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(CASE REPORT)

The discovery of multiple myeloma during the evolution of lupus nephropathy: A case report and literature review

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Abstract

Introduction: Systemic lupus erythematosus (SLE) has been proven to be independently associated with higher proportions of malignancies, particularly hematological patterns. We report a patient who developed multiple myeloma on underlying lupus nephropathy with poor outcome.

Observation: It was a 48-year-old male patient followed in pneumology for bronchial dilatation secondary to pulmonary tuberculosis who consulted nephrology for an impure nephrotic syndrome without extra-renal signs and a renal biopsy outlining advanced endo and extra-capillary glomerulonephritis with 38% activity. The etiological investigation had revealed lupus. Despite 2 therapeutic protocols based on MMF + corticoids then cyclophosphamide + corticoids, there was no remission. He underwent conservative treatment for chronic kidney disease with stable renal function including a GFR of 27 ml/min/1.73m^2. Two years after the discovery of lupus disease, the patient presented with a bleeding syndrome with a blood count showing normocytic normochromic anaemia at 4.1 g/dl, leukopenia at 830/mm^3 and thrombocytopenia at 49000/mm^3. The bone marrow count performed on the basis of this pancytopenia showed a plasmocytosis in 38% with a dysmorphic erythroblastic lineage (basophilic punctation and laminated cytoplasm), an absent megakaryocytic lineage and the presence of numerous naked plasma cells and dysmorphic plasma cells, numerous hemophagocytic macrophages and siderophages. Plasma protein electrophoresis did not show a monoclonal peak. The outcome was poor. Death occurred 3 days after his hospitalization in a medullary insufficiency course.

Conclusion: Lupus can be the starting point for the development of a hematological malignancy at a later stage. On the other hand, cancer can induce spontaneous autoimmune manifestations or secondary to anti-tumor therapies. In our case it was a patient who developed myeloma 2 years after the onset of lupus with a poor outcome leading to death.

Keywords: Lupus; Myeloma; Renal failure; Cancer

1. Introduction

The role of the immune system in the risk of cancer occurrence is an interesting topic and, as a result, the association between autoimmunity and cancer has been under investigation for over a decade [1]. An autoimmune disease may represent the starting point for the subsequent development of a solid cancer or hematological malignancy. On the other hand, cancer can induce autoimmune manifestations spontaneously or as a result of anti-tumor therapy. The dilemma sometimes remains to distinguish between autoimmune paraneoplastic syndrome or genuine autoimmune disease, especially if the diagnosis was concomitantly set [2]. Systemic lupus erythematosus (SLE) has been shown to be independently associated with higher proportions of malignancies, particularly hematological malignancies [3]. In a large cohort assessing the risk of SLE-related cancer, 10/644 cases of multiple myeloma were reported [4]. We report a patient who developed multiple myeloma in lupus nephropathy.

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2. Result and observation

This was a 48-year-old patient with a history of pulmonary tuberculosis with sequelae of bronchial dilatation. In January 2018 he consulted a nephrologist for an impure nephrotic syndrome without extra-renal symptoms. The renal biopsy showed advanced endo and extra capillary glomerulonephritis with 38% activity. An etiological investigation revealed lupus. The initial treatment consisted of a combination of mycophenolate mofetil (MMF), corticosteroids and hydroxychloroquine. The outcome was labelled by an absence of remission. A change of treatment protocol was made with the combination of cyclophosphamide/corticoids in induction and then azathioprine/corticoids in maintenance. The patient did not respond favorably to the treatment, leading to treatment discontinuation.

In 2019, the kidney function was still stable with a clearance of 27.31 ml/min/1.73m^2 (table 1) under conservative treatment (nephroprotector, vitamin D supplementation, erythropoiesis stimulating agent and correction of all other progression factors of chronic kidney disease). An arteriovenous fistula for hemodialysis and a hepatitis B vaccination were performed.

In July 2020, he presented with a sudden onset of heavy rectal bleeding complicated by cardiovascular collapse. He was urgently admitted to hospital and underwent blood transfusions. Emergency investigations revealed severe pancytopenia with normocytic normochromic anaemia at 4.1 g/dl, leukopenia at 830/mm3 and thrombocytopenia at 49,000/mm3 (table 1). Creatinine level was 81.5 mg/L with a glomerular filtration rate (GFR) of 8.55 ml/min/1.73m2. Digestive endoscopy was not performed due to the patient's instability.

On the basis of the hemorrhage and severe thrombocytopenia, combined with other hematological lineages impairment, the medullogram was carried out. The results (figure 1) of this investigation showed a 38% plasmacytosis associated with:

- A dysmorphic erythroblastic lineage (basophilic punctation and laminated cytoplasm);
- Absent megakaryocytic lineage;
- And the presence of numerous naked plasma cells and dysmorphic plasma cells, numerous hemophagocytic macrophages and siderophages.

The diagnosis of multiple myeloma associated with macrophage activation syndrome was made in the context of lupus nephropathy. Plasma protein electrophoresis did not show a monoclonal peak.

The evolution was fatal with a hemorrhagic syndrome consisting of rectal bleeding, epistaxis, hemoptysis and conjunctival hyperaemia. Death occurred 3 days after hospitalization in a state of bone marrow failure. The rest of the investigations could not be carried out.

3. Discussion

Our case consisted of a patient who developed multiple myeloma after 2 years of evolution of lupus nephropathy. The association of lupus and multiple myeloma (MM) is relatively rare in the literature. A cohort study reported a single case of MM in 70 lupus patients [5], and a large case-control study showed a high risk of MM in subjects with a family history of SLE, but no personal history of SLE [6]. This may suggest an underlying genetic predisposition to both diseases and likely a common pathway.

SLE is known to cause polyclonal activation of B cells [7], whereas monoclonal proliferation appears to be a rare event. Plasma cell dyscrasias (monoclonal gammopathy of undetermined significance (MGUS) and MM) have also been associated with chronic inflammatory processes, but not specifically with SLE [8]. Possible underlying mechanisms for this association include chronic B-cell activation, immunosuppressive therapy and EBV viral infection [9, 10], but further studies are needed to demonstrate this possible link.

Anemia in SLE is often microcytic and of peripheral or regenerative origin, which was not found in our patient. In CKD, it consisted of an aregenerative normocytic normochromic, but the leukopenia and thrombocytopenia in our patient suggested a new lupus disease attack. This anaemia was worsened by the gastro-intestinal hemorrhage, which was itself favored by the thrombocytopenia. These acute cytopenias ruled out the hypothesis of a drug cause because our patient was no longer under immunosuppressive treatment during this period. Regarding the kidney, we noted an accutisation of the CKD at stage 5. On the basis of these associated hematological disturbances, the medullogram might clearly outline the origin of these attacks. The presence of hemophagocytic macrophages in the bone marrow was in favor of MAS,

which could explain the thrombocytopenia and the severe leukopenia. However, the other elements of this syndrome were not investigated because of the early death of our patient after 3 days of hospital stay.

4. Appendix

Table 1 Overview of biological parameters

Parameters	30/08/2018	09/11/2018	08/07/2020
Haemoglobin (g/dl)	9.9	10.8	4.1
MCV (fl)	92.8	94.1	97.7
MCH	30.7	31	31.5
Leukocytes (/mm3)	16260	16930	830
Platelets (/mm3)	286000	283000	49000
Urea (g/l)	1.46	1	-
Creatininemia (mg/l)	39.71	29.9	81.5
Clearance (GFR)	19.77	27.31	8.55
Natremia (mmol/l)	145	146	-
Kalemia (mmol/l)	4.06	4.37	-
Calcemia (mg/l)	96	97	-
Protidemia (mg/l)	-	-	53
Albuminemia (g/l)	-	-	24.2
Alpha-1 (g/l)	-	-	6.2
Alpha-2 (g/l)	-	-	9.4
Beta-2 (g/l)	-	-	3.2
Beta-3 (g/l)	-	-	3.3
Gamma (g/l)	-	-	12.6
CRP (mg/l)	-	2.99	-
Proteinuria (g/24h)	2.05	-	-

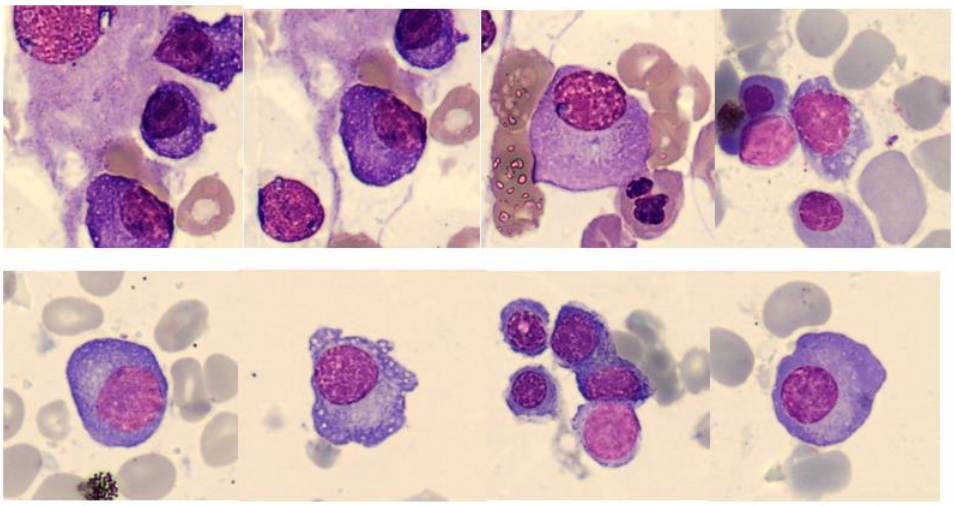

Figure 1 Medullogram showing plasma cell proliferation

5. Conclusion

SLE can be the starting point for the development of a hematological malignancy at a later stage. On the other hand, cancer can induce spontaneous autoimmune manifestations or secondary to anti-tumor therapies. In our case, a patient developed myeloma 2 years after the onset of lupus with a poor outcome leading death.

Compliance with ethical standards

Acknowledgments

All authors contributed to this work. They read and approved the final version of the manuscript. The authors would like to thank the biologist colleagues from the Aristide Le Dantec hospital for the results of the medullogram.

Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of informed consent

The informed consent of the patient's family was obtained.

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