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RESEARCH ARTICLE
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DIAGNOSTIC CHALLENGES IN ACUTE MONOBLASTIC /MONOCYTIC LEUKEMIA IN CHILDREN OF QUETTA BALUCHISTAN

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ABSTRACT

Background: Particularly in low-resource areas with poor pediatric healthcare facilities, such as Quetta, Baluchistan, acute monoblastic/monocytic leukemia (AMoL) poses special diagnostic challenges.

Objective: To investigate the difficulties in diagnosing AMoL in children, with an emphasis on clinical obstacles, laboratory shortcomings, and institutional constraints.

Methods: 100 people participated in the qualitative study, which included pediatric patients, caregivers, and medical professionals. Semi-structured interviews were used to gather the data, which were then subjected to thematic analysis.

Results: Financial difficulties, irregular cytochemical labeling, a shortage of qualified morphologists, and restricted access to flow cytometry and molecular testing were among the main obstacles. Misunderstandings and delays in diagnosis were frequent.

Conclusion: For quick and precise AMoL diagnosis in underprivileged pediatric populations, it is essential to improve infrastructure, training, and reasonably priced diagnostics.

Keywords: Acute Monoblastic/Monocytic Leukemia (AMoL), Pediatric Leukemia Diagnosis, Diagnostic Challenges

INTRODUCTION

Pediatric AML cases consist of 15–24% of all leukemia and Acute Monoblastic/Monocytic Leukemia (AMoL) is among these cases.

AML-M5, sometimes called AMoL, is the term used by the French American British group when 80% or more of blast cells in the bone marrow or peripheral blood are monocytic and there are at least 30% blasts. The Wright-Giemsa or May-Grünwald-Giemsa procedures are used to evaluate stained smears (4–6). In that same year, the WHO defined AML, not otherwise specified (NOS), to refer to AMoL and decided that a total of 20% of blasts is needed, if the majority are monocytes. All in all, the presence of specific morphology in AMoL can guide whether the case should be classified as AML or as having a rare genetic variant not recognized in the WHO classification.

Acute monoblastic leukemia is named AML-M5a when 80% or more of the monocytic cells are monoblasts. If blast cells are more developed and mostly monocytes, the type of leukemia is known as acute monocytic leukemia (AML-M5b). Some of the main features of AMoL include raised white blood cell counts, many infiltrates in the skin, gums and the central nervous system and an increased chance of coagulation and bleed-related issues (19–21).

It is sometimes hard to detect AMoL and MRD, as leukemic monocyte cells can closely resemble the healthy monocytes. Used methods for classifying different cells in the monocytic group are cytomorphology, cytochemistry, flow cytometry, cytogenetics and molecular biology (22, 23).

The review lists the main diagnostics used for patients with immature myeloid leukemia. The cytoplasm is With only a few azurophilic granules, small vacuoles and a total absence of Auer rods, the cells become numerous and stain well with basophilic dyes. Some experts think that the pseudopods reveal a membrane only after they develop a distinct translucent feature (24–27).

Generally, myeloperoxidase (MPO) does not stain mature monocytes and monoblasts, yet it can exceptionally be seen in promonocytes. MPO (1, 29) can be seen as a strong marker of granulocytic cells.

Negative or weak NSE can be found in some AMoL cases, but there are often many monocytes that show up very well and positively using cytochemistry, making cytochemistry a valuable method for monocytic leukemia. Myeloid-type cells can be distinguished from monocytic cells since either NSE is not expressed or there is just a small amount of expression (1, 29). Yet, NSE sometimes brings surprising and uneasy-to-understand results and making samples is not a simple task. To get the right results, the process needs to take place in labs regularly with the help of capable morphologists.

Sodium fluoride in NSE staining makes it easier to distinguish the cells in monocytic group from those in myeloid group 1. Apart from the commonly used methods, there are few others, including Sudan black and naphthol AS-D chloroacetate esterase, that are used only occasionally in routine clinical tests. Despite this trait, monoblasts are often HLA-DR negative and positive for tartrate-sensitive acid phosphatase. With the help of these three stains, one can interpret the various results of embryo examinations (24-26). This study aims to explain and show the barriers encountered when trying to detect AMoL in young people living in Quetta, Baluchistan.

LITERATURE REVIEW

It is often challenging for doctors to diagnose AMoL, a type of AML, in young people. Since their features are similar to normal monocytes, identifying leukemic monoblasts is challenging. Places like Quetta, Baluchistan, that do not have access to advanced tests in diagnostics and may lack knowledge about hematopathology make such situations worse.

AMoL belongs to AML-M5, a type of leukemia identified by the predominate presence of monocytic cells in the blood, by the FAB categorization. Depending on how mature monocytic cells are, this type of leukemia is further divided into M5a (acute monoblastic leukemia) and M5b (acute monocytic leukemia). These diagnoses are often indicated by increased white blood cells and their presence in the skin, gums or central nervous system. Since these symptoms may appear in other illnesses as well, it is challenging to diagnose AMoL when there are no tests available.

Doctors use visual examinations of cells to help in diagnosing leukemia. Yet, in AMoL, it is not easy to tell these apart since they resemble each other. Monoblasts are large, with round-oval nuclei having fine chromatin and obvious nucleoli inside, along with a lot of basophilic cytoplasm and some spaces that look like vacuoles. When they are more developed into promonocytes, they may be difficult to identify because their appearance fluctuates a lot. A study on 12 cases of pure acute monocytic

leukemia emphasizes the importance of morphologists being able to discern AMoL from reactive monocytosis when blast cells are unclear [32].

Tissue samples were generally examined using NSE cytochemical staining to identify monocytic cells in the past. It can be recognized as part of the myeloid lineage because monoblasts and promonocytes have a high level of NSE activity while this activity is suppressed by sodium fluoride. Nevertheless, having the correct supplies and equipment and knowing the proper techniques are important because these methods can be less accurate in poorly equipped laboratories [33]. In a similar way, myeloperoxidase (MPO) cannot help much in AMoL diagnosis, as it is negative in monocytic blasts and positive in granulocytic cells [34].

CD14, CD64, CD11b and CD33 surface markers make flow cytometry immunophenotyping more accurate in determining different cell types. Even though multiparametric flow cytometry is emerging, it is still limited in Quetta and other similar areas. The similarities seen in the expression of monocytic markers in both cancerous and healthy cells may make it hard to clearly distinguish the differences. Diagnosis is more challenging because the markers CD34 and HLA-DR are expressed differently in AMoL cases [35].

Better diagnosis is achieved through the study of genetics and molecules. Frequently, genetic alterations involving KMT2A are found in pediatric AMoL and play a part in diagnosis and outlook. Since molecular diagnostics are very expensive and the infrastructure is lacking, access to them is almost impossible in Balochistan [36]. Also, WHO classification systems are often not used widely as there are still many genetic disorders related to AMoL that have not been recognized by WHO [37].

It is also challenging to detect small, remaining groups of cancer cells after treatment (MRD) in AMoL. Sometimes, resemblance between regrowing normal monocytes and remaining leukemic monocytes occurs after chemotherapy, making it difficult to confirm the presence of the leukemia. MRD monitoring will not work properly unless clear protocols and advanced tools are used. For children, timely detection of early relapses is crucial because it determines their chances of survival.

In clinical practice, AMoL tends to be severe and may lead to internal bleeding, blood clotting throughout the body and buildup of white blood cells in certain areas. This makes it harder for diagnostic teams, as they must act quickly to diagnose and commence therapy. If it takes time to identify diseases because laboratories are limited, the impact can be negative in regions such as Quetta where the medical system faces heavy pressure [39].

When an extramedullary presentation resembles a different disease, it adds to the challenges in making the right diagnosis. At first, cutaneous nodules and enlarged gums may seem like simple hyperplasia or infections. A study indicated that misinterpreting these infections delayed the diagnosis in some cases of pediatric AMoL [40].

To deal with these challenges, a strategy involving three steps in diagnosis has been set up in Balochistan. This requires supporting subsidized molecular testing, establishing flow cytometry facilities at the regional level and enhancing education in cytomorphology. Another step toward fixing the gap would be teaming up with international organizations and major cities.

Overall, the challenges of diagnosing AMoL in children include changes in cell shape, different chemical reactions and scarce available resources. Even though these new technologies are helpful, applying them in places like Quetta requires investment in necessary infrastructure, training and assistance from the government.

RESEARCH OBJECTIVE

The main goal of this study is to explore the reasons why it is hard to diagnose acute monoblastic/monocytic leukemia (AMoL) in children living in Quetta. It aims to examine the aspects of disease that complicate early and accurate diagnosis and outlines the resources that are missing and the problems in timely detection. The purpose of the study is to uncover what is preventing timely detection and treatment of AMoL in children, considering the facilities available in local hospitals, access to modern diagnostics and understanding among healthcare workers. The main purpose is to facilitate progress in the diagnosis and care of children with leukemia in this poor area.

METHODOLOGY

The objective of this study was to look into the difficulties in diagnosing acute monoblastic/monocytic leukemia (AMoL) affecting children in Quetta, Balochistan. People were selected in a purposive way, with 100 participants taking part in the study. The participants were pediatric patients with AMoL, their guardians and others involved such as pediatricians, hematologists and lab assistants who took part in the diagnosis. To better understand the problems patients face during diagnosis, I used in-depth and semi-structured interviews. To allow individuals to talk freely about their experiences, we interviewed them with open-ended questions instead of surveys. Agreement was obtained ahead of the interviews which were recorded and transcribed in detail, followed by analysis to discover recurring issues facing the healthcare system. The process was approved by the required review board and ensured everyone's privacy.

RESULTS

Table 1: Common Themes Identified from Interviews

Main Theme	Sub-Themes	Frequency (n=100)	Representative Quotes
Diagnostic Delays	Late referrals, misdiagnosis, slow lab turnaround	68	"It took almost a month to know it was leukemia."
Resource Limitations	Lack of flow cytometry, unavailability of molecular testing	74	"We had to send samples to Karachi."
Lack of Specialist Training	Inexperienced morphologists, misinterpretation of smears	55	"Initial reports said infection, not leukemia."
Financial Constraints	Cost of advanced diagnostics, lack of subsidized care	63	"We couldn't afford private testing, so we waited."

Table 2: Perceived Diagnostic Barriers by Participant Category

Participant Category	Primary Diagnostic Barrier Reported	Number of Participants	Remarks
Pediatricians	Limited access to diagnostic tools	35	Need for training in recognizing AMoL signs
Hematologists	Delay in lab processing and misinterpretation of results	20	Emphasis on lack of skilled lab technicians
Laboratory Technicians	Inadequate equipment and reagents	25	Complaints about outdated staining techniques
Caregivers	Financial and travel burden, lack of information	20	Many unaware of what leukemia actually is

Table 3: Diagnostic Tools Reported as Unavailable or Underutilized

Diagnostic Tool	Availability at Study Site	Reported Impact on Diagnosis	Mentioned by Participants (n)
Flow Cytometry	No	Delay in confirming lineage	78
Molecular Genetic Testing (e.g., KMT2A)	No	Inability to classify leukemia type	66
Cytochemical Staining (NSE/MPO)	Partially	Misleading results due to inconsistent techniques	58
Trained Morphologist Interpretation	Limited	Misclassification of monoblasts	61

MRD Monitoring Tools	No	Missed early relapse	52

DISCUSSION

Based on the study's results, the authors mention a variety of challenges to correctly diagnosing AMoL in kids living in Quetta. In Table 1, you can see that there are three main themes among the most frequent issues: not having specialized training (55), a lack of resources (74) and being delayed with diagnoses (68) are some of the reasons. The evidence shows that the process of making a diagnosis in these cases is often separated, leading to long waits, first diagnoses that are sometimes off the mark and lacking laboratory support. A member of the group commented that they didn't know it was leukemia for almost a month, underlining the length of the diagnostic process for many people.

The secondary set of diagnostic problems given in Table 2 covers different roles of people involved. Hematologists pointed out that sometimes tests are misinterpreted and there are delays in making the report, while pediatricians commonly said that getting access to advanced equipment was often an issue. Many pain points in MPO and NSE staining arose from employees relying on old equipment and having inconsistent processes for cytochemical staining. Twenty of the caregivers mentioned difficulties with money and not understanding leukemia; this often resulted in putting off getting care for the patient.

Table 3 shows the results of a survey where 78 participants said that flow cytometry to identify and validate the markers of AMoL was not possible at where they worked. Sixteen experts pointed out that if molecular genetic tests such as KMT2A mutation analysis, are not available, it complicates the subtyping of leukemia. There was a large number of inconsistencies and not many qualified morphologists which meant cytochemical labeling was not always reliable (n=61). One important limitation found was that MRD monitoring is not done after treatment, as stated by 52 patients.

All told, inadequacies have been identified in the way AMoL is trained, the necessary equipment is provided and the funds available which all add to the difficulty of providing prompt and correct diagnoses in this area. Addressing these issues is necessary to better the outcomes in children with leukemia.

CONCLUSION

This research found that diagnosing AMoL in children in Quetta, Baluchistan, is a major difficulty for health professionals. Among these obstacles are not having modern machines like flow cytometry and molecular testing, skipping cytochemical staining, not having enough talented morphologists and the burden that families face in paying for treatment. As a result, it can become harder to diagnose a patient on time, led by these various elements. Some important steps to take include making diagnostic services more accessible, improving training and building up laboratory facilities. Clearances of these hurdles improve the diagnosis and outcomes for children in short supply areas.

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