WEGENER'S GRANULOMATOSIS IN A 20-YEARS-OLD WOMAN PRESENTING WITH SEVERE ODYNOPHAGIA, AND RECURENT EYE COMPLAINTS: A RARE CASE REPORT

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ABSTRACT

Wegener's granulomatosis, or granulomatosis with polyangiitis (GPA), presents a diagnostic and therapeutic challenge due to its diverse clinical manifestations. In a recent case encountered in our Emergency Department (ED), a 20-year-old female presented with a distressing seven-day history of severe odynophagia, rendering her unable to consume both solids and liquids due to the intensity of pain. This alarming symptomatology was accompanied by painful swellings over the outer part of both eyes, indicating potential ocular involvement, a recognized aspect of Wegener's granulomatosis. Further investigation revealed a positive cytoplasmic antinuclear antibody (c-ANCA) at a titre of 1:160, a pivotal immunological marker contributing to the diagnostic confirmation of the underlying autoimmune process. Nasopharyngeal biopsies undertaken in this case exhibited characteristic findings, including fibrinoid necrosis with inflammatory cell infiltration, alongside vascular abnormalities such as dilatation and bleeding. These histopathological insights into the disease's impact on the upper respiratory tract emphasized the multisystemic nature of Wegener's granulomatosis, reinforcing the need for a comprehensive and multidisciplinary approach to diagnosis and management. This clinical scenario underscores the importance of recognizing odynophagia as a potential indicator of disease activity in Wegener's granulomatosis. The integration of clinical, immunological, and histopathological findings is paramount in elucidating the complex nature of this autoimmune disorder. The positive c-ANCA titre and characteristic biopsy results provide critical information guiding appropriate therapeutic interventions and highlighting the need for vigilant monitoring of the patient's multisystem involvement. This case not only contributes to our understanding of the diverse presentations of Wegener's granulomatosis but also underscores the significance of a holistic approach in managing the complexities associated with this challenging autoimmune condition.

Keyword: - *Wegener's granulomatosis, nasopharyngeal biopsies, vascular dilatation, bleeding.*

1. INTRODUCTION

Wegener's granulomatosis is characterized by agranulomatous arteritis involving the upper and lower respiratory tracts, progressive glomerulonephritis and systemic symptoms attributable to small vessel vasculitis [1]. The clinical manifestations of vasculitides are diverse,typically, this involves the lungs or kidneys. Wegener's granulomatosis (WG) is an antineutrophil cytoplasmic antibody (ANCA)-associated small vessel vasculitides [2].

Wegener's granulomatosis, presents a formidable clinical landscape characterized by a diverse range of manifestations, each contributing to the complexity of this autoimmune disorder. Arteritis, a hallmark feature, involves inflammation of blood vessels without granuloma formation, affecting the upper and lower respiratory tracts. This inflammatory process can lead to the development of nodules, cavities, or infiltrates in the lungs, necessitating a comprehensive and nuanced approach to respiratory care [3], [4]. Pulmonary involvement, therefore, stands as a pivotal aspect of Wegener's granulomatosis, contributing significantly to the morbidity associated with the disease.

Central to the diagnostic framework of Wegener's granulomatosis is the association with antineutrophil cytoplasmic antibodies (ANCAs), with particular emphasis on the presence of proteinase 3-antineutrophil cytoplasmic antibodies (PR3-ANCA). These autoantibodies play a dual role as diagnostic markers and key contributors to the immunopathogenesis of the vasculitis observed in this disorder. The identification of PR3-ANCA not only aids in confirming the diagnosis but also opens a window into the intricate immune mechanisms that underlie the vascular inflammation characteristic of Wegener's granulomatosis [5], [6].

In addition to respiratory manifestations, Wegener's granulomatosis often involves the kidneys, leading to progressive glomerulonephritis [7]. Vigilant monitoring and therapeutic interventions are essential to mitigate the long-term organ damage associated with renal involvement. The intricate interplay between vascular inflammation and renal pathology underscores the systemic nature of this disorder, emphasizing the need for a holistic and multidisciplinary approach to patient care.

Systemic symptoms further contribute to the clinical complexity of Wegener's granulomatosis, with patients frequently experiencing fever, fatigue, and weight loss [6], [8]. These symptoms, indicative of the systemic impact of the disease, highlight the importance of addressing not only organ-specific manifestations but also the overall well-being of the affected individual. A comprehensive treatment approach should aim at alleviating symptoms, controlling inflammation, and preventing organ damage, necessitating a collaborative effort from specialists across various medical disciplines.

As our understanding of Wegener's granulomatosis continues to evolve, ongoing research endeavors strive to refine diagnostic methods and therapeutic strategies. The pursuit of targeted and personalized treatment approaches holds promise for improving outcomes and enhancing the quality of life for individuals grappling with the complexities of this autoimmune disorder. The multidimensional nature of Wegener's granulomatosis demands a continual commitment to advancing medical knowledge and clinical practice to meet the evolving challenges posed by this intricate and challenging condition.

2. CASE REPORT

A 20-year-old female presented to our Emergency Department (ED) with a seven-day history of severe odynophagia for solids and liquids, with inability to eat due to pain. she complained painful and swellings over the outer part of both eyes. The complaints have been repeated several times. Over the previous three years, she was diagnosed with Wegener Syndrome and routinely go to Hasan Sadikin Hospital in Bandung. She regulary takes prednison 45 mg once daily. There was no history of redness of eyes, blurring of vision, diplopia, dry eyes, hemoptysis, fever, oliguria, hematuria, skin rash, tingling, burning or weakness in extremities, headache, seizures or altered sensorium.

On the examination, revealed bilateral swelling diagnosed as soft tissue swelling by our ophthalmologist. There was no uveitis or retinal involvement. She looked unwell, but was hemodynamically stable and afebrile. The patient was normotensive and systemic examination was unremarkable. There were a crust covering the nasal cavity of the dextra oropharynx.

Initial laboratory studies revealed a white blood cell count of $4{,}9\times10^9$/L (4.4 to 11.0×109/L), hemoglobin level of 12,1 g/L (12,3-15,3 g/dl) and platelet level of 190×10^9/L. Blood urea nitrogen and creatinine were normal. On patient chest radiograph were normal. There were no lung involvment and cardiomegaly. Measurement of cytoplasmic antinuclear antibody (c-ANCA) was positive at a titre of 1:160. Nasopharingeal biopsies revealed fibrinoid necrosis with inflammatory cell infiltration. There were vascular dilatation and bleeding. No sign of malignancy.

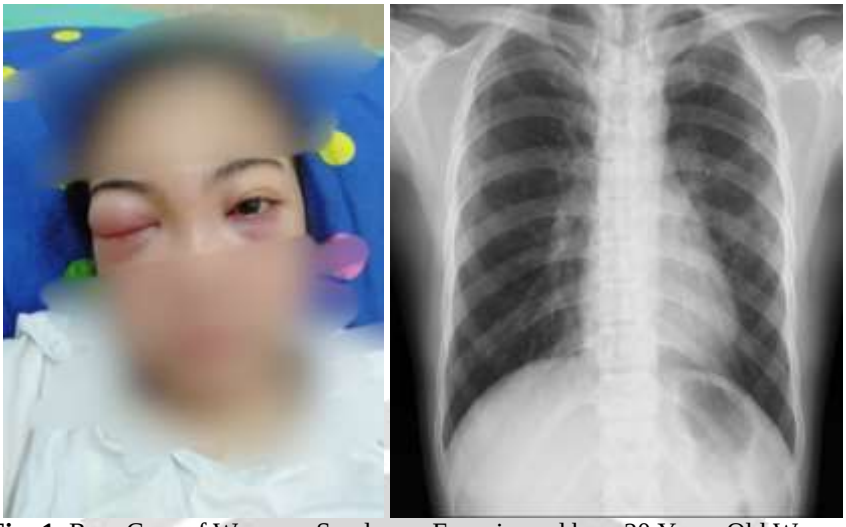

Fig -1: Rare Case of Wegener Syndrome Experienced by a 20 Years Old Woman

Wegener's granulomatosis was diagnosed on the basis of ear, nose and throat involvement (nasal ulcerations), positive c-ANCA and biopsies of a nasopharingeal biopsy showing fibrinoid necrosis with inflammatory cell infiltration. Treatment was initiated with cyclophosphamide 200 mg once daily and metylprednisolon 125 mg once daily.

3. CASE DISCUSSION

Granulomatosis with polyangiitis (GPA), formerly known as Wegener's granulomatosis, is typically considered when individuals exhibit prolonged, perplexing symptoms. The initial presentation is marked by a diverse array of nonspecific symptoms, primarily affecting the upper respiratory tract with nasal congestion, discomfort during swallowing, sinus inflammation, and structural changes in the septum, leading to the distinctive saddle nose deformity. The multifaceted nature of these symptoms underscores the complexity of diagnosing GPA, necessitating a comprehensive understanding of its varied clinical manifestations [9].

Ocular involvement in GPA is frequently characterized by inflammation of the outer eye layers, specifically scleritis and conjunctivitis. The American College of Rheumatology has established diagnostic criteria with a specificity of 92% and sensitivity of 88%. These criteria include the identification of red blood cell casts in urine sediment, abnormal findings on chest radiography, the presence of mouth ulcers or nasal secretions, and the detection of granulomatous inflammation through biopsy [10]. This stringent diagnostic framework aims to enhance the accuracy of GPA diagnosis, recognizing the diverse clinical manifestations and ensuring a comprehensive evaluation of the disease.

GPA is classified as a small-vessel vasculitis associated with antineutrophil cytoplasmic autoantibody (ANCA) positivity. The diagnostic criteria outlined by esteemed bodies such as the American College of Rheumatology (ACR) and the Chapel Hill Consensus Conference (CHCC) acknowledge the clinical diversity inherent in GPA, emphasizing that ANCA presence is not mandatory for an accurate diagnosis. The ACR and CHCC criteria emphasize a comprehensive evaluation, considering clinical manifestations, histopathological evidence, and other pertinent factors to ensure a nuanced and accurate diagnosis [11].

The diagnostic parameters specified by the American College of Rheumatology (ACR) require the fulfillment of two or more criteria, demonstrating a specificity of 92% and sensitivity of 88%. These criteria encompass diverse clinical and histopathological aspects, such as red blood cell casts in urine sediment, abnormalities in chest radiography, mouth ulcers or nasal secretions, and the presence of granulomatous inflammation identified through biopsy [10]. This meticulous diagnostic framework emphasizes a comprehensive assessment, integrating both clinical and histological evidence to enhance the precision and reliability of the GPA diagnosis.

A patient with GPA presented with a sore throat, and a nasopharyngeal biopsy revealed fibrinoid necrosis, inflammatory cell infiltration, and dilatation of blood vessels with associated bleeding. These histological findings align with characteristic features of GPA, emphasizing the importance of histopathological assessments in the diagnostic process. In the ocular domain, inflammation of the outer eye layers, including scleritis and conjunctivitis, emerged as prominent clinical indicators of GPA. This ocular involvement aligns with the systemic nature of GPA,

reinforcing the significance of integrating both clinical observations and histopathological evidence to enhance diagnostic accuracy [9].

However, it is imperative to underscore that the diagnostic criteria outlined by the American College of Rheumatology (ACR) do not mandate the presence of ANCA for a definitive diagnosis of GPA. The recognition of GPA extends beyond serological markers, acknowledging the nuanced and diverse clinical presentations that may not universally manifest with ANCA positivity [11].

The presence of ANCA, specifically proteinase 3 (PR3)-ANCA, is a characteristic feature in a significant proportion of GPA cases. Despite this association, the absence of ANCA does not exclude the possibility of GPA, emphasizing the complexity and heterogeneity of the disease. The ACR's diagnostic stance underscores a comprehensive approach that incorporates various clinical, radiological, and histopathological parameters, ensuring that the absence of ANCA does not hinder accurate identification and diagnosis of GPA [11].

Notably, ANCA presence is not pathognomonic for GPA, as it can manifest in various infectious, neoplastic, and autoimmune contexts, including inflammatory bowel disease, sclerosis cholangitis, and other rheumatological diseases. The broad spectrum of conditions associated with ANCA underscores the importance of a comprehensive diagnostic approach that integrates clinical, serological, and histopathological findings [11]. While ANCA detection can be a valuable indicator, its presence alone lacks the specificity required for an isolated GPA diagnosis. The diagnostic process necessitates careful consideration of the entire clinical context, including the patient's medical history, symptoms, imaging results, and histopathological evidence. This awareness of the multifactorial etiology of ANCA presence contributes to a more discerning diagnostic process, preventing the misattribution of ANCA-related findings to GPA in cases where other underlying conditions may be at play [11]. The clinician's astute evaluation becomes paramount in distinguishing GPA from a broader array of medical entities with overlapping serological markers, ensuring accurate diagnosis and appropriate therapeutic interventions.

4. CONCLUSIONS

Granulomatosis with polyangiitis (formerly Wegener's granulomatosis) comes under consideration typically when an individual endures prolonged and perplexing symptoms that resist straightforward explanation. The initial clinical presentation is characterized by a diverse array of symptoms, which often poses a diagnostic challenge owing to their nonspecific nature. Manifestations commonly span a spectrum of upper and lower respiratory tract issues and may extend to involve renal structures. The array of symptoms encompassing Wegener's granulomatosis reflects the systemic nature of the disease, contributing to its complexity in early detection. Respiratory symptoms, such as nasal obstruction, pain during swallowing, sinus inflammation, and potential structural changes like the formation of a saddle nose, underscore the affliction's predilection for the upper respiratory tract. Concurrently, lower respiratory tract involvement may present as cough, hemoptysis, and pulmonary infiltrates. Additionally, Wegener's granulomatosis has the propensity to affect the kidneys, leading to a range of renal manifestations. This multifaceted clinical spectrum emphasizes the importance of a comprehensive clinical evaluation when suspecting Wegener's granulomatosis, acknowledging the varied presentations that necessitate a meticulous diagnostic approach. The amalgamation of respiratory and renal symptoms underscores the systemic nature of the disease, warranting a holistic assessment to facilitate timely and accurate diagnosis, enabling prompt initiation of appropriate therapeutic interventions.

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