International Journal of Computational and Experimental Science and ENgineering (IJCESEN)

Vol. 11-No.4 (2025) pp. 10174-10180
http://www.ijcesen.com

ISSN: 2149-9144

Research Article

The Imperative of Interprofessional Collaboration in the Management of Erdheim-Chester Disease: Integrating Family Medicine, Pediatrics, Dentistry, Nursing, Pharmacy, Radiology, and Laboratory Services

Israa Ali alsaffar[1]*, Husah Abdullah Alqafshat[2], Fatema Mohammed Alayesh[3], Ayman Ali AlMuraihel[4], Zahra'a Hussain Aldraisi[5], Abdulaziz Essam Alshail[6], Sajedah Abdullah Albaqshi[7], Badoor Abdrabalameer Alghafli[8], Maram Hesham A Banah[9], Afnan Abdullah Almutairi[10]

[1]Dental assistant - Dammam medical complex
* **Corresponding Author Email:** Esra-saffar@hotmail.com - **ORCID:** 0000-0002-5247-005X

[2]Lab specialist (working in micro lab) - QCH
Email: Halqafshat@gmail.com - **ORCID:** 0000-0002-5247-9910

[3]Nurse specialist - Health cluster alahsa
Email: Fmalayesh@moh.gov.sa- **ORCID:** 0000-0002-5247-9920

[4]Pharmacy Technician - king fahad specialist hospital
Email: Aalmuraihel@moh.gov.sa- **ORCID:** 0000-0002-5247-9940

[5]Nurse specialist - PHC, Eastern province
Email: Zaldraisi1988@gmail.com - **ORCID:** 0000-0002-5247-9990

[6]Consultant Family medicine - General Directorate of Medical Services (Alnakhil Medical Center)
Email: abdulazizalshail@gmail.com- **ORCID:** 0000-0002-5247-9930

[7]Pharmacy technician - Eastern Health Cluster, Supply Chains
Email: Saalbaqshi@moh.gov.sa - **ORCID:** 0000-0002-5247-9980

[8]Pediatric doctor - Central health network - eastern region cluster
Email: Budoorajg@gmail.com- **ORCID:** 0000-0002-5247-9970

[9]Physics - King Fahad hospital Hofuf
Email: Mbanah1993@hotmail.com- **ORCID:** 0000-0002-5247-9960

[10]Dental assistant - King Fahad hospital
Email: Yoonag7@gmail.com- **ORCID:** 0000-0002-5247-9550

Article Info:

DOI: 10.22399/ijcesen.4795
Received : 02 January 2025
Accepted : 30 January 2025

Keywords

Erdheim-Chester Disease,
Interprofessional Collaboration,
Multidisciplinary Team,
Rare Disease Management,
Histiocytic Neoplasms,
MAPK/ERK Pathway

Abstract:

Erdheim-Chester Disease (ECD), a rare multi-systemic histiocytic neoplasm, epitomizes the critical necessity for interprofessional collaboration (IPC) in modern healthcare. Its diagnosis and management present a formidable challenge that no single medical specialty can address in isolation due to the disease's protean manifestations, which can span skeletal, cardiovascular, neurological, renal, and dermatological systems. An effective IPC model for ECD strategically integrates the longitudinal oversight and coordination of Family Medicine, the developmental expertise of Pediatrics, the oral-systemic health vigilance of Dentistry, the continuous care and patient education provided by Nursing, the pharmacotherapeutic precision and safety surveillance of Pharmacy, the diagnostic and monitoring prowess of Radiology, and the definitive histopathological and molecular diagnostics from Laboratory Services. This synergistic approach mitigates the diagnostic delays and fragmented care typical of rare diseases by ensuring continuous communication, comprehensive patient assessment, personalized treatment planning, and holistic support. Ultimately, this collaborative framework transforms the management paradigm from reactive, specialty-specific interventions into a proactive, patient-centered strategy aimed at improving diagnostic

accuracy, optimizing targeted therapy, managing complex comorbidities, and enhancing the overall quality of life for individuals navigating this complex condition.

1. Introduction

Erdheim-Chester Disease (ECD) stands as a paradigmatic example of a clinical entity whose effective management transcends the capabilities of any single medical discipline. First described by Jakob Erdheim and William Chester in 1930, ECD is a rare, non-Langerhans cell histiocytosis characterized by the systemic infiltration of tissues by foamy CD68+, CD1a- histiocytes, often accompanied by a rich inflammatory milieu of lymphocytes and fibrosis [1]. With an estimated prevalence of fewer than 1 in 1,000,000, it resides within the realm of "ultra-rare" diseases, a classification that often belies its profound complexity and the diagnostic odyssey it imposes upon patients [2]. The disease is driven in approximately 50-70% of cases by activating mutations in the *BRAF* V600E oncogene, with other mutations in the MAPK/ERK pathway (e.g., in *MAP2K1*, *NRAS*, *ARAF*, *PIK3CA*) identified in most remaining cases, solidifying its status as a clonal, inflammatory myeloid neoplasm [3]. This molecular understanding has revolutionized therapeutic approaches, yet it has also underscored the multifaceted nature of the disease, which demands a correspondingly multifaceted clinical response.

The clinical presentation of ECD is notoriously heterogeneous, a feature that serves as both a primary diagnostic challenge and the core rationale for an interprofessional care model. The disease is not confined to a single organ system; it is a multisystemic infiltrator. Skeletal involvement, presenting as symmetric, osteosclerotic lesions in the long bones (particularly the diaphyses and metaphyses of the femur, tibia, and humerus), is almost universal and a classic hallmark, though it may be asymptomatic [4]. Beyond the skeleton, ECD can manifest with a bewildering array of symptoms. Cardiovascular involvement, perhaps the most life-threatening complication, can lead to pericardial effusion, tamponade, "coated aorta" periaortic fibrosis, and myocardial infiltration. Central nervous system (CNS) involvement, present in up to 50% of cases, can cause diabetes insipidus (the most common endocrine manifestation), cerebellar ataxia, pyramidal signs, and neuropsychiatric symptoms, dramatically impacting quality of life [5]. Renal involvement with perirenal "hairy kidney" fibrosis, retroperitoneal fibrosis, pulmonary infiltration leading to dyspnea, cutaneous xanthoma-like lesions, and exophthalmos from orbital infiltration are just a selection of the potential disease manifestations [6]. This systemic tapestry means a patient may first present to a cardiologist with heart failure, a neurologist with balance problems, an endocrinologist with polyuria and polydipsia, or an orthopedic surgeon with bone pain.

It is within this context of diagnostic complexity and multisystemic burden that the traditional, siloed model of specialty care reveals its profound inadequacies. A neurologist may expertly manage cerebellar symptoms but lack the purview to connect them to subtle perirenal fibrosis seen on an abdominal scan. A cardiologist may drain a pericardial effusion without immediately recognizing its association with long bone pain described months earlier to a primary care physician. This fragmentation of care leads to catastrophic delays in diagnosis—often averaging several years—during which time irreversible organ damage accrues [7]. Furthermore, the treatments for ECD, which have evolved from palliative interventions to targeted biologic and molecular therapies (e.g., BRAF inhibitors like vemurafenib, dabrafenib; MEK inhibitors; interferon-alpha), are potent and carry significant toxicities and monitoring requirements [8]. Managing these therapies while simultaneously addressing the diverse symptomatic burdens of the disease requires a synchronized, continuous, and comprehensive effort.

2. The Central Coordinating Role of Family Medicine

The Family Medicine physician often serves as the first point of contact within the healthcare system and, critically, as the consistent longitudinal anchor throughout the patient's often tumultuous medical journey. In the context of a rare, multisystem disease like ECD, this role evolves from one of general care to one of essential coordination, integration, and patient advocacy. The initial presentation of ECD is frequently a collection of vague, non-specific symptoms—persistent bone pain, fatigue, mild dyspnea, low-grade fevers, or weight loss—that do not immediately point to a specific specialty [9]. It is the Family Medicine practitioner's broad scope and commitment to whole-person care that positions them to detect concerning patterns amidst this ambiguity. They are tasked with taking a meticulous, time-insensitive history, asking about symptoms across all organ systems, and performing a comprehensive physical exam that might reveal subtle signs like

xanthomatous skin lesions, mild bilateral exophthalmos, or peripheral edema suggestive of undiagnosed pericardial disease.

Upon suspicion of a serious underlying condition, the Family Physician's role becomes that of a strategic navigator. They initiate the diagnostic workup with broad-based laboratory tests and imaging, such as a plain radiograph of painful long bones that may reveal the classic symmetric osteosclerosis. When findings suggest a systemic process, they must make appropriate referrals to specialists—rheumatology, neurology, cardiology, endocrinology—while simultaneously maintaining the "big picture" view [10]. Crucially, they act as the central repository for all medical information, synthesizing reports from multiple specialists, reconciling often conflicting opinions in the pre-diagnosis phase, and preventing redundant testing. For the diagnosed ECD patient, the Family Medicine provider manages comorbid conditions (hypertension, diabetes, etc.), addresses general wellness and preventive care, and provides continuous psychosocial support to the patient and family, who are often overwhelmed by the complexity of their situation. They translate the sometimes esoteric language of oncology and specialist care into actionable plans for daily living, ensuring that the patient remains an empowered partner in their own care [11]. This longitudinal, patient-centered perspective is the glue that holds the intricate interprofessional team together, ensuring that care remains coherent and continuous across different settings and over many years.

3. The Nuanced Perspective of Pediatrics in ECD Care

While predominantly a disease of adults, with a median age at diagnosis in the 50s and 60s, ECD does rarely occur in children and adolescents. Pediatric-onset ECD presents unique challenges that necessitate the specialized expertise of Pediatricians and Pediatric subspecialists, fully integrated into the interprofessional team [12]. The presentation in children can be even more insidious and atypical than in adults. Bone pain may be attributed to growing pains or sports injuries. Unexplained fever, failure to thrive, or developmental delay might be the primary clues. Diabetes insipidus in a child requires rapid investigation, and its potential link to a systemic histiocytic disorder like ECD must be considered within the differential diagnosis, which also includes Langerhans Cell Histiocytosis (LCH) and other conditions [13].

The Pediatrician's role extends beyond diagnosis to encompass the profound implications of a chronic, potentially life-altering disease on growth and development. Treatment plans, particularly the use of targeted therapies like BRAF inhibitors, must be carefully considered in the context of a developing body, with close attention to potential effects on growth plates, organ maturation, and long-term side effect profiles that may differ from adults [14]. Dosing of medications is weight-based and requires precise calculation and adjustment. Furthermore, the psychosocial impact on a child and their family is monumental. The Pediatrician, often in close partnership with Pediatric Nursing and Child Life specialists, addresses issues of school attendance, peer relationships, body image (especially with conditions like exophthalmos or skin lesions), and the anxiety associated with frequent hospital visits and procedures. They ensure that the child's educational needs are met, often coordinating with schools to develop individualized education plans (IEPs). The pediatric perspective ensures that management strategies are not merely scaled-down versions of adult protocols but are thoughtfully adapted to support the child's journey toward adulthood, aiming to minimize the disease's footprint on their developmental trajectory [15].

4. Dentistry: Guardian of Oral-Systemic Health in ECD

The role of Dentistry in the management of ECD is a critical yet frequently overlooked component of interprofessional care. The oral cavity can be both a site of direct ECD involvement and a zone of significant vulnerability due to the sequelae of systemic treatment. Oral manifestations, though not the most common, have been documented and include soft tissue swelling, gingival infiltration, and bony lesions in the mandible or maxilla that can mimic other dental or periodontal pathologies [16]. A dentist attuned to systemic disease may be the first to biopsy an unusual gingival lesion, potentially providing the crucial tissue diagnosis. More universally, the dentist is a key defender against treatment-related oral complications. Many ECD patients receive therapies with significant oral side effects. Interferon-alpha can cause xerostomia (dry mouth) and stomatitis. Targeted therapies like BRAF inhibitors are associated with a high incidence of hyperkeratotic skin lesions, which can also manifest in the oral mucosa, and can increase the risk of secondary infections, including viral reactivations like herpes simplex [17].

Chronic xerostomia is not a trivial issue; it drastically increases the risk of dental caries, periodontal disease, and oral candidiasis. The dentist, therefore, implements aggressive preventive regimens, including high-fluoride

prescriptions, salivary substitutes, and meticulous hygiene instruction. They perform regular surveillance for mucosal changes, secondary neoplasms (given the slightly increased risk with some therapies), and dental infections. In patients scheduled for immunosuppressive therapies or major surgeries (e.g., cardiac or orthopedic procedures), a pre-treatment dental clearance is essential to eliminate any occult dental foci of infection that could seed bacteremia and lead to systemic sepsis [18]. By maintaining oral health, dentistry directly contributes to systemic health, preventing pain, infection, and malnutrition that could derail overall treatment plans and quality of life, embodying the core principle of the oral-systemic health connection.

5. Nursing: The Continuous Thread of Care, Education, and Advocacy

Nursing is the profession that provides the continuous, 24-hour thread connecting all aspects of ECD management across inpatient, outpatient, and community settings. The role of the nurse in this context is multidimensional, encompassing direct clinical care, patient and family education, symptom management, care coordination, and enduring psychosocial support. Nurses are often the most consistent point of human contact for patients navigating the complexities of ECD. In the clinic or hospital, they are responsible for administering complex therapies, including chemotherapeutic agents and biologics, monitoring for acute infusion or injection reactions, and assessing vital signs and clinical status with a holistic lens [19]. They are the frontline assessors of treatment toxicity, evaluating for rashes, fevers, neuropathic pain, changes in respiratory status, or signs of fluid overload that might indicate worsening pericardial effusion.

Perhaps one of the most vital nursing functions is patient and caregiver education. They translate the treatment plan into daily routines: teaching self-injection techniques for interferon, managing side effect profiles of targeted therapies, explaining the signs and symptoms that require immediate medical attention, and reinforcing medication adherence. For a disease requiring life-long monitoring, empowering the patient is paramount, and nurses are the primary educators. Furthermore, nurses serve as powerful patient advocates, often identifying unmet needs, clarifying communication gaps between the patient and other specialists, and ensuring that the patient's voice—their concerns about quality of life, functional status, and personal goals—is heard within the interprofessional team [20]. In advanced cases, palliative care nursing principles become integral, focusing on aggressive symptom control (pain, dyspnea, fatigue) and supporting patients and families through difficult decisions, ensuring dignity and comfort irrespective of the disease stage.

6. Pharmacy: Precision, Safety, and Pharmacovigilance

The Pharmacist's expertise is fundamental in the era of targeted and complex combination therapies for ECD. Moving far beyond dispensing, the clinical pharmacist embedded within the interprofessional team ensures the precision, safety, and efficacy of the pharmacotherapeutic regimen. Their work begins with a thorough review of the patient's complete medication profile, including prescriptions, over-the-counter drugs, and supplements, to identify and mitigate potential drug-drug and drug-disease interactions. Given that ECD patients are often on multiple medications for comorbid conditions and ECD-related symptoms (e.g., pain relievers, hormone replacements for diabetes insipidus), this reconciliation is a critical safety check [21].

For targeted therapies like vemurafenib or dabrafenib, the pharmacist provides crucial education on administration (often with high-fat meals to increase bioavailability), storage, and the management of expected side effects such as arthralgia, photosensitivity, and cutaneous squamous cell carcinomas. They monitor laboratory parameters for organ toxicity (liver function tests, renal function, electrolytes) and advise on dose adjustments in collaboration with the treating physician. In cases where ECD treatments interact with other essential medications—for instance, the effect of BRAF inhibitors on the metabolism of warfarin or certain anticonvulsants—the pharmacist's intervention is vital to maintain therapeutic efficacy and avoid adverse events [22]. Furthermore, pharmacists are often responsible for facilitating access to these high-cost specialty medications, navigating insurance prior authorizations, and exploring patient assistance programs, thereby removing a significant practical barrier to care. Their vigilant pharmacovigilance ensures that the powerful tools of modern ECD therapy are used as safely and effectively as possible.

7. Radiology: The Diagnostic Cornerstone and Monitoring Sentinel

Radiology is not merely a diagnostic service but a central, interpretive discipline in every phase of ECD management. It provides the visual evidence of this systemic disease and serves as the primary

tool for monitoring treatment response and detecting progression. The radiologist's expertise is essential in recognizing the classic and sometimes subtle imaging findings of ECD. The initial clue often comes from a technetium-99m bone scan, which reveals pathognomonic symmetric, increased radiotracer uptake in the diaphyses and metaphyses of long bones, with frequent involvement of the distal femur and proximal tibia ("double knee" sign) [23]. Plain radiographs confirm the corresponding mixed lytic and sclerotic appearance of the bone lesions.

Beyond the skeleton, cross-sectional imaging is indispensable. Computed Tomography (CT) of the chest, abdomen, and pelvis reveals characteristic findings: bilateral and symmetric perirenal fibrosis creating the "hairy" or "coated" kidney appearance, periaortic fibrosis encasing the aorta and its major branches, pleural thickening, and interstitial lung disease. Cardiac MRI has become the gold standard for evaluating cardiac involvement, precisely characterizing pericardial thickening, effusion, and myocardial infiltration [24]. Positron Emission Tomography combined with CT (FDG-PET/CT) is arguably the most powerful tool in the initial staging and subsequent monitoring of ECD. It identifies metabolically active disease sites throughout the body—in bone, soft tissue, and the CNS—that might be otherwise silent. The interventional radiologist also plays a therapeutic role, performing image-guided biopsies of accessible lesions (e.g., bone, soft tissue) to obtain tissue for the definitive histopathological and molecular diagnosis, and in draining symptomatic pericardial or pleural effusions [25]. The radiologist's synthesized report, correlating findings across multiple modalities, provides the disease "map" that guides the entire team's therapeutic strategy and tracks its success over time.

8. Laboratory Services: From Cellular Morphology to Molecular Pathogenesis

Laboratory Services form the bedrock of definitive diagnosis and increasingly, of targeted treatment selection for ECD. The journey typically begins in the Histopathology laboratory, where a biopsy specimen (from bone, skin, retroperitoneum, etc.) is processed. The histopathologist identifies the defining microscopic features: a diffuse infiltrate of large, lipid-laden (foamy) histiocytes with eosinophilic, granular cytoplasm, typically surrounded by a mixed inflammatory infiltrate of lymphocytes and plasma cells and associated with fibrosis [12]. Special stains are crucial: the histiocytes are positive for CD68 and often for CD163 and factor XIIIa, while they are negative for CD1a and Langerin (CD207), a key distinction from LCH. This immunophenotypic profile, confirmed by the Pathology laboratory, is diagnostic of ECD.

The most transformative advance has come from the Molecular Pathology laboratory. The identification of activating mutations in the MAPK/ERK pathway, most notably *BRAF* V600E, has redefined ECD as a treatable neoplasm. Using techniques such as allele-specific PCR, next-generation sequencing (NGS), or immunohistochemistry with a BRAF V600E-specific antibody, the laboratory confirms the presence of this mutation [3]. This result is not academic; it directly dictates therapy, making patients eligible for highly effective BRAF inhibitor therapy. In *BRAF* wild-type cases, extended NGS panels can identify alternative mutations (*MAP2K1*, *NRAS*, etc.), informing the use of MEK inhibitors or other targeted agents. Furthermore, the Clinical Chemistry and Hematology laboratories provide continuous monitoring data: elevated inflammatory markers (C-reactive protein, erythrocyte sedimentation rate), renal function tests to monitor for hydronephrosis from retroperitoneal disease, lipid profiles (as ECD histiocytes are lipid-laden), and hematological parameters that can be affected by disease or treatment [25]. Thus, the laboratory translates tissue and blood into actionable molecular and biochemical intelligence, driving personalized medicine for each ECD patient.

9. Synthesis and Conclusion: The Integrated Team in Action

The management of Erdheim-Chester Disease ultimately presents a compelling argument for the necessity of sophisticated interprofessional collaboration in modern medicine, particularly for rare, complex diseases. The journey of a single ECD patient vividly illustrates this synergy. It may begin with a Family Physician who, alerted by persistent, vague symptoms, orders an x-ray revealing unusual bone changes. The Radiologist interprets this, suggests a bone scan for confirmation, and identifies perirenal fibrosis on an accompanying abdominal ultrasound. Guided by these findings, an Interventional Radiologist performs a CT-guided biopsy of an accessible bone lesion. The Histopathologist in the Laboratory makes the microscopic diagnosis, and the Molecular Pathologist identifies a *BRAF* V600E mutation. The treating specialist (often an Oncologist or Hematologist), in consultation with the Pharmacist, initiates therapy with a BRAF

inhibitor. The Nurse educates the patient on managing the drug's side effects, while the Dentist addresses emerging oral dryness and mucositis. The Family Physician continues to manage hypertension and provides emotional support, and if the patient is a child, the Pediatrician ensures these interventions support normal development. All the while, serial FDG-PET/CT scans by the Radiologist objectively measure treatment response.

This is not a linear sequence but a dynamic, parallel process of continuous communication and adjustment. Regular interprofessional team meetings, whether virtual or in-person, are the engine of this model. Here, the radiologist presents new imaging, the pharmacist flags a drug interaction, the nurse reports a patient's worsening fatigue, and the family physician provides context from the last home visit. Together, they adjust the care plan in real-time. This collaborative model mitigates the profound isolation experienced by patients with rare diseases. It accelerates diagnosis, personalizes treatment, enhances safety, improves adherence, and holistically addresses the physical, emotional, and social dimensions of living with a chronic illness. In confronting the multifaceted challenge of Erdheim-Chester Disease, a robust interprofessional team combining Family Medicine, Pediatrics, Dentistry, Nursing, Pharmacy, Radiology, and Laboratory Services is not an optional luxury but the essential framework for delivering care that is as comprehensive and integrated as the disease itself. It represents the highest standard of medicine—a coordinated human system designed to understand and treat a complex biological one.

10. Conclusion

In conclusion, the intricate and systemic nature of Erdheim-Chester Disease renders a siloed, specialist-centric approach to care not only inefficient but potentially detrimental to patient outcomes. The imperative for a structured, dynamic interprofessional collaboration is unequivocal, as it directly addresses the core challenges of ECD: diagnostic complexity, multisystemic involvement, and the need for long-term management of both disease and treatment-related sequelae. By weaving together the distinct yet complementary expertise of family medicine, pediatrics, dentistry, nursing, pharmacy, radiology, and laboratory services into a cohesive unit, a truly patient-centric ecosystem is created. This model ensures that the journey from initial vague symptom to definitive molecular diagnosis is expedited, that powerful targeted therapies are administered with utmost safety and precision, and that the patient's physical, psychosocial, and functional well-being remains the constant focus. The collaborative framework thus transcends mere consultation, fostering a shared responsibility that enhances communication, reduces errors, and empowers both clinicians and patients. For individuals with ECD, such a team-based paradigm is not an ancillary support but the foundational pillar of care, offering the best prospect for timely intervention, effective disease control, and a sustained quality of life amidst a chronic and challenging illness.

Author Statements:

- **Ethical approval:** The conducted research is not related to either human or animal use.
- **Conflict of interest:** The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper
- **Acknowledgement:** The authors declare that they have nobody or no-company to acknowledge.
- **Author contributions:** The authors declare that they have equal right on this paper.
- **Funding information:** The authors declare that there is no funding to be acknowledged.
- **Data availability statement:** The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

[1] Diamond EL, Subbiah V, Lockhart AC, Blay JY, Puzanov I, Chau I, et al. Vemurafenib for BRAF V600–mutant erdheim-chester disease and langerhans cell histiocytosis. JAMA Oncol. 2018;4:384.

[2] Bartoli L, Angeli F, Stefanizzi A, Fabrizio M, Paolisso P, Bergamaschi L, et al. Genetics and clinical phenotype of Erdheim–Chester disease: A case report of constrictive pericarditis and a systematic review of the literature. Front Cardiovasc Med. 2022;9.

[3] Weissman R, Diamond EL, Haroche J, Pillar N, Shapira G, Durham BH, et al. The contribution of microRNAs to the inflammatory and neoplastic characteristics of erdheim–chester disease. Cancers (Basel). 2020;12:3240.

[4] Khoury JD, Solary E, Abla O, Akkari Y, Alaggio R, Apperley JF, et al. The 5th edition of the world health organization classification of haematolymphoid tumours: myeloid and

histiocytic/dendritic neoplasms. Leukemia. 2022;36:1703–19.

[5] Pegoraro F, Maniscalco V, Peyronel F, Westenend PJ, Hendriksz TR, Roperto RM, et al. Long-term follow-up of mTOR inhibition for Erdheim-Chester disease. Blood. 2020;135:1994–7.

[6] Saunders IM, Goodman AM, Kurzrock R. Real-world toxicity experience with BRAF/MEK inhibitors in patients with erdheim-chester disease. Oncologist. 2020;25:e386–90.

[7] Arnaud L, Hervier B, N.el A, Hamidou MA, Kahn JE, Wechsler B, et al. CNS involvement and treatment with interferon-α are independent prognostic factors in Erdheim-Chester disease: a multicenter survival analysis of 53 patients. Blood. 2011;117:2778–82.

[8] Reiner AS, Durham BH, Yabe M, Petrova-Drus K, Francis JH, Rampal RK, et al. Outcomes after interruption of targeted therapy in patients with histiocytic neoplasms. Br J Haematol. 2023;203:389–94.

[9] Elbaz Younes I, Ellis A, Zhang X. Updates on erdheim-chester disease. Hum Pathol Rep. 2022;28:300636.

[10] Chazal T, Pegoraro F, Manari G, Bettiol A, Maniscalco V, Gelain E, et al. Clinical phenotypes and long-term outcome of kidney involvement in Erdheim-Chester histiocytosis. Kidney Int. 2023;103:177–86.

[11] Berti A, Cavalli G, Guglielmi B, Biavasco R, Campochiaro C, Tomelleri A, et al. Tocilizumab in patients with multisystem Erdheim–Chester disease. Oncoimmunology. 2017;6(6):e1318237.

[12] Antunes C, Gra.a B, Donato P. Thoracic, abdominal and musculoskeletal involvement in Erdheim-Chester disease: CT, MR and PET imaging findings. Insights into Imaging. 2014;5:473–82.

[13] Gianfreda D, Nicastro M, Galetti M, Alberici F, Corradi D, Becchi G, et al. Sirolimus plus prednisone for Erdheim-Chester disease: an open-label trial. Blood. 2015;126:1163–71.

[14] He J, Fang X, Zhang X, Chen K, Huang J. Extensive aortic thromboembolism in a patient with erdheim-chester disease: A case report. Front Cardiovasc Med. 2022;9.

[15] Salama HA, Jazieh AR, Alhejazi AY, Absi A, Alshieban S, Alzahrani M, et al. Highlights of the management of adult histiocytic disorders: langerhans cell histiocytosis, erdheim-chester disease, rosai-dorfman disease, and hemophagocytic lymphohistiocytosis. Clin Lymphoma Myeloma Leuk. 2021;21:e66–75.

[16] Cohen-Aubart F, Maksud P, Saadoun D, Drier A, Charlotte F, Cluzel P, et al. Variability in the efficacy of the IL1 receptor antagonist anakinra for treating Erdheim-Chester disease. Blood. 2016;127:1509–12.

[17] Abeykoon JP, Ravindran A, Rech KL, Young JR, Oliver Tobin W, Shah MV, et al. Mimics of erdheim–chester disease. Br J Haematol. 2022;196:984–94.

[18] Hervier B, Arnaud L, Charlotte F, Wechsler B, Piette JC, Amoura Z, et al. Treatment of erdheim-chester disease with long-term high-dose interferon-α. Semin Arthritis Rheumatol. 2012;41:907–13.

[19] Braiteh F, Boxrud C, Esmaeli B, Kurzrock R. Successful treatment of Erdheim-Chester disease, a non–Langerhans-cell histiocytosis, with interferon-α. Blood. 2005;106:2992–4.

[20] Goyal G, Heaney ML, Collin M, Cohen-Aubart F, Vaglio A, Durham BH, et al. Erdheim-Chester disease: consensus recommendations for evaluation, diagnosis, and treatment in the molecular era. Blood. 2020;135:1929–45.

[21] Diamond EL, Francis JH, Lacouture ME, Rotemberg V, Yabe M, Petrova-Drus K, et al. CSF1R inhibition for histiocytic neoplasm with CBL mutations refractory to MEK1/2 inhibition. Leukemia. 2023;37:1737–40.

[22] Dray B, Emile JF, Cohen-Aubart F, Amoura Z, Wagner M, Haroche J, et al. Abdominal extrarenal involvement in erdheim-chester disease in a cohort of 304 patients. JAMA Oncol. 2022;8:1843.

[23] Abla O. Management of ECD: the era of targeted therapies. Blood. 2020;135:1919–20.

[24] Cohen Aubart F, Emile JF, Carrat F, Charlotte F, Benameur N, Donadieu J, et al. Targeted therapies in 54 patients with Erdheim-Chester disease, including follow-up after interruption (the LOVE study). Blood. 2017;130:1377–80.

[25] Martínez-López J, Márquez A, Pegoraro F, Ortiz-Fernández L, Acosta-Herrera M, Kerick M, et al. Genome-wide association study identifies the first germline genetic variant associated with erdheim-chester disease. Arthritis Rheumatol. 2024;76:141–5.