TEMPI Syndrome: Disease Progression and Response to Treatment

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Learning Objectives

- Raise awareness among clinicians for this particularly rare disorder
- Understand disease progression and highlight response to treatment over the span of approximately 10 years
- Describe proposed pathophysiology of TEMPI syndrome

Introduction

TEMPI syndrome, characterized by telangiectasias, erythrocytosis and elevated erythropoietin, monoclonal gammopathy, perinephric fluids collections, and intrapulmonary shunting was only recently first described in 2011. To our knowledge, there are fewer than 15 reported cases worldwide.

Case Description

A 58-year-old male with a diagnosis of TEMPI syndrome was admitted for acute worsening of chronic hypoxia. In 2009, the patient was diagnosed with polycythemia vera. Two years later, he began to have a clinical constellation of hypoxemia, mild clubbing, and telangiectasias. The patient had evidence of intrapulmonary shunting on nuclear perfusion study, IgG kappa monoclonal gammopathy, and bilateral peri-renal fluid collections on CT scan, supporting a diagnosis of TEMPI syndrome.

In 2012, the patient was trialed on separate therapies of bortezomib and lenalidomide, both without sustained clinical response. While on daratumumab therapy, monoclonal protein levels and erythropoietin level improved. However, intrapulmonary shunt increased from 40% to 56% and daratumumab was discontinued.

In 2019, treatment with autologous stem cell transplantation was considered, but later deemed too risky of treatment. His chronic hypoxemia continued to worsen, requiring multiple hospitalizations. Unfortunately, the patient succumbed to his disease due to a rapidly declining hypoxemic respiratory failure.

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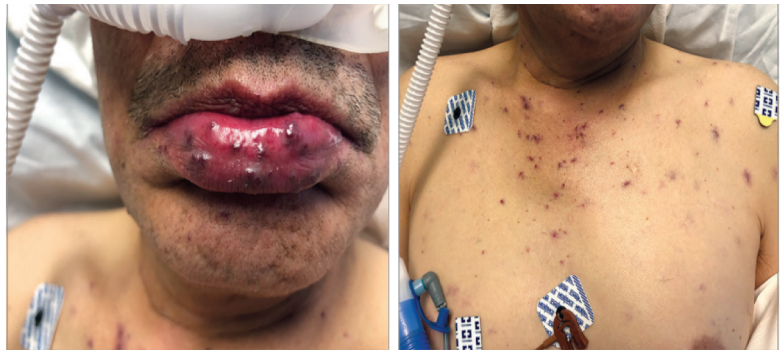

Figure I: Mucocutaneous manifestations of TEMPI syndrome (A) lower lip telangiectasias (B) scattered skin telangiectasias over the chest[6]

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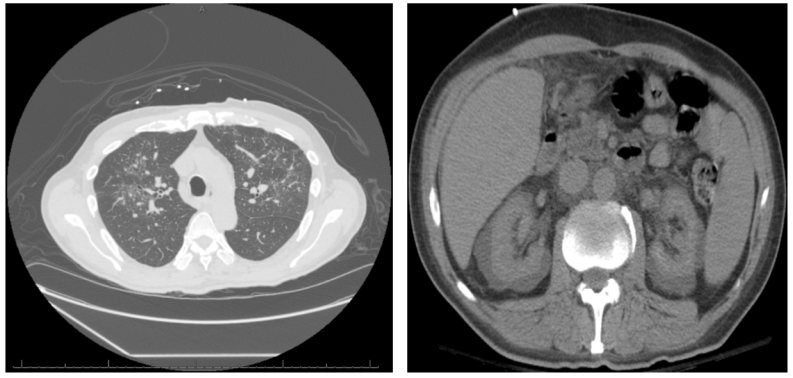

Figure II: CT Chest (2019) with persistent areas of reticulation and ground glass opacities bilaterally, related to intrapulmonary shunting

Figure III: CT Abdomen, Pelvis (2019) with small, moderate bilateral perinephric fluid

Discussion

According to the reported cases, the disease affects middle-aged males across all ethnic groups and countries. Erythrocytosis as the first presenting. symptom, as seen in our patient, seems to be a common motif[1].

In our patient, erythrocytosis was followed by evidence of slight hypoxemia and then monoclonal gammopathy. Intrapulmonary shunting, perinephric abscess and telangiectasia were later discovered.

It has been hypothesized that plasma cell dyscrasia plays a causative role given marked improvement of symptoms in a patient who was treated with bortezomib[2]. Similarly, treatment with anti-CD 38 monoclonal antibody, daratumumab, yielded complete resolution of symptoms in two patients providing an additional support for this theory[3].

Conversely, it has been theorized that inhibition of hypoxia-inducible factor-1 alpha (Hif-1a) and down-stream transcription of vascular endothelial growth factor rather than apoptosis of malignant plasma cells may explain the reversal of symptoms with bortezomib since it affects the function of Hif-1a[4,5].

However, the exact pathophysiology of TEMPI syndrome remains uncertain.

Conclusion

The treatments above did not result in reversal of the syndrome, in contrast to previously reported cases. Further studies are needed to determine the underlying pathophysiology and whether these therapies improve survival.

References

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