Elsedfy and Gamal
Egyptian Journal of Medical Human Genetics (2023) 24:28
https://doi.org/10.1186/s43042-023-00407-z

Egyptian Journal of Medical Human Genetics

CASE REPORT Open Access

Congenital hypothyroidism: a case report of an Egyptian child with congenital heart disease, pelvic kidney and cavernous transformation of portal vein

Heba Elsedfy[1] and Radwa Gamal[2*]

Abstract

Background A case of thyroid hormone deficiency which presented at birth. Thyroid hormones are essential for brain development and normal cognitive function. Common symptoms of congenital hypothyroidism (CH) include constipation, decreased activity, increased sleep and feeding difficulty. Common signs include dry skin, macroglossia and umbilical hernia. If congenital hypothyroidism is left untreated after birth, it can lead to permanent intellectual disability and growth failure.

Case presentation.

Here, we report a 10.5-year-old female with the typical features of CH. She is the sixth in order of birth of consanguineous Egyptian parents. No family history of similar condition. Our patient had primary CH caused by thyroid agenesis. She had congenital heart disease, pelvic kidney, cavernous transformation of portal vein and parenchymatous liver disease.

Conclusions Congenital hypothyroidism is associated with an elevated risk of congenital anomalies. Clinical suspicion of symptoms and signs of congenital hypothyroidism are important for early diagnosis and prevention of serious problems that are related to congenital hypothyroidism.

Keywords Congenital hypothyroidism, Congenital heart disease, Cavernous transformation of portal vein

Background

We present a case of CH with a late diagnosis. If CH is left untreated after birth, it can lead to permanent intellectual disability and growth failure [1]. Thyroid hormones are important for normal growth hormone and insulin-like growth factor 1 (IGF-1) functions. Normal brain development and cognitive function depend on delivery of adequate thyroid hormone in the first 2–3 years of life [2].

Thyroid organogenesis comprises a complex process. Several genes are expressed during thyroid gland formation. A high frequency of other congenital defects, mostly cardiac, has been described in infants with CH. These defects detected by neonatal screening are supporting a role of genes in development of CH [3, 4].

Here, we report a case with the typical features of congenital hypothyroidism which was diagnosed late.

*Correspondence:
Radwa Gamal
drradwagamal@yahoo.com
[1] Paediatrics Department, Ain Shams University, Cairo, Egypt
[2] Medical Genetics Department, Ain Shams University, Cairo, Egypt

Case presentation

The case was a 10.5-year-old female, sixth in order of birth of consanguineous marriage. The patient was delivered vaginally at term. No problems were noted during pregnancy. The patient was admitted to newborn intensive care unit for 29 days for cyanosis resulting from a complete atrioventricular canal (CAVC) and pulmonary stenosis which were surgically repaired at the age of 2 years. She was kept on medication for heart failure.

She was referred with a complaint of excessive daytime sleepiness and constipation. Genetic consultation was ordered for dysmorphic features. There was no family history of a similar condition. The patient lived in Cairo in a family of low socioeconomic level.

On examination, her weight was 20 kg (below 3rd centile), her height was 91 cm (below 3rd centile), arm span was 92 cm, and her skull circumference was 51 cm (below 3rd centile). The patient had dry skin, coarse features, hairy forehead, depressed nasal bridge, upward slanting palpebral fissures, macroglossia, short neck, nail clubbing, hypertrichosis and median sternotomy scar.

Abdominal examination revealed distended abdomen, hepatomegaly and umbilical hernia. Neurologic examination and genital examination were apparently normal. She had intellectual disability (IQ test was 51). Fundus examination revealed dilated tortuous vessels.

Investigations revealed low free thyroxine (FT4) of 0.15 ng/dl (0.86–1.4), free triiodothyronine (FT3) 21.39 ng/dl (105–207) and thyroid stimulating hormone (TSH) of more than 150 mU/L (0.35–5.5). Serum total bilirubin was 2.4 mg/dl (0.2 to 1.3), and serum direct bilirubin was 1.7 mg/dl (0–0.3). Alanine transaminase, aspartate transaminase and albumin levels were normal.

Her karyotype was normal. An abdominal-pelvic ultrasound with portal duplex revealed parenchymatous liver disease with dilated hepatic veins, cirrhotic liver, chronic portal vein thrombosis with cavernous transformation of portal vein with average flow of 15 cm/s^2 and right pelvic kidney with bilateral grade 1 nephropathy. Neck ultrasonography revealed no thyroid tissue. Tc-99 m pertechnetate thyroid scintigraphy revealed faint ill-defined tracer uptake seen at anatomical site of the thyroid gland (Fig. 1). Antithyroglobulin antibodies and thyroid peroxidase antibodies levels were normal.

Echocardiography revealed large primum atrial septal defect 10 mm with bidirectional flow, multiple muscular ventricular septal defects, pulmonary band, and dilated right and left ventricle with heavy trabeculation. Skeletal survey revealed bilateral irregular femoral epiphyses, cardiomegaly, multiple Wormian bones related to lambdoid suture and delayed bone age (Figs. 2, 3, 4, 5, 6, 7, 8, 9, 10 and 11).

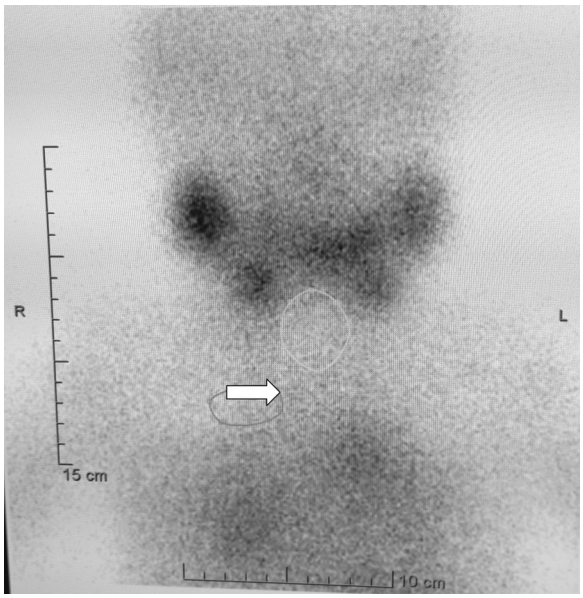

Fig. 1 Thyroid scan shows faint ill-defined tracer uptake seen at anatomical site of the thyroid gland (arrow)

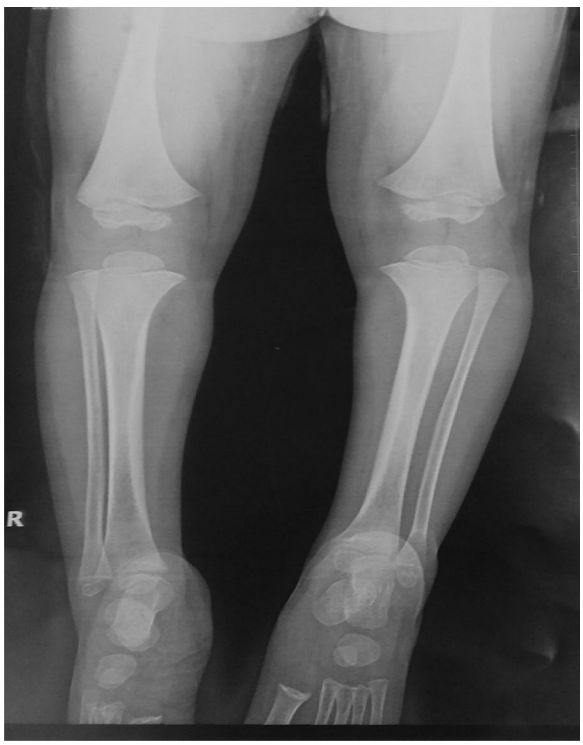

Fig. 2 Bilateral irregular femoral epiphyses

After diagnosis at the age of 10.5 year, she had been treated with levothyroxine at a dose of 100 µg daily. Within one week after the initial treatment, there was improvement in her bowel habits and sleep pattern.

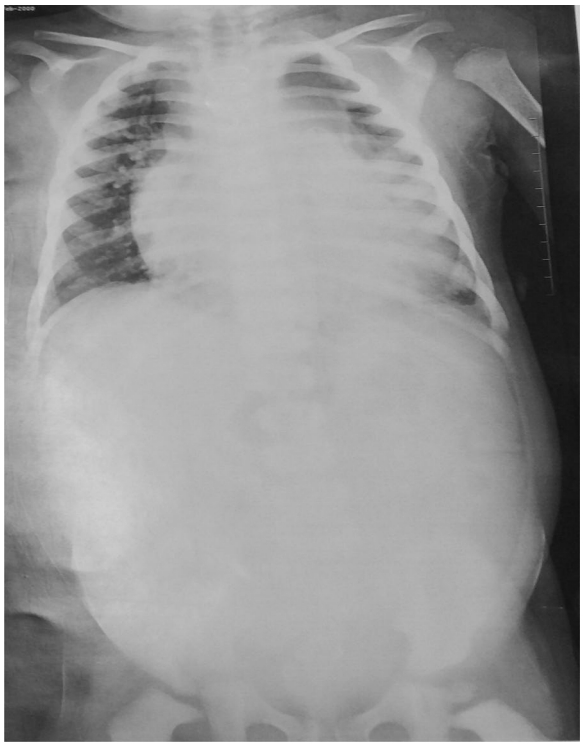

Fig. 3 Cardiomegaly

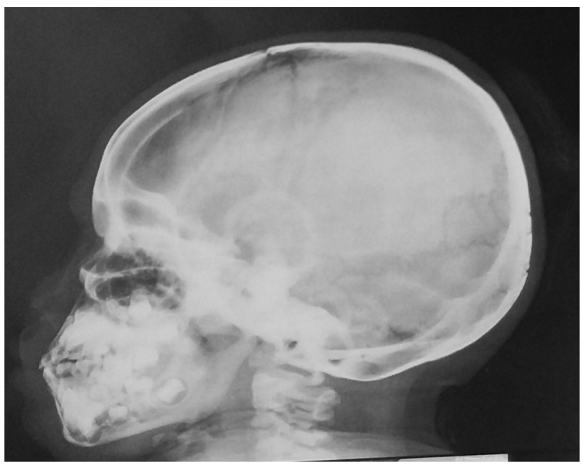

Fig. 4 Multiple Wormian bones related to lambdoid suture

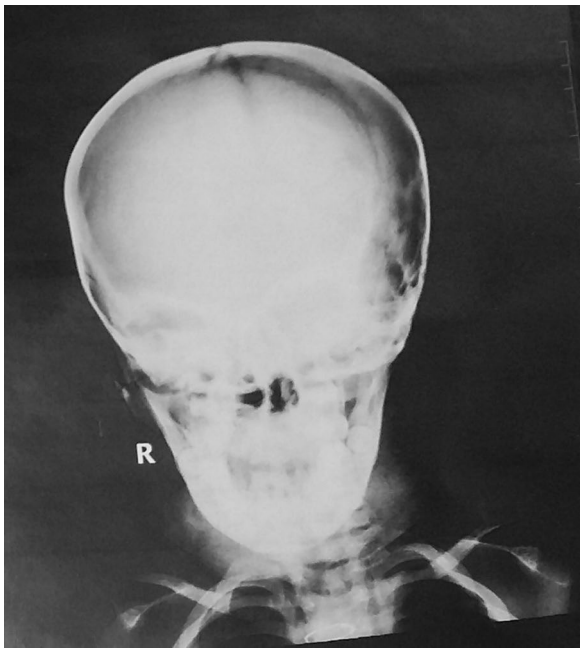

Fig. 5 .

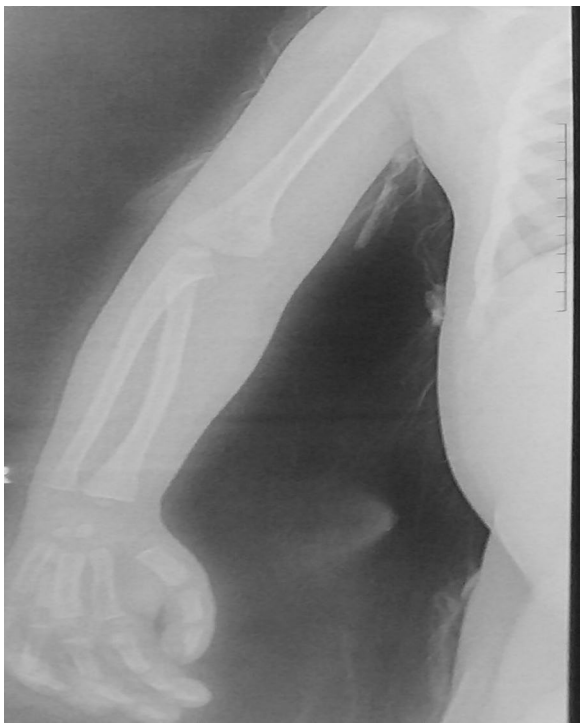

Fig. 6 .

Discussion

Most infants with CH may show no effects at birth due to transplacental passage of some maternal thyroid hormone [5]. Central nervous system and skeleton might be affected if the hypothyroidism develops during fetal life [6].

CH is classified into primary, secondary or peripheral etiologies. Primary causes of CH include thyroid dysgenesis and thyroid dyshormonogenesis. Thyroid dysgenesis is a consequence of abnormal thyroid gland organogenesis in which the thyroid gland is absent,

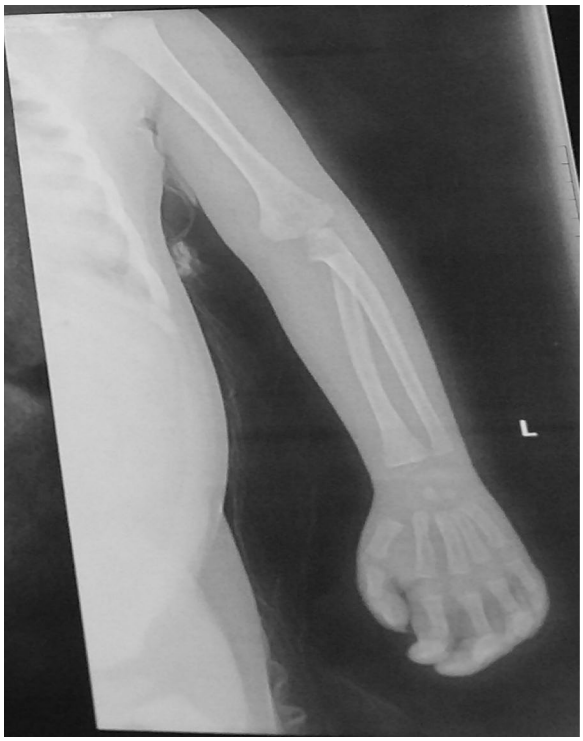

Fig. 7 Delayed bone age

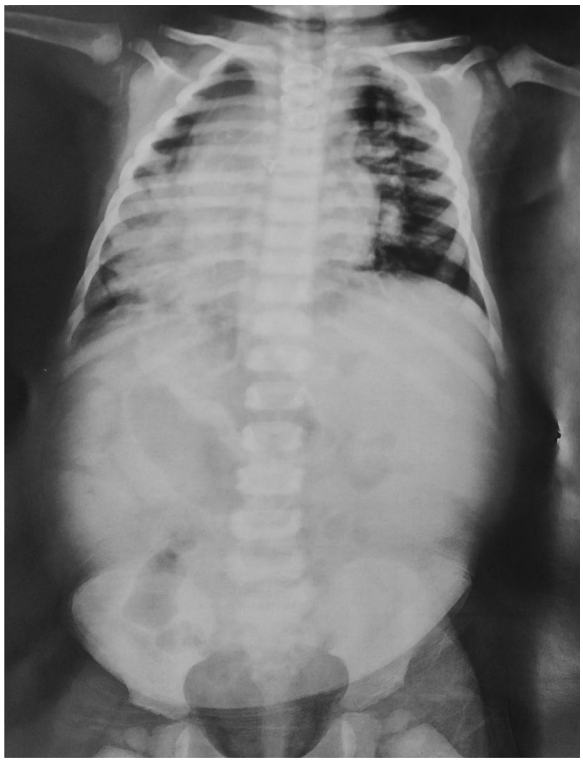

Fig. 8 .

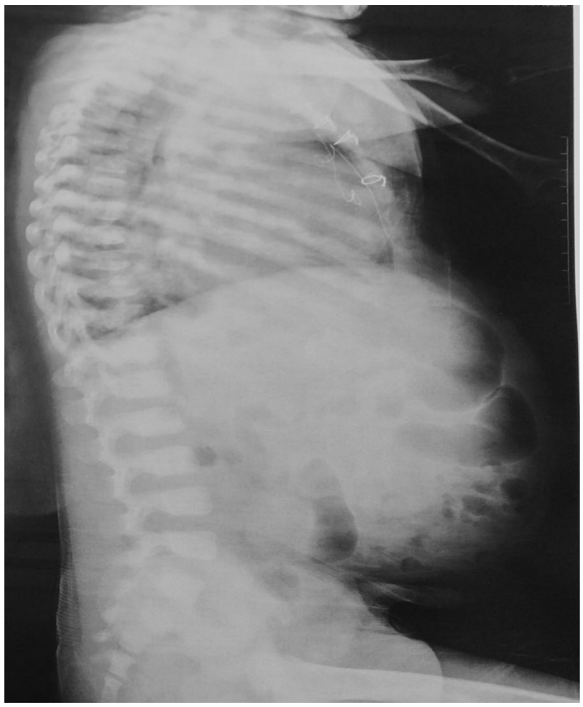

Fig. 9 .

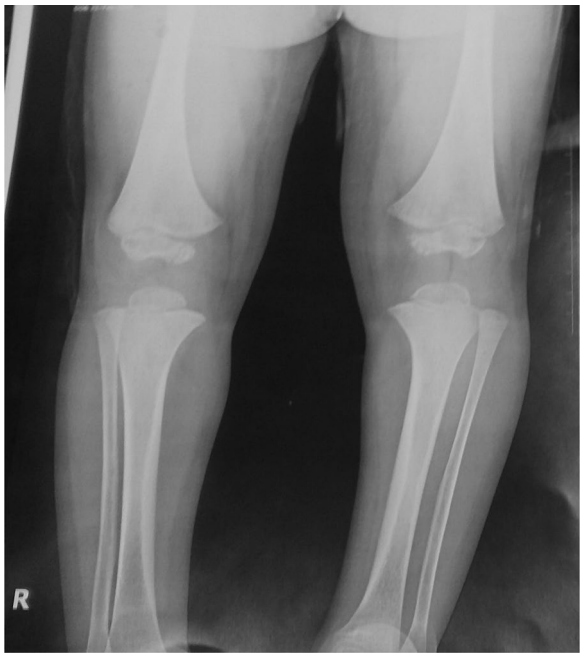

Fig. 10 Bilateral irregular femoral epiphyses

hypoplastic, or abnormally located. Our patient had an absent thyroid gland.

Thyroid dysgenesis represents 80–85% of patients with primary CH [7]. Genes associated with thyroid

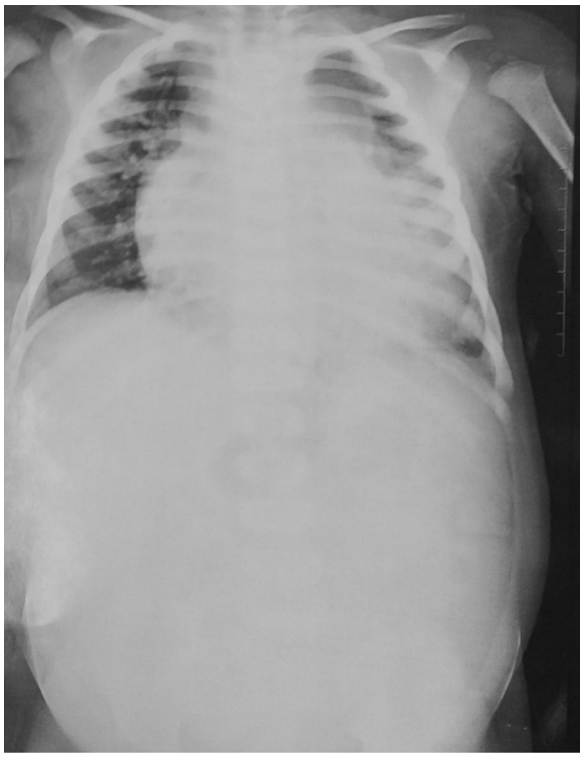

Fig. 11 Cardiomegaly

dysgenesis include: PAX8, FOXE1, NKX2-1, NKX2-5 and HHEX [8].

In addition, syndromic hypothyroidism is a form of CH associated with defects in other organ systems [7].

Most cases of primary CH are sporadic; however, the inheritance mode is unclear and polygenic, multifactorial and monogenic inheritances have all been proposed [9]. Our patient had no family history of a similar condition.

The diagnosis of CH is confirmed by a low FT4 level and elevation of serum TSH. Other diagnostic tests, such as thyroid sonography, thyroid radionuclide uptake and scan or serum thyroglobulin determination may help find the underlying etiology, but the treatment may be started without these tests [7]. Our patient had high TSH level and low FT4, FT3 with no thyroid tissue detected by thyroid ultrasonography or thyroid scan confirming the diagnosis of primary CH.

Common symptoms of CH include constipation, decreased activity, increased sleep and feeding difficulty. Common signs include dry skin, large fontanels, macroglossia and umbilical hernia which were detected in our patient [8].

CH is associated with risk of congenital anomalies. There is relationship between the cardiovascular system and thyroid gland [9]. Minor alteration of thyroid hormone can change blood pressure, cardiac contractility and vascular resistance due to the presence of the thyroid hormone receptors on these tissues [9]. In previous study of infants with CH, the majority of extra thyroidal congenital malformations were cardiac [3]. Our patient had complete atrioventricular canal and pulmonary stenosis.

Other reported malformations include cleft palate and neurologic abnormalities which were not detected in our patient [10].

Our patient had parenchymatous liver disease with dilated hepatic veins, cirrhotic liver related to heart failure. Cardiac cirrhosis is secondary to hepatic congestion due to cardiac dysfunction [11]. Congestive hepatopathy occurs by impaired hepatic venous outflow secondary to a right-sided cardiac failure and is usually subclinical [12]. Symptomatic patients with congestive hepatopathy present with mild jaundice, malaise and intermittent right upper quadrant pain secondary to dilatation of the liver capsule. Treatment of congestive hepatopathy consists of improvement of cardiac output and treatment of the underlying cardiac disease [12, 13].

The complications of cardiac cirrhosis are affected by the complications of the underlying liver dysfunction and cardiac abnormality. Portal hypertension, variceal bleeding, hepatic encephalopathy, recurrent ascites and hepatopulmonary syndrome can be detected secondary to cardiac cirrhosis [10].

Our patient had chronic portal vein thrombosis with cavernous transformation of portal vein which was not reported before in CH. It is a complication of liver cirrhosis caused by heart failure. Portal vein thrombosis (PVT) is a blockage of the portal vein with thrombosis. Chronic PVT can cause portal cavernoma leading to secondary portal hypertension [14]. Portal vein thrombosis is a severe complication of liver cirrhosis [14].

Interpretation of the pathogenesis of PVT in liver cirrhosis can occur by Virchow's triad which includes local vessel injury, decreased blood flow and hypercoagulable state [15]. Patients with liver cirrhosis usually have hepatic sinusoid destruction, fibrous tissue proliferation, and vascular occlusion leading to decreased portal vein velocity into the liver. Several studies have revealed that portal vein velocity of < 15 cm/s detected by Doppler ultrasound increases the risk of developing PVT by 10–20 folds [16, 17]. The most common cause of local vessel injury for liver cirrhosis-related PVT is abdominal surgery [14]. Patients with liver cirrhosis usually have an elevated level of intestinal endotoxin leading to hypercoagulable status [18].

In addition, various changes in the coagulation-fibrinolytic system have been reported in patients with thyroid hormone deficiency [19]. The effect of thyroid hormone on the coagulation fibrinolytic system is

mainly mediated by the interaction between the hormone and its receptors [19].

Hypothyroidism is associated with an increased risk of bleeding; however, some studies revealed an increased risk of unprovoked deep venous thrombosis in patients with subclinical hypothyroidism [20, 21]. Studies with a larger number of patients should be conducted to detect the risk of thrombosis in patients with hypothyroidism.

Children with CH have an increased risk of congenital urologic and renal anomalies [22]. Kumar et al. reported that children with CH are significantly prone to renal and urinary tract anomalies, especially hydronephrosis and renal agenesis [9]. Autosomal recessive polycystic kidney disease and glomerulocystic kidney disease were reported before in patients with CH. Our patient had pelvic kidney which was not reported before in patients with CH.

Ophthalmic pathology was determined in patients with CH including significant refractive errors [23]. Fundus examination of our patient revealed dilated tortuous vessels. The retinal venules usually present as both dilated and tortuous preceding and during a vascular occlusive event with different etiologies of thrombosis [24]. The thrombosis will lead to a buildup of pressure within the capillary and venous system causing the leakage of blood into the retina [25]. This could be caused by various changes in the coagulation-fibrinolytic system described in patients with CH.

Radiographic features of CH include fragmented ossification centers mainly at the hips, Wormian bones, abnormal vertebral flattening with broadening of ribs and delayed bone age [26, 27]. Our patient had bilateral irregular femoral epiphyses, multiple Wormian bones related to lambdoid suture and delayed bone age.

The mainstay of treatment of CH and complications that are related to it is early diagnosis and thyroid hormone replacement [28]. Unfortunately, our patient was diagnosed late. She had intellectual disability which could have been prevented by early screening and treatment with levothyroxine.

Levothyroxine alone is the medication of choice for the treatment of CH [29].

Conclusions

Congenital hypothyroidism is associated with an elevated risk of congenital anomalies. Clinical suspicion of symptoms and signs of CH are important for early diagnosis and prevention of serious problems that are related to CH.

Acknowledgements
Not applicable.

Author contributions
HE and RG had made substantial contributions to the conception, design of the work, analysis, interpretation of data; had drafted the work and substantively revised the work, had approved the submitted version and had agreed to be personally accountable for the author's own contributions and had ensured that questions related to the accuracy or integrity of any part of the work are appropriately investigated, and documented in the literature. All authors read and approved the final manuscript.

Funding
Not applicable.

Availability of data and materials
All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Declarations

Ethics approval and consent to participate
The study was approved by Ethical Committee at the faculty of medicine, Ain Shams University, Cairo, Egypt.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Received: 9 November 2022 Accepted: 22 March 2023
Published online: 31 March 2023

References

1. Persian L, Brabant G, Dattani M, Bonomi M, Feldt-Rasmussen U, Fliers E et al (2018) European thyroid association (Eta) guidelines on the diagnosis and management of central hypothyroidism. Eur Thyroid J 7(5):225–237
2. Rastogi MV, LaFranchi SH (2010) Congenital hypothyroidism. Orphanet J Rare Dis 5(1):1–22
3. Olivieri A, Stazi MA, Mastroiacovo P, Fazzini C, Medda E, Spagnolo A, Study Group for Congenital Hypothyroidism et al (2002) A population-based study on the frequency of additional congenital malformations in infants with congenital hypothyroidism: data from the Italian Registry for Congenital Hypothyroidism (1991–1998). J Clin Endocrinol Metab 87(2):557–62
4. Reddy PA, Rajagopal G, Harinarayan CV, Vanaja V, Rajasekhar D, Suresh V et al (2010) High prevalence of associated birth defects in congenital hypothyroidism. Int J Pediatr Endocrinol 2010:940980
5. Kooistra L, Laane C, Vulsma T, Schellekens JM, van der Meere JJ, Kalverboer AF (1994) Motor and cognitive development in children with congenital hypothyroidism: a longterm evaluation of the effects of neonatal treatment. J Pediatr 124:903–909
6. Vulsma T, Gons MH, de Vijlder JJ (1989) Maternal-fetal transfer of thyroxine in congenital hypothyroidism due to a total organification defect or thyroid agenesis. N Engl J Med 321(1):13–16
7. Park S, Chatterjee VK (2005) Genetics of congenital hypothyroidism. J Med Genet 42:379–389
8. Sun F, Zhang JX, Yang CY et al (2018) The genetic characteristics of congenital hypothyroidism in China by comprehensive screening of 21 candidate genes. Eur J Endocrinol 178(6):623–633
9. Szinnai G (2014) Genetics of normal and abnormal thyroid development in humans. Best Pract Res Clin Endocrinol Metab 28(2):133–150
10. Rastogi MV, LaFranchi SH (2010) Congenital hypothyroidism. Orphanet J Rare Dis 5:17
11. Ahmadi N, Ahmadi F, Sadiqi M, Ziemnicka K, Minczykowski A (2020) Thyroid gland dysfunction and its effect on the cardiovascular system: a comprehensive review of the literature. Endokrynol Pol 71(5):466–478

12. Kumar J, Gordillo R, Kaskel FJ, Druschel CM, Woroniecki RP (2009) Increased prevalence of renal and urinary tract anomalies in children with congenital hypothyroidism. J Pediatr 154(2):263–266
13. Rodriguez Ziccardi M, Pendela VS, Singhal M (2022) Cardiac Cirrhosis. In: StatPearls. StatPearls Publishing, Treasure Island
14. El Hadi H, Di Vincenzo A, Vettor R, Rossato M (2020) Relationship between heart disease and liver disease: a two-way street. Cells 9(3):567
15. Hollenberg SM, Waldman B (2016) The circulatory system in liver disease. Crit Care Clin 32(3):331–342
16. Hepatobiliary Disease Study Group, Chinese Society of Gastroenterology, Chinese Medical Association. Consensus for management of portal vein thrombosis in liver cirrhosis (2020, Shanghai). J Dig Dis. 2021;22(4):176–186.
17. Zocco MA, Di Stasio E, De Cristofaro R et al (2009) Thrombotic risk factors in patients with liver cirrhosis: correlation with MELD scoring system and portal vein thrombosis development. J Hepatol 51(4):682–689
18. Stine JG, Wang J, Shah PM et al (2018) Decreased portal vein velocity is predictive of the development of portal vein thrombosis: a matched case-control study. Liver Int 38(1):94–101
19. Xu XB, Guo XZ, De Stefano V et al (2019) Nonselective beta-blockers and development of portal vein thrombosis in liver cirrhosis: a systematic review and meta-analysis. Hepatol Int 13(4):468–481
20. Carnevale R, Raparelli V, Nocella C et al (2017) Gut-derived endotoxin stimulates factor VIII secretion from endothelial cells. Implications for hypercoagulability in cirrhosis. J Hepatol. 67(5):950–956
21. Squizzato A, Romualdi E, Buller HR, Gerdes VEA (2007) Thyroid dysfunction and effects on coagulation and fibrinolysis: a systematic review. J Clin Endocrinol Metab 92(7):2415–2420
22. Danescu LG, Badshad A, Matta F, Yeakoub AY, Malloy D, Stein PD (2008) Risk of venous thromboembolism in patients hospitalized with hypothyroidism. Chest 134(4):s46002
23. Wei WT, Liu PP, Lin SM, Peng CC, Wang JH, Huang HK, Loh CH (2020) Hypothyroidism and the risk of venous thromboembolism: a nationwide cohort study. Thromb Haemost 120(3):505–514
24. Yousefichaijan P, Dorreh F, Rafeie M et al (2015) Congenital anomalies of kidney and upper urinary tract in children with congenital hypothyroidism; a case-control study. J Renal Inj Prev 4(4):120–126
25. Kurtul BE, Ozer PA, Kabatas EU, Gürkan A, Aycan Z (2016) Ophthalmic manifestations in children with congenital hypothyroidism. J Pediatr Ophthalmol Strabismus 53(1):29–34
26. Kolar P (2014) Risk factors for central and branch retinal vein occlusion: a meta-analysis of published clinical data. J Ophthalmol 2014(4):724–780
27. Kriechbaum K, Michels S, Prager F et al (2008) Intravitreal Avastin for macular oedema secondary to retinal vein occlusion: a prospective study. Br J Ophthalmol 92:518–522
28. Digeorge AM (1992) Congenital hypothyroidism. In: Behrman RE, Kliegman RM, Nelson WE, Vaughan VC (eds) Nelson textbook of pediatrics, 14th edn. WB Saunders, London, pp 1417–1420
29. van Trotsenburg P, Stoupa A, Léger J, Rohrer T, Peters C, Fugazzola L et al (2021) Congenital hypothyroidism: a 2020–2021 consensus guidelines update-An ENDO-European reference network initiative endorsed by the european society for pediatric endocrinology and the European Society for Endocrinology. Thyroid 31(3):387–419

Publisher's Note