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Case Report

# Granulomatosis With Polyangiitis as a Trigger for Acute Myeloid Leukemia

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We are presenting a case of granulomatosis with polyangiitis (GPA) triggering acute myeloid leukemia (AML).

A 38-year-old woman, without previous diseases, went to emergency department (ED) for fever, dyspnea and anosmia and she had these symptoms during the last 10 days. Chest X-ray showed consolidations in the right upper lobe and left lower lobe (Fig. 1). Also, laboratory tests revealed neutrophilia ($8.17 \times 10^9$/L) without leukocytosis or eosinophilia and as well as elevated acute phase reactants, without renal failure.

Thoracic computed tomography (CT) confirmed the radiographic findings and manifested a necrotic core in consolidation in the right upper lobe (Fig. 2A and B). Moreover, CT of paranasal sinuses evidenced extensive sinus occupation (Fig. 2C). Microbiological cultures were negative. Antineutrophil cytoplasmic antibodies with cytoplasmic pattern (c-ANCA) were positive at 1/320 titer and anti-proteinase 3 (PR3) antibodies had a concentration of 60 IU/mL (normal is less than 10 IU/mL). In addition, a fibrobronchoscopy was performed with transbronchial biopsies showing vasculitis and granulomas with fibrinoid necrosis (Fig. 2D). After obtaining 13 points of the 2022 ACR/EULAR diagnostic criteria, the diagnosis of GPA was established (score ≥5). So, induction treatment with prednisone 30 mg/24 h was started and rituximab 604 mg weekly was administered weekly for 4 weeks. After three months, the patient went to ED for asthenia presenting leukocytosis ($19.2 \times 10^9$/L) with monocytosis ($8.36 \times 10^9$/L). Peripheral blood morphology evidenced 48% of blasts confirming the diagnosis of AML.

Hematologic malignancies and ANCA-associated vasculitis (AAVs) are related. Several studies have reported the increased incidence of bladder carcinoma, AML, cutaneous squamous cell carcinoma, lung cancer, colorectal carcinoma and lymphoma in AAVs due to immunosuppression, treatment and tissue inflammation. Furthermore, AAVs may present as paraneoplastic vasculitis.[1,4]

Cyclophosphomide has been replaced by rituximab in induction and maintenance treatment of AAVs because of its dose-dependent oncogenicity (skin cancer, myeloid malignancies and bladder cancer).[2] Rituximab increases the risk of infection, produces hypogammaglobulinemia and neutropenia, but cumulative exposure does not increase the risk of malignancy.[3–5]

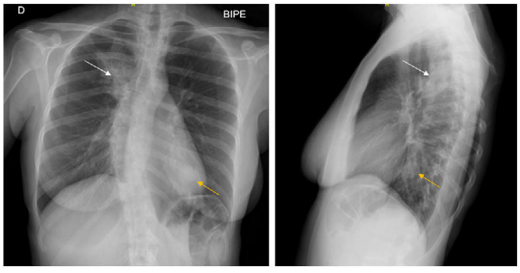


**Fig. 1.** Posteroanterior and lateral chest radiograph with consolidation in the right upper lobe (white arrow) and left lower lobe (yellow arrow).

Overall cancer risk is higher in patients with GPA than other AAVs. It can be explained by PR-3 which is an autoantigen at the crosstalk of autoimmunity and hematopoietic proliferation and is overexpressed in several hematological malignancies.[4] PR3 is the target antigen for c-ANCA and is essential for associating GPA and hematological malignancies. It is endothelially expressed on mature neutrophils and monocytes and is inhibited by alpha-1 antitrypsin. It induces endothelial apoptosis, angiogenesis, regulation of myeloid lineage differentiation and inhibition of T-lymphocyte proliferation. In hematological malignancies, there is overexpression of PR3 due to the action of G-CSF and defects in its suppression.[4,5]

The association of GPA with AML has been described in few cases in the literature, mainly in paraneoplastic vasculitis and patients treated with cyclophosphamide. In our case, the patient does not present initial alterations in the hemogram, so it is not a paraneoplastic syndrome and the AML was later, which confirms the exceptionality of the case. PR3 plays a key role in the hematological oncogenesis of GPA. The exceptional evolution presented in this case shows us the importance of close follow-up in search of hematologic malignancies in patients with AAVs.

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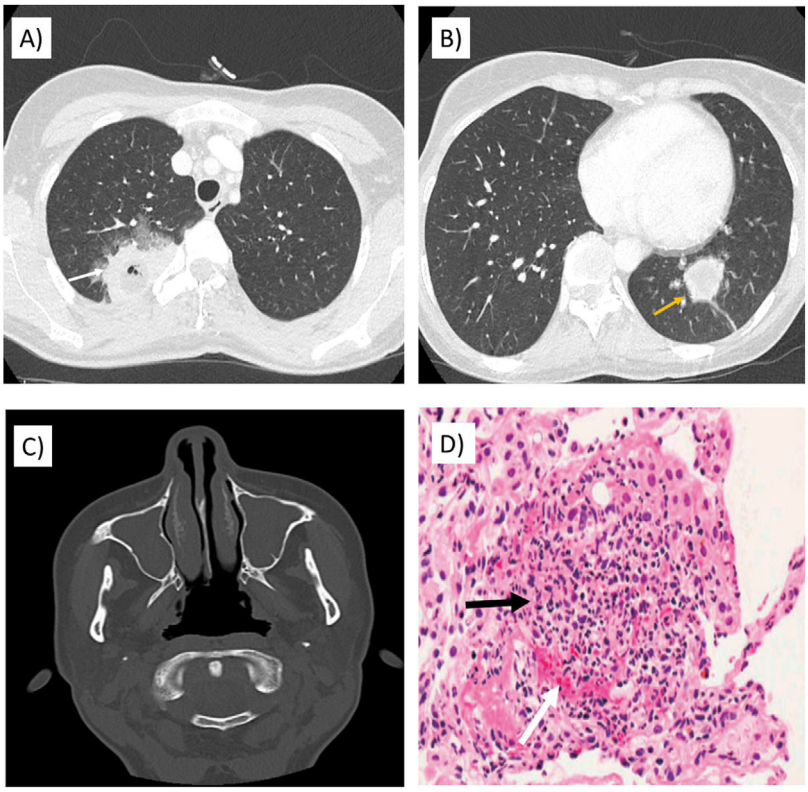


**Fig. 2.** (A) Thoracic computed tomography (CT) with consolidation in the posterior segment of the right upper lobe with necrotic core (white arrow). (B) Thoracic CT with consolidation in the medial basal segment of the left lower lobe (yellow arrow). (C) CT of paranasal sinuses with complete occupation of both maxillary sinuses. (D) Histologic section of transbronchial biopsy in posterior segment of right upper lobe with presence of lung parenchyma with air spaces replaced by inflammatory cellularity of lymphohistiocytic predominance, granuloma (black arrow) and vascular inflammation with fibrinoid necrosis (white arrow).

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## Conflict of Interests

The authors state that they have no conflict of interests.

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