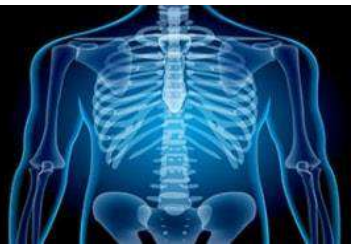
International Journal of Radiology and Diagnostic Imaging



E-ISSN: 2664-4444
P-ISSN: 2664-4436
www.radiologypaper.com
IJRDI 2022; 5(3): 54-59
Received: 20-04-2022
Accepted: 02-06-2022

Pravinkumar Bharde
Senior Resident, Department of Radiology, Osmania General Hospital, Hyderabad, Telangana, India

VD Praveenkumar Gorrela
Senior Resident, Department of Radiology, Osmania General Hospital, Hyderabad, Telangana, India

Srujana Pilli
Assistant Professor, Department of Radiology, MGM Hospital, Warangal, Telangana, India

Chinmayee M
Bidar Institute of Medical College, Bidar, Karnataka, India.

Corresponding Author:
Pravinkumar Bharde
Senior Resident, Department of Radiology, Osmania General Hospital, Hyderabad, Telangana, India

Cranial extramedullary hematopoiesis with pancreatic secondary hemochromatosis in a beta thalassemia patient: A case report

Pravinkumar Bharde, VD Praveenkumar Gorrela, Srujana Pilli and Chinmayee M

DOI: http://dx.doi.org/10.33545/26644436.2022.v5.i3a.276

Abstract
Thalassemia is one of the most worrying hemolytic disorder with wide range of evolving clinical alterations based on the type, severity of affected hematopoietic mechanisms and repeated transfusions to correct underlying anemia.
We present a 13 year old female patient diagnosed with thalassemia major showing features of cranial extra medullary hematopoiesis with severe intracranial infections in the form of cerebellar abscess and otomastoiditis extending in to adjacent sinus venouses, Iron deposition in liver & pancreas and incidental findings of uncomplicated horse shoe kidney.
Extra medullary hematopoiesis is a catch up mechanism at the failing medullary hematopoeising to keep in check the hemoglobin levels without causing much physiological imbalance.
EMH usually affects visceral structures like liver, spleen lymph nodes and thorax. Less commonly pleura, lungs, GIT, breast, skin, kidneys, adrenals and rarely the cranium and intracranial structures. Here, we present one of the rare presentations of cranial EMH in the background of severe intracranial infection.

Keywords: pleura, lungs, GIT, breast, skin, kidneys, adrenals

Introduction
Thalassemia is an inherited autosomal recessive hematological disorder causing microcytic hemolytic anemia. The severity and diverse clinical presentations depend on the type of gene affected, severity of anemia, chronicity of problem and transfusion dependence [1].
The alpha and beta thalassemias reflect the respective deficient genes with relative increase of other globin chains causing varying levels of hemolysis. Beta Thalassemias are classified in to Trait with one gene defect. Intermedia with two gene defect with moderate decrease of beta chains and Major with severe deficient beta chains [1].
Extra medullary hematopoiesis is a catch up compensatory mechanism at the failed bone marrow hematopoiesis for various reasons [2, 3]. Thus, it is seen in severe hemoglobinopathies, myelofibrotic and proliferative diseases [4].
EMH accounts to 15% of thalassemia patients, who receive under or inadequate treatment. The EMH mechanism involves recruitment of multipotential cells from other tissues like liver, spleen, lymph nodes, paraspinal regions, kidney, pleura and intestine and rarely intracranium [5, 6] to pace up hematopoiesis to make up for failing hemoglobin synthesis at the marrow.
There are a few reports where EMH has involved some rare places such as the perirenal and paravertebral region, paranasal sinuses, clivus, meninges, spinal and epidural spaces, prostate, adrenals, pleura, breast, thymus, kidney, sweat gland, broad ligament and retroperitoneal space. This unusual phenomenon, especially when it involves the central nervous system (CNS), can act as a space-occupying lesion [7, 8] and lead to neurological deficits.

Case report
A 13 year old female patient presented to hospital with fever, acute left ear pain, 2 episodes of vomitings and 5 episodes of seizures.

Also she complained of vague abdominal pain and pain over left parietal region for the last 1 month and SOB for 2 days. She got splenectomy performed 5 years earlier, diagnosed with Type 1 diabetes mellitus for 4 years and was on intermittent blood transfusion every 2 months to correct anemia.

On physical examination, pulse rate was 110 bpm, blood pressure was 110/80, oral temperature was 39.6 °C, and saturation was 84% on room air. The physician noticed swelling behind the left ear. The patient's abdomen was slightly distended with hepatomegaly. The patient had been evaluated by a pediatrician and was diagnosed with left otomastoiditis with intracranial complication.

Patient lab investigation revealed that hemoglobin (Hb) was 5.9 gm/dL, with mean corpuscular volume (MCV) - 70.9 fl and mean corpuscular haemoglobin (MCH) - 22.8pg. Her peripheral blood film showed microcytic hypochromic anaemia with anisocytosis, macrocytes, schistocytes, poikilocytes and target cells. The haemoglobin was subjected to Hb electrophoresis, and the results revealed that HbA-4.7%, HbA2-3.6%, HbF-89.9%, and HbS-0. The sickling test was negative.

MRI scan of the brain and abdomen was performed on a 1.5-Tesla BRIVO MR355 whole-body scanner (GE Medical Systems, Milwaukee, WI) equipped with echo-speed gradients.

The scan showed marked bony expansion of skull vault with scattered, varying sized multiple well defined moderately enhancing, T1 – Iso to hyper; T2, FLAIR and DWI – hypo intense lesions(Figure 1).

T2/Flair hyper intensity was observed in the left middle ear and mastoid air cells along with loss of flow void in the left transverse and sigmoid sinus, corresponding MRV showed filling defects in the respective sinuses – Left Otomastoiditis with intracranial extension, thrombosis of adjacent dural sinuses like transverse and sigmoid sinuses(Figure 2).

T2/Flair hyper intense lesion measuring 36*24mm was noted in the left cerebellar hemisphere causing mass effect over left cerebellar peduncle, anteriorly displacing pons and effacing adjacent 4th ventricle causing obstructive hydrocephalus. It showed central restriction on DWI, no blooming on GRE and peripheral ring enhancement on contrast – Cerebellar Abscess with significant edema & mass effects (Figure 2).

MRI of liver and pancreas showed significant T1&T2 signal drop – Hemochromatosis due to multiple blood transfusions (Figure 3). Non-enhancement computed tomography of abdomen revealed increased liver and pancreatic density with pancreatic calcification and incidental Horse-Shoe kidney (Figure 3&4).

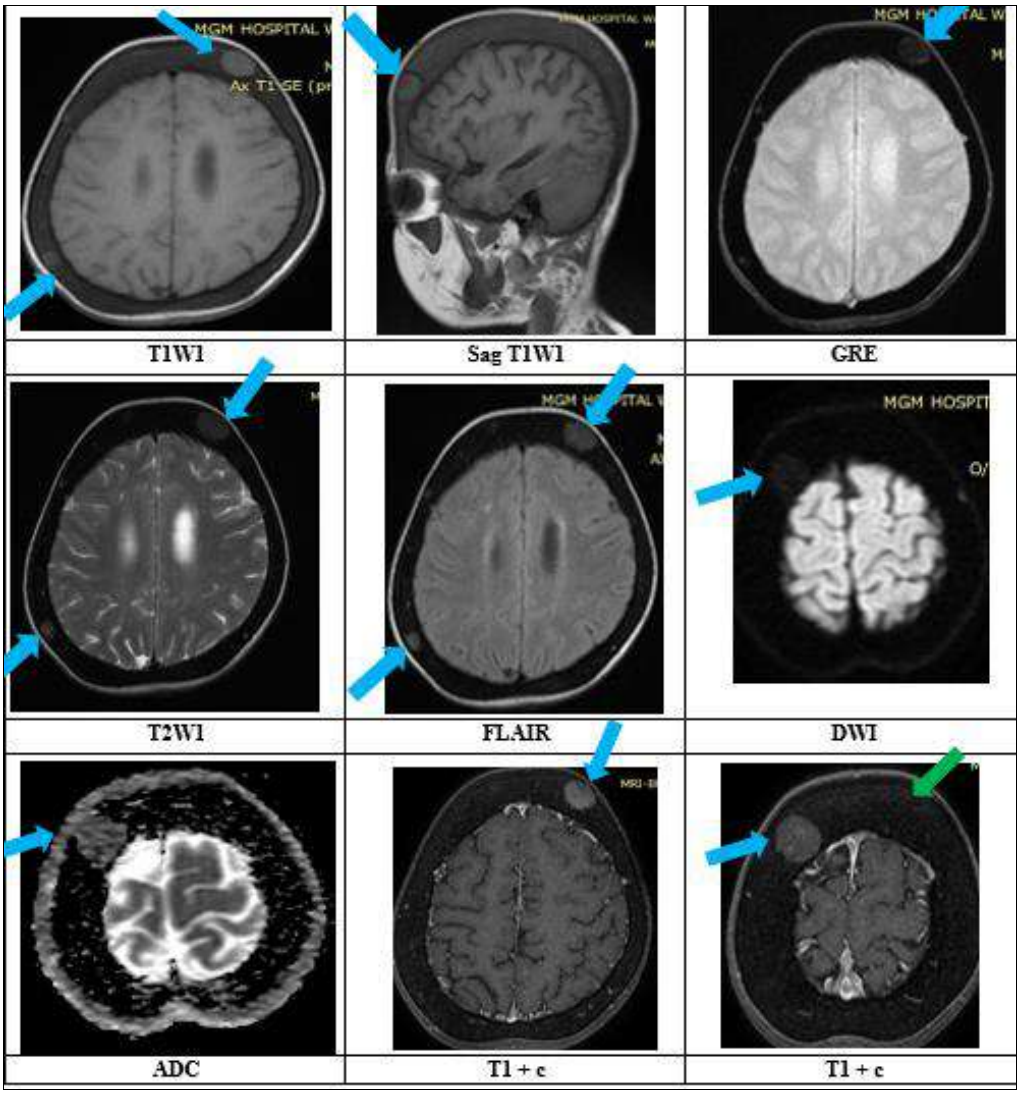


Fig 1: MR images of brain showing green arrow: widening of diploic spaces and blue arrow: homogenously enhancing soft tissue masses (EMH) within skull vault.

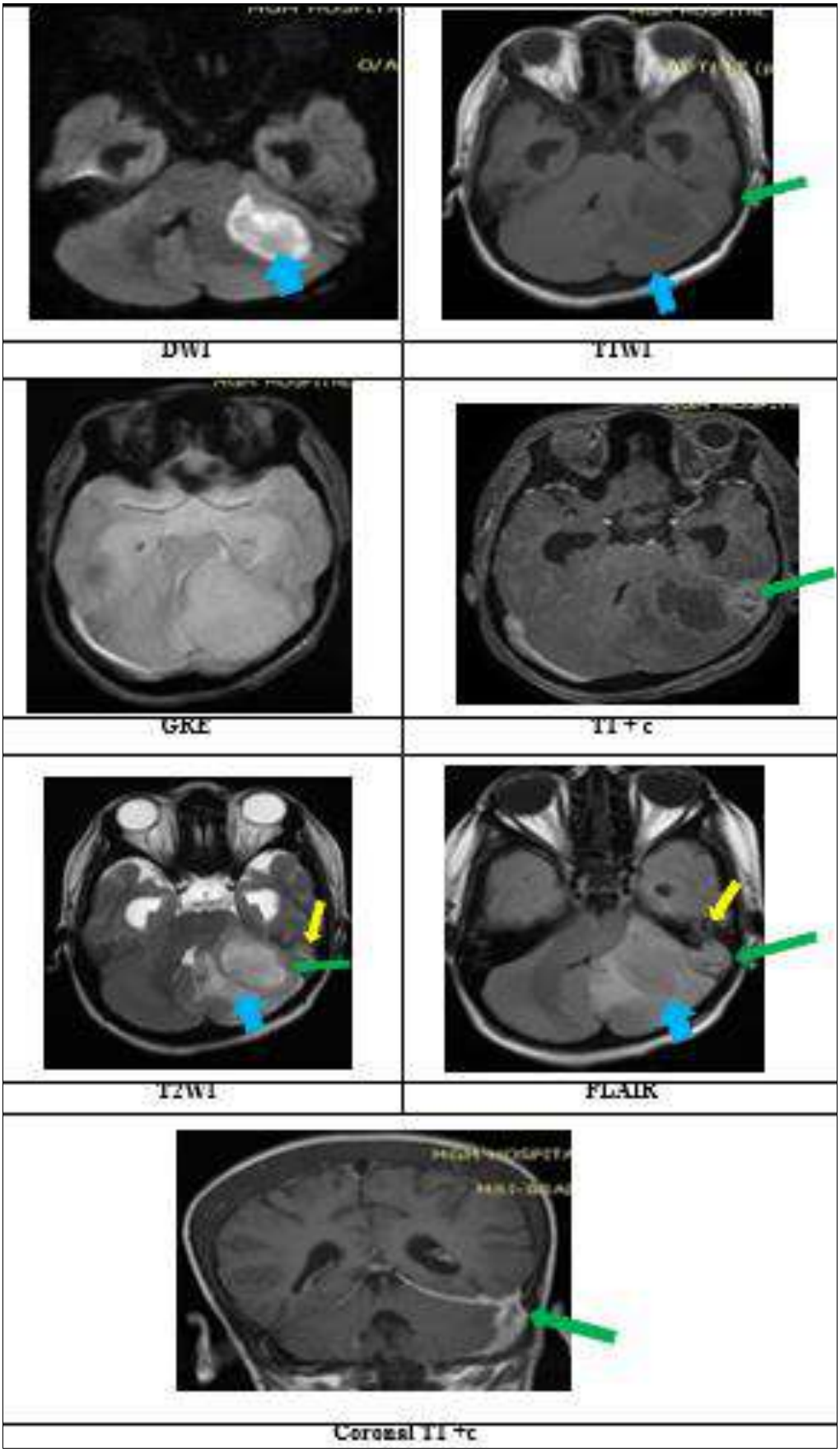


Fig 2: MR images of brain showing yellow arrow: left otomastoiditis, blue arrow: left cerebellar abscess and green arrow: left transverse and sigmoid sinus thrombosis along with tentorial and Dural enhancement

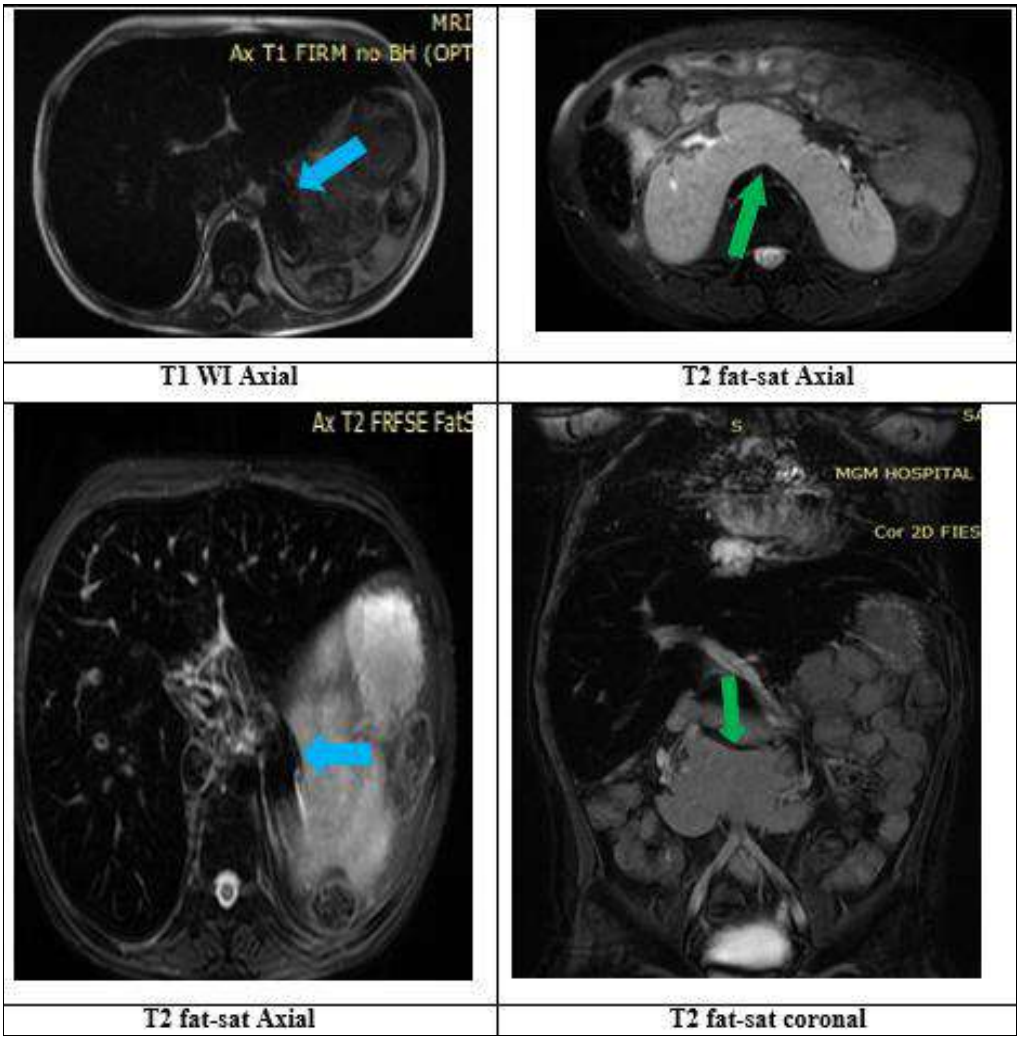


Fig 3: MR images of liver showing blue arrow T1W1: decreased intensity in the liver, T2WI: marked signal loss in liver and pancreas. Green arrow horse shoe kidneys

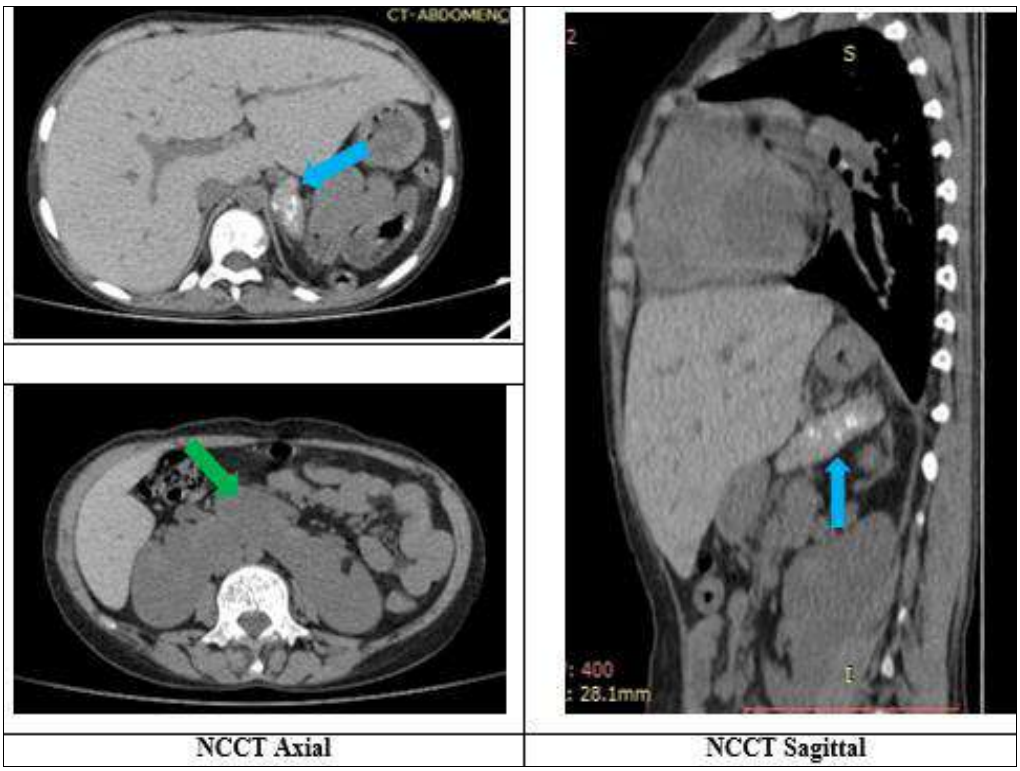


Fig 4: NCCT of the abdomen showing the blue arrow pancreas and green arrow horseshoe kidneys. Homogenously increased liver and pancreas density up to 94HU (normal 45-67 HU)

Based on the patient's case history, lab and imaging findings, she was diagnosed with Beta thalassemia major with features showing widened diploic spaces with multiple extra medullary hematopoietic tissues in the cranial vault. Left otomastoiditis with thrombosis of the left transverse and sigmoid sinus and left cerebellar abscess with obstructive hydrocephalus. An incidental horse shoe kidney and secondary hemochromatosis involving liver and pancreas.

Discussion

Hematopoiesis is the formation and maturation of blood elements. When the primary sites of hematopoiesis in the adults fail as in myelofibrosis and hemoglobinopathies (especially thalassemia and sickle cell disease), various extramedullary sites take on the role of blood formation [9].Several other clinical entities can also lead to EMH like hemolytic anaemia, primary and secondary myelofibrosis, leukaemia, lymphoma and bone metastasis, and myelodysplastic syndromes, characterized by abnormal morphology and inadequate production of blood cells, while the uncommon intracranial EMH occurs without predisposing bone marrow disorders [10]. EMH most often involves the spleen, the liver, and paraspinal regions of the thorax. However, in addition to these common sites of EMH, the process can involve virtually any organ or tissue. Reported sites include abdominal viscera, pleura, lymph nodes, adrenal glands, breast, thymus, kidneys, gastrointestinal tract, and intracranial structures [9, 11, 12]. Isolated intracranial EMH occurs most often in association with hemangioblastomas; it has also been observed in two intracranial lipomas, a meningioma, a few subdural hematomas, an encephalocele, a tumor like a mass of papillary endothelial hyperplasia, and a pilocytic astrocytoma [13]. There are two main groups in EMH. The first group shows paraosseous foci that may result from herniation of medullary tissue from the underlying bone. It is seen in hemolytic disorders such as thalassemia and sickle cell anaemia, where the marrow has tremendous activity. The second group shows extraosseous soft tissue foci, which may arise from multipotential stem cells. This happens when the marrow activity is ineffective, as in idiopathic myelofibrosis or, rarely, with toxic or tumoral marrow destruction [14]. Intracranial EMH is extremely rare [15]. Most patients do not have signs and symptoms related directly to the disorder. Most foci of EMH are noted as incidental findings in imaging studies or postmortem examinations. However, occasionally EMH in the intracranial or intraspinal epidural space can lead to serious neurogenic complications (increased intracranial pressure, hemiplegia, altered levels of consciousness, or visual disturbances, including subdural haemorrhage, delirium, increased intracranial pressure, papilledema, coma, motor and sensory impairment, and limb paralysis due to direct mass effect upon adjacent structures) [14, 15, 16, 17]. The most frequently reported causes of intracranial involvement by EMH are thalassemia (50%) and myelofibrosis (31%) [18]. In the central nervous system (CNS), Cranial nerves, spinal canal, cranial dura, falx, cerebral parenchyma, optic nerve sheath, and diploic space of the skull are involved. Falx is the most commonly involved site. EMH can manifest as smooth juxta osseous homogeneous masses in the skull (in the epidural space, dura matter, venous sinuses) or in the spine (in the epidural space). Unlike the other locations of EMH, which are usually asymptomatic, CNS masses can cause various symptoms e.g., seizures, cranial nerve deficits (when located at the skull base), increased intracranial pressure (if compressing Dural sinuses), myelopathy if compressing the spinal cord. Bone changes in the skull and the vertebrae may show the specific findings of the underlying disease (*e.g.*, expanded diploic space, "hair on end", or osteosclerosis).

Diagnosis of EMH is based on the clinical circumstances, laboratory data, and the use of different diagnostic imaging modalities[18]. In cases with intracranial EMH, the CT appearance is characterized by the heterogeneous lobulated soft tissue density mass[19].MRI is the diagnostic investigation of choice, where in the Intracranial EMH appears as unique or multiple iso- or hyperintense extra-axial masses appended to the meninges, with homogeneous enhancement after contrast administration. These masses are usually lobular, well-circumscribed masses of intermediate signal intensity on T1-weighted images and low signal intensity on T2-weighted images. These masses may show significant enhancement after gadolinium administration [20, 21]. MRI demonstrates a high signal intensity rim representing fatty tissue on both T1- and T2-weighted images [22].The multiple intracranial extra-axial EMH can mimic multiple meningiomas, lymphoma, myeloma, leukaemia, neuroblastoma, and other metastatic malignant diseases. In addition, the differential diagnoses include epidural hematoma, abscess, chloroma, granulomatous diseases like tuberculosis and sarcoidosis, and pachymeningeal thickening related to rheumatoid disease [23].

The treatment options for EMH are regular transfusion therapy, Nutritional support and low dose radiation therapy (1000-3000cGy). Surgical treatment is least recommended due to excessive bleeding and a higher rate of recurrence. In case of symptomatic EMH, irradiation or decompression by partial/complete removal of structures causing compression is the recommended therapy. EMH usually regresses or disappears after medical treatment.

Hemochromatosis is classified as (a) primary (genetic disturbance) and (b) secondary (chronic diseases or multiple transfusions). Iron overload can also be classified depending on the deposition patterns (Parenchymal or reticuloendothelial). These patterns can help to differentiate among the possible causes of hemochromatosis. In the Parenchymal pattern of deposition, decreased signal intensity is observed in the liver and the pancreas, while in the spleen and the bone marrow, signal intensity is preserved. In the reticuloendothelial deposition pattern, the signal intensity of the pancreas is generally preserved, except when the volume of blood infused goes beyond the storage capacity of the reticuloendothelial system, leading to parenchymal deposition. Computed tomography (CT) and MR imaging can be used to detect iron overload. Non-enhanced CT shows a homogeneous increase in the attenuation of the hepatic parenchyma to 72 HU or more. This case suggests that EMH must be taken into consideration when masses with characteristic radiologic appearance are identified in patients with various blood dyscrasias.

Conclusion

In conclusion, iron overload is a relatively common presentation associated with various pathologies. EMH presents as hematopoietic masses in several typical and

atypical body locations. Typical locations are the liver, spleen, lymph nodes and paravertebral region, and atypical locations are the intra-spinal canal, Presacral region, nasopharynx and paranasal sinuses. Knowledge of these typical and atypical EMH locations should be interpreted together with the patient's clinical history to reach the correct diagnosis. MR imaging has a fundamental role because it can contribute to the diagnosis in a non-invasive way. The disease is often clinically silent. Knowledge of the imaging findings, the patterns of distribution, and associated diseases can facilitate diagnosis and help in further management of patient.

References

1. Galanello R, Origa R. Beta-thalassemia. Orphanet journal of rare diseases. 2010 Dec;5(1):1-5.
2. Kim CH. Homeostatic and pathogenic extra medullary hematopoiesis. Journal of blood medicine. 2010;1:13.
3. Yang X, Chen D, Long H, Zhu B. The mechanisms of pathological extramedullary hematopoiesis in diseases. Cellular and Molecular Life Sciences. 2020 Jul;77(14):2723-38.
4. Papavasiliou C. Clinical expressions of the expansion of the bone marrow in the chronic anemias: The role of radiotherapy. International Journal of Radiation Oncology* Biology* Physics. 1994 Feb 1;28(3):605-12.
5. Ohtsubo M, Hayashi K, Fukushima T, Chiyoda S, Takahara O. Intracranial extramedullary haematopoiesis in postpolycythemic myelofibrosis. The British Journal of Radiology. 1994 Mar;67(795):299-302.
6. Tabesh H, Shekarchizadeh A, Mahzouni P, Mokhtari M, Abrishamkar S, Abbasi Fard S. An intracranial extramedullary hematopoiesis in a 34-year-old man with beta thalassemia: a case report. Journal of medical case reports. 2011 Dec;5(1):1-4.
7. Haider S, Ortiz-Neira C, Shroff M, Gilday D, Blaser S. Intracranial involvement in extramedullary hematopoiesis: case report and review of the literature. Pediatric radiology. 2005 Jun;35(6):630-4.
8. Tayari N, Ahrar MH, Jafarpishe MS. Case report of the extramedullary hematopoiesis presented as a hyper vascular intracranial mass. Advanced biomedical research, 2013, 2.
9. SANEEI TM, Birang SH, Shahnazi M, Hemadi H. Large splenic mass of extramedullary hematopoiesis.
10. Chernak BJ, Rampal RK. Extramedullary hematopoiesis in myeloproliferative neoplasms: Pathophysiology and treatment strategies. In International review of cell and molecular biology. Academic Press. 2021 Jan 1;365:97-116.
11. Miyake H, Matsuda M, Iyomasa S, Mizuno K. Presacral extramedullary hematopoiesis. Surgery. 2004 Jan 1;135(1):112-3.
12. Al-Habib H, Hadzikaric N. Spinal cord compression due to intraspinal extramedullary hematopoiesis in thalassemia intermedia. Neurosciences Journal. 2007 Jul 1;12(3):261-4.
13. Palma JA, Dominguez PD, Riverol M. Intracranial extramedullary hematopoiesis associated with multiple myeloma. Neurology. 2013 Apr 23;80(17):1620.
14. Kaya H, Cerci SS. Tc-99m nanocolloid scintigraphic imaging of intracranial meningeal extramedullary hematopoiesis in a patient with idiopathic myelofibrosis. Annals of nuclear medicine. 2006 Oct;20(8):565-8.
15. Lee CM, Salzman KL, Blumenthal DT, Gaffney DK. Intracranial extramedullary hematopoiesis: brief review of response to radiation therapy. American journal of hematology. 2005 Feb;78(2):151-2.
16. Singer A, Maldjian P, Simmons MZ. Extramedullary hematopoiesis presenting as a focal splenic mass: a case report. Abdominal imaging. 2004 Nov;29(6):710-2.
17. Koch BL, Bisset 3rd GS, Bisset RR, Zimmer MB. Intracranial extramedullary hematopoiesis: MR findings with pathologic correlation. AJR. American journal of roentgenology. 1994 Jun 1;162(6):1419-20.
18. Haidar S, Ortiz-Neira C, Shroff M, Gilday D, Blaser S. Intracranial involvement in extramedullary hematopoiesis: Case report and review of the literature. Pediatric radiology. 2005 Jun;35(6):630-4.
19. Zhang HZ, Li Y, Liu X, Chen BR, Yao GH, Peng YN. Extramedullary hematopoiesis: a report of two cases. Experimental and Therapeutic Medicine. 2016;12(6):3859-62.
20. Demir MK, Yapıcıer Ö, Onat E, Toktaş ZO, Akakın A, Urgun K, *et al*. Rare and challenging extra-axial brain lesions: CT and MRI findings with clinico-radiological differential diagnosis and pathological correlation. Diagnostic and Interventional Radiology. 2014 Sep;20(5):448.
21. Tillema JM, Pirko I. Neuroradiological evaluation of demyelinating disease. Therapeutic advances in neurological disorders. 2013 Jul;6(4):249-68.
22. Zimny A, Zińska L, Bladowska J, Neska-Matuszewska M, Sąsiadek M. Intracranial lesions with high signal intensity on T1-weighted MR images–review of pathologies. Polish Journal of Radiology. 2013 Oct;78(4):36.
23. Debard A, Demasles S, Camdessanche JP, Duband S, Mohammedi R, Antoine JC. Dural localization of extramedullary hematopoiesis. Report of a case. Journal of neurology. 2009 May 1;256(5):837.