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Chronic myelogenous leukemia: a case report from Azal hospital, Sana'a, Yemen

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ABSTRACT

Chronic myelogenous leukemia (CML) is a myeloproliferative disorder that is always associated with the presence of the BCR-ABL gene. In this article, we report the case of a 38 years old male patient who presented with fever, fatigability, abdominal pain, and blurred vision. Investigations confirmed CML with leukemoid retinal hemorrhage and anemia. The patient was immediately administered imatinib 400 mg daily for two weeks and then hydroxyurea (500 mg daily) was add. After 4 months, the white blood cells, hemoglobin, and basophils returned to normal values, retinal hemorrhages improved, and the patient's general health improved.

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1. INTRODUCTION

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm caused by a reciprocal translocation [t(9;22)(q34;q11.2)] that leads to the fusion of ABL1 gene sequences (9q34) downstream of the BCR gene sequence (22q11) and is cytogenetically visible on the Philadelphia chromosome (Ph) [1]. Chronic myeloid leukemia (CML) is a chronic myeloproliferative stem cell disorder that results in the proliferation of all hematopoietic lineages but manifests prominently in the granulocytic series. Cell maturation proceeds fairly normally. Tyrosine kinase inhibitors (TKI) have changed the natural history of CML [2]. In less than 10 years, the prognosis of chronic myeloid leukemia has changed from that of a fatal disease to a disorder amenable to lifelong oral medication, and is compatible with a normal lifespan [3]. Chronic myeloid leukemia (CML) has been a "model disease" with a long history. It begins with the first discovery of leukemia and the description of the Philadelphia Chromosome and ends with the current goal of achieving treatment-free remission after targeted therapies [4]. In comparison to imatinib, second-generation inhibitors

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used as first-line treatment lead to faster and deeper molecular remissions accompanied by different adverse event profiles [5]. Over the past two decades, TKI have become the foundation of CML treatment. The choice between imatinib and newer TKIs needs to be balanced against the known toxicity and efficacy data for each drug [6]. Clinical trials have demonstrated that CML patients treated with TKI who achieved and maintained deep molecular responses could discontinue their treatment after several years without facing overt signs of disease relapse [7]. Patients diagnosed with chronic myelogenous leukemia (CML) in chronic phase can now have a life expectancy comparable to that of the general population thanks to the use of tyrosine kinase inhibitor (TKI) therapies [8, 9]. Small molecule inhibitors and monoclonal antibodies directed at relevant cancer-related proteins have been instrumental in delivering successful treatments of some blood malignancies, such as imatinib with CML, tamoxifen with ER-positive breast cancer, and trastuzumab for HER2-positive breast cancer [10].

2. CASE PRESENTATION

A 38 years old male presented to the internal medicine clinic of our hospital with complaints of abdominal pain, dyspepsia, anorexia, nausea, fatigue, low-grade fever, and sweating. In addition, the patient had blurred vision. He had an unknown case of any medical illness. Physical examination revealed tachycardia (128 beats per minute) and low-grade fever; otherwise, the patient was normal. The patient confirmed that these symptoms had started after 2 weeks. Like most male Yemenis, he is a khat chewer, but a nonsmoker. A full blood count (FBC) showed white blood corpuscles (WBCs) 342000, anemia: hemoglobin (Hb) 9.5, neutrophilia: 78.7%, lymphopenia: 6.3%, and basophilia: 7.2%, but normal platelets: 316000. Blood film tests in two different laboratories showed blast cells of approximately 4% and commented on a case of CML. The renal and hepatic functions were normal. Ophthalmological examination revealed a retinal hemorrhage, as shown in figures 1 and 2. The patient refused to undergo bone marrow aspiration and a BCR-ABL1 genetic test was not performed. The patient was diagnosed with chronic chronic stage. Imatinib was initiated at a dose of 400 mg daily, followed by hydroxyurea (500 mg daily). FBC was measured frequently, as shown in the table; WBC, basophils, and hemoglobin all improved dramatically. Abdominal pain, dyspepsia, anorexia, nausea, fatigue, low-grade fever, and sweating improved. In addition, he claimed that his vision had improved. The patient's overall status generally improved. We asked the patient to repeat an ophthalmological examination, but like many Yemeni patients, he stopped attending after his health improved.

Date	$WBC * 10^{5}$	Basophils%	Haemoglobin g/dl
01-Oct-23	342.9	7.2	9.5
17-Oct-23	130.4	12.1	10.6
23-Oct23	38.05	9	10.8
28-Oct23	13.97	7	12.7
4-Nov23	16.3	3.1	13.3
11-Nov23	31.44	1.2	13
28-Jun23	9.96	0.9	15.6

Result table showing WBC count, basophils concentration and haemoglobin in our patient with continuous administration of imatinib and hydroxyurea.

3. DISCUSSION

Imatinib was first used for the treatment of CML in 2008 [11]. This is one of the major success stories in modern cancer medicine. Moreover, it was the first tyrosine kinase inhibitor to be used [12]. Since then, more than 70 protein have been approved [13]. Imatinib and three second-generation TKIs (bosutinib, dasatinib, and nilotinib) are the first-line therapies for CML in the chronic phase (CML-CP) [14]. At the beginning of the diagno-





Figure 1. Retinal haemorrhage.



Figure 2. Retinal haemorrhage report.



sis, we attempted to assure our patient; however, he reacted with anxiety and phobia. However, at every visit, we let him know of his improvement in investigations, which were reflected in his mood. After 4 months, his CBC was within the normal range, and his symptoms markedly improved. Moreover, he claimed that his vision had improved. At this stage, the patient disappeared. We attempted to contact him to repeat ophthalmological examination. After 4 months from his last visit, exactly in the 3rd of June, 2024, the patient came to perform the CBC test, unfortunately he showed the following results WBC 179.09, neutrophils 91.3% and basophils 1.2%. Moreover, he confessed cessation of treatment in the last 4 months. We asked the patient to resume treatment with imatinib (400 mg/day) and hydroxyurea (500 mg/day).

4. **DISCUSSION**

Imatinib was first used for CML in 2008 [11]. It is one of the major success stories of modern cancer medicine. Moreover, it is the first tyrosine kinase inhibitor to be used [12]. Since then more than 70 protein kinase inhibitors were approved [13]. Imatinib and the three second-generation TKIs (bosutinib, dasatinib and nilotinib) are the frontline therapy of CML in the chronic phase (CML-CP), [14]. In the beginning of diagnosis, we tried to assure our patient, however he reacted with anxiety and phobia. But in every visit we let him to know his improvement in investigations, which were reflected on his mood. After 4 months his CBC is within normal range, his symptoms were markedly improved. Moreover, he claimed improvement in his vision. At this stage the patient disappeared. We tried to contact him to repeat ophthalmological examination. After 4 months from his last visit, exactly in the 3rd of June, 2024, the patient came to perform the CBC test, unfortunately he showed the following results WBC 179.09, neutrophils 91.3% and basophils 1.2%. Moreover, he confessed cessation of treatment the last 4 months. We asked him to resume treatment with Imatinib 400 mg/d and hydroxyurea 500 mg/d.

5. CONCLUSION

CML is a dangerous malignant disease and should be diagnosed early for a good prognosis. Protein kinase inhibitors are the cardinal treatment in this case. The addition of hydroxyurea improves response. It seems

HUMAN ETHICS

Consent was obtained from our patient in this study.

that long-term treatment with these two drugs prevents relapse.

REFERENCES

- Afaf EG Osman and Michael W Deininger. "Chronic Myeloid Leukemia: Modern therapies, current challenges and future directions". In: *Blood reviews* 49 (2021), p. 100825. URL: doi:doi:%2010.1016/j.blre.2021.100825.
- [2] Jorge Cortes, Carolina Pavlovsky, and Susanne Saußele. "Chronic myeloid leukaemia". In: *The Lancet* 398.10314 (2021), pp. 1914–1926. URL: doi:doi:%2010.1016/S0140-6736(21)01204-6.
- [3] Jane F Apperley. "Chronic myeloid leukaemia". In: *The Lancet* 385.9976 (2015), pp. 1447–1459. URL: doi:10.1016/ S0140-6736(13)62120-0.
- [4] Valentina R Minciacchi, Rahul Kumar, and Daniela S Krause. "Chronic myeloid leukemia: a model disease of the past, present and future". In: *Cells* 10.1 (2021), p. 117. URL: doi: 10.3390/cells10010117.
- [5] Dominik Heim, Monika Ebnöther, and Geneviève Favre. "Chronic myeloid leukemia-update 2020". In: *Ther. Umschau. Revue therapeutique* 76.9 (2019), pp. 503–509. URL: doi: 10.1024/0040-5930/a001124.
- [6] Naranie Shanmuganathan, Devendra Keshaorao Hiwase, and David Morrall Ross. "Treatment of chronic myeloid leukemia: assessing risk, monitoring response, and optimizing outcome". In: *Leuk. & lymphoma* 58.12 (2017), pp. 2799– 2810. URL: doi:10.1080/10428194.2017.1312377.
- [7] Delphine Rea and Jean-Michel Cayuela. "Treatment-free remission in patients with chronic myeloid leukemia". In: *Int. journal hematology* 108 (2018), pp. 355–364. URL: doi: 10.1007/s12185-017-2295-0.
- [8] Delphine Rea and Jean-Michel Cayuela. "Treatment-free remission in patients with chronic myeloid leukemia". In: *Int. journal hematology* 108 (2018), pp. 355–364. URL: doi: 10.1007/s12185-022-03446-1.
- [9] Massimo Breccia et al. "Measuring prognosis in chronic myeloid leukemia: what's new?" In: *Expert Rev. Hematol.* 14.6 (2021), pp. 577–585. URL: doi:10.1080/17474086.2021. 1938534.
- [10] Hon Yan Kelvin Yip and Antonella Papa. "Signaling pathways in cancer: therapeutic targets, combinatorial treatments, and new developments". In: *Cells* 10.3 (2021), p. 659. URL: doi: 10.3390/cells10030659.
- [11] Simone Claudiani and Jane F Apperley. "The argument for using imatinib in CML". In: *Hematol. 2014, Am. Soc. Hematol. Educ. Program Book* 2018.1 (2018), pp. 161–167. URL: doi:doi:10.1182/asheducation-2018.1.161.
- [12] Lillian R Klug et al. "New treatment strategies for advancedstage gastrointestinal stromal tumours". In: *Nat. reviews Clin. oncology* 19.5 (2022), pp. 328–341. URL: doi:10.1038/ s41571-022-00606-4.
- [13] Philip Cohen, Darren Cross, and Pasi A Jänne. "Kinase drug discovery 20 years after imatinib: progress and future directions". In: *Nat. reviews drug discovery* 20.7 (2021), pp. 551–569. URL: doi:10.1038/s41573-021-00195-4.
- [14] Jayastu Senapati et al. "Management of chronic myeloid leukemia in 2023–common ground and common sense". In: *Blood cancer journal* 13.1 (2023), p. 58. URL: doi:10.1038/ s41408-023-00823-9.