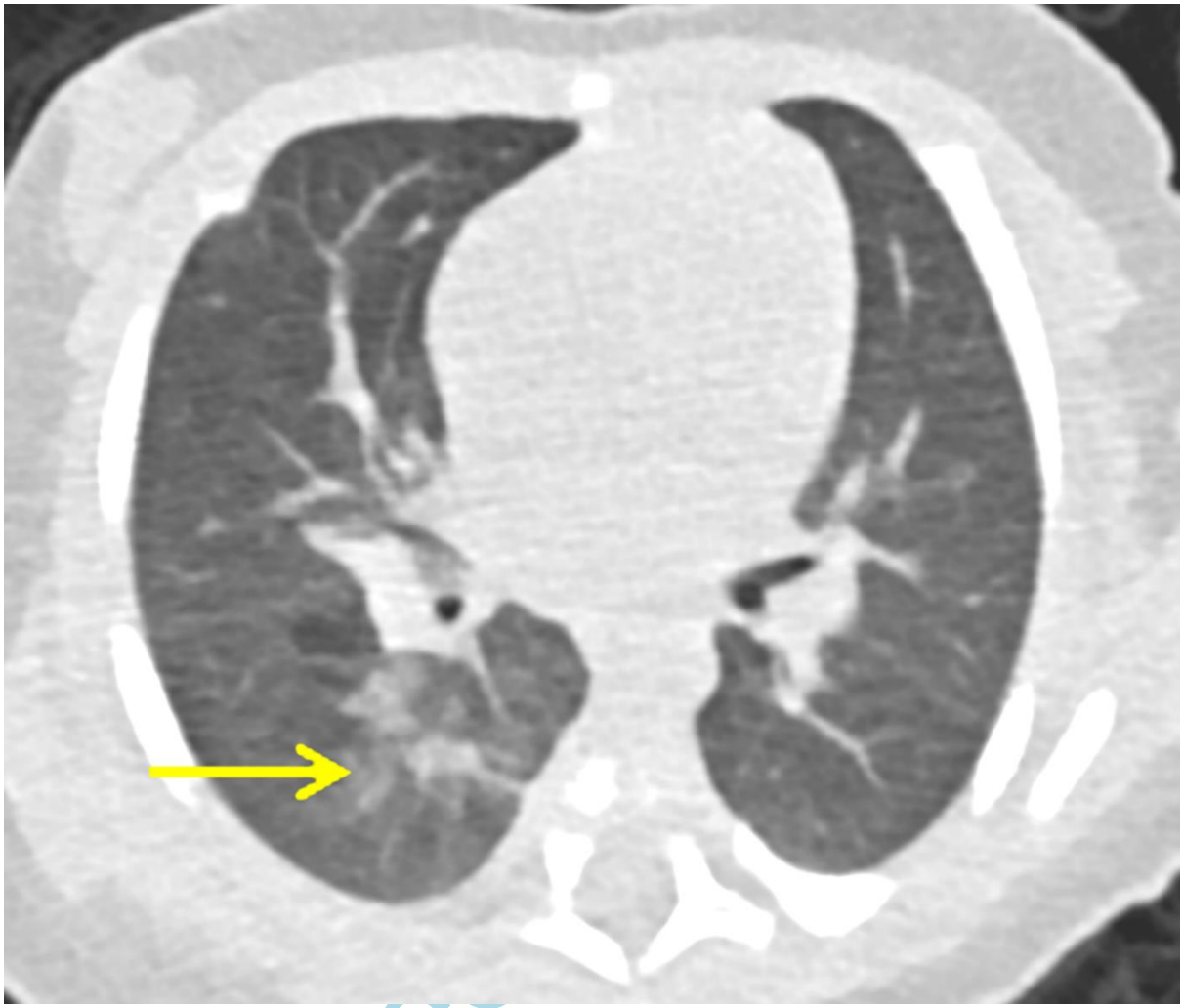

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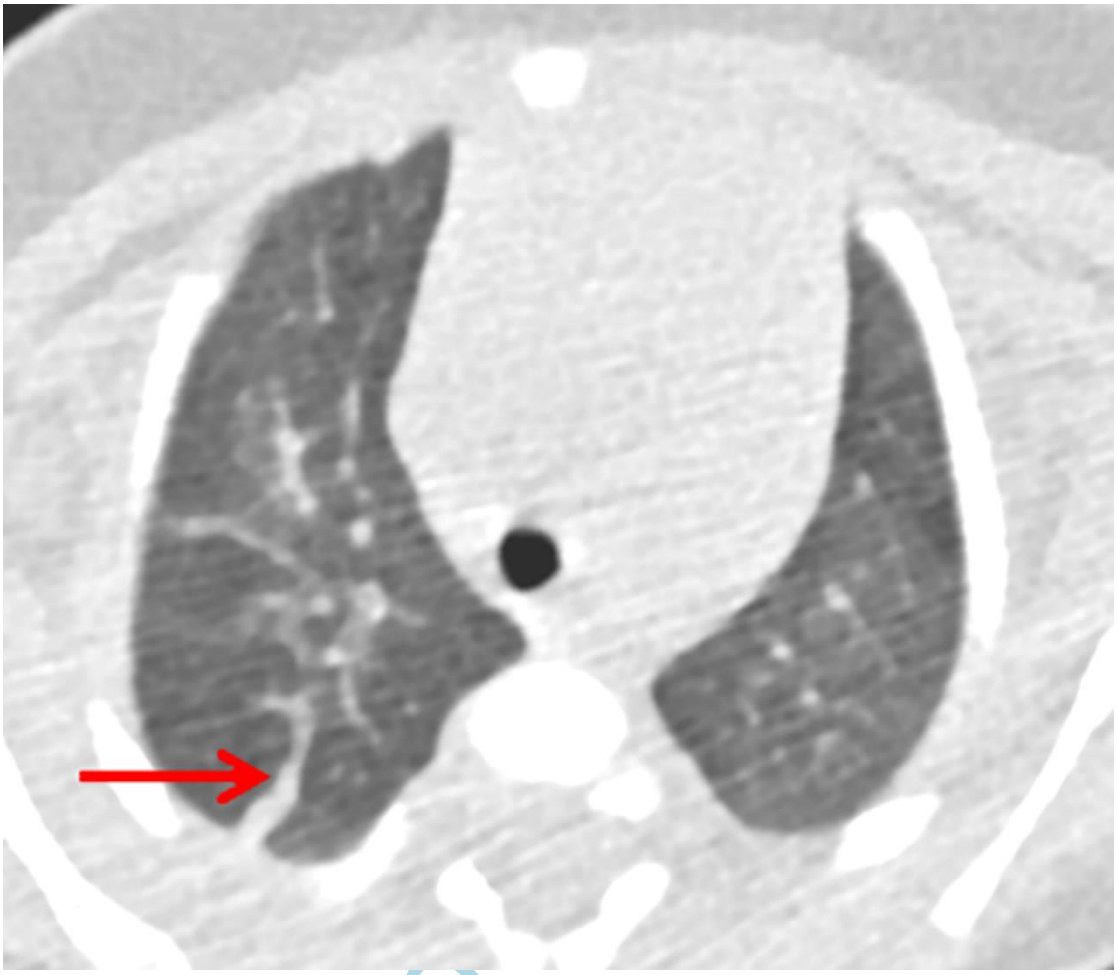

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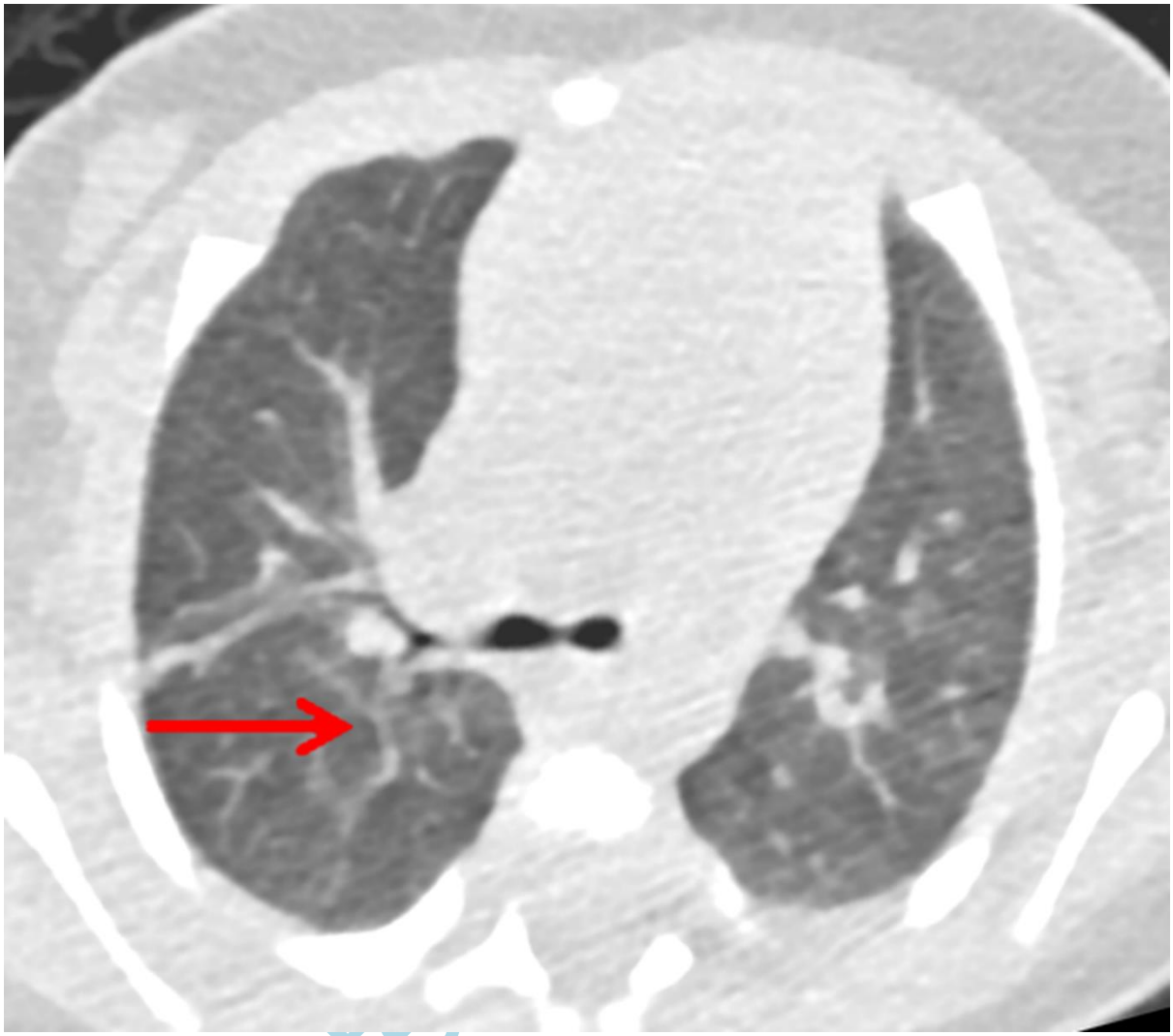

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