



REVISTA MÉDICA DEL
HOSPITAL GENERAL
DE MÉXICO

www.elsevier.es/hgmx



REVIEW ARTICLE

Morphology of leukaemias



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Received 4 April 2015; accepted 11 June 2015

Available online 29 October 2015

KEYWORDS

Diagnostic techniques and procedures;
Lymphoid leukaemia;
Myeloid leukaemia;
Cellular morphology

Abstract Acute leukaemias are characterised by uncontrolled proliferation of immature blood cells with lymphoid or myeloid lineage. Morphological classification is based on the identification of the leukaemia cell line and its stage of differentiation. The first microscopic descriptions dating from the 1930s pointed to 2 different types of leukaemia cells: lymphoid and myeloid. In 1976, the consensus that led to the French-American-British (FAB) classification was achieved. This includes criteria for identifying myeloid and lymphoid leukaemias, and gives a list of morphological subtypes, describing how these affect the patient's prognosis. Today, despite new classifications based on sophisticated studies, FAB classification is widely used by experts due to its technical simplicity, good diagnostic reliability and cost-effectiveness.

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PALABRAS CLAVE

Técnicas y procedimientos diagnósticos;
Leucemia linfóide;
Leucemia mieloide;
Morfología celular

Morfología de las leucemias

Resumen Las leucemias agudas se caracterizan por proliferación descontrolada de células progenitoras de estirpe linfóide o mieloide. La clasificación morfológica se basa en la identificación de la línea celular de la célula leucémica y de la etapa de diferenciación. Desde las primeras descripciones microscópicas durante el primer tercio del siglo XIX se plantearon dos tipos distintos de las células leucémicas: linfóides y mieloides. Fue hasta 1976 cuando se logró el consenso que dio origen a la clasificación Franco-Americano-Británica (FAB) que conserva la gran división entre mieloides y linfóides, además de asignar subtipos a partir de características morfológicas, destacando la traducción directa que tienen sobre el pronóstico del paciente. Hoy

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en día a pesar de contar con clasificaciones que consideran estudios más sofisticados, la clasificación FAB es ampliamente usada por expertos debido a su sencillez técnica, buena fiabilidad diagnóstica y precio económico.

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Background

The word leukaemia (originally *leukämie* in German) comes from the Greek words *leukos* (λευκός): white and *haima* (αἷμα): blood. The modern term leukaemia was first proposed by Rudolf Virchow in 1846.¹ Unsurprisingly, the term was suggested after examining infected blood under the microscope, an instrument that was first invented in the 17th century, but only perfected 2 centuries later and used by physicians to identify alterations in tissues and cells.

The famous French physician Alfred Armand Louis Marie Velpeau (1795–1867) is credited with providing the first anatomical and pathological description of leukaemia. The patient was a 63-year-old man called Monsieur Vernis, who earned his living selling flowers and lemonade in Paris, and complained of fever, weakness, and an enlarged liver and spleen. Velpeau performed the autopsy on the patient, observing a greatly enlarged spleen weighing 4.5 kg and noting that the blood was very thick with a consistency similar to that “of porridge”. Under the microscope, he observed a large quantity of “globules of pus in the blood”. Velpeau reported the histological and anatomical findings in this patient to the Royal Academy of Medicine in Paris, and the article was published in March of 1827. A few years later, in 1839, Alfred François Donné, also a Paris-based physician and an enthusiast of microscopy as a diagnostic tool, described the case of a woman with splenomegaly and increased levels of “mucous globules” in the blood. The case caught the attention of one of Donné’s foreign disciples, the English pathologist John Hughes Bennett (1812–1875). On returning to his native land, Bennett came across a similar case of organ enlargement and changes in the consistency and colour of the blood, which he described in detail in the *Edinburgh Medical and Surgical Journal* (1845). Six years later, Bennett dubbed this pathology “leukocytosis”.^{1,2}

Five or six weeks after publication of Bennett’s report, a report titled *Weisses Blut* (white blood, in German) was published in the German journal *Neue Notizen aus Gebiete der Natur-und Heilkunde*. The article reported the case of a 50-year-old cook by the name of Maria Straide, with a 4-year history of chronic fatigue and abdominal distension. On physical examination, the patient presented an enlarged, slightly tender spleen, oedema of the lower limbs, and diarrhoea. She had complained of epistaxis that was lasting for 8 days, rash, and weakness. The autopsy showed loss of colour in all organs, “white spots” on the liver, and a greatly enlarged spleen. Microscopic findings were “everywhere in the blood vessels a mass closely resembling pus was found, with colourless corpuscles”. The author of the report was the young 24-year-old German pathologist Rudolf Virchow (1821–1902). These observations gave rise to

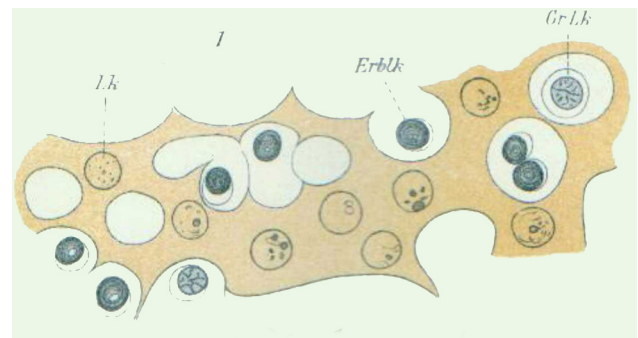


Figure 1 First published sketch of the origin of leukaemic cells, by Ernst C. Neumann. Public domain image, taken from: Wikimedia Commons.

the term leukaemia (*leukämie*). Although Virchow was quick to praise Bennett and addressed him with great respect, the appearance of his report so soon after Bennett’s, proposing a different name for the same condition, sparked considerable controversy.^{2,3}

The next major step in the story of leukaemia morphology occurred in 1869, when both blood and bone marrow were studied under the microscope. Studying bone fragments, Franz Ernst C. Neumann (1834–1918), a German pathologist born in Königsberg, pupil of Hermann Ludwig F. von Helmholtz (1821–1894) and Virchow, was the first to show that haematopoiesis takes place in the bone marrow. He hypothesised that blood originates from a common precursor, which he called a stem cell (*Stammzelle* in German) (Fig. 1).^{4,5} Neumann also suggested that, in addition to the lymphatic and splenic leukaemias proposed by Virchow, there was another type of leukaemia that originated in the bone marrow. He called this “myeloid leukaemia”, and his theory was later validated by Bizzozero.^{1,3}

The last breakthrough in this brief history of the morphology of leukaemia was spearheaded by Paul Ehrlich (1854–1915). While still a medical student, Ehrlich developed the technique of cell staining, and observed for the first time the cytoplasmic components and different types of nuclei in blood cells, for which he coined the terms acidophils and basophils.⁶

Morphology of acute leukaemias

Acute leukaemias are characterised by the uncontrolled proliferation of myeloid or lymphoid progenitor cells.¹ Their morphological classification is based on the identification of the leukaemia cell line and stage of cell differentiation.^{1,6}

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