DISCUSSION

This is the first case of e13a3 BCR-ABL fusion variant to be reported from India. The most recent meta-analysis by Baccarani et al. 2019 puts emphasis on the fusion RNA variant. According to Baccarini et al, transcript identity is a variable which may assist in fine tuning the already successful treatment strategy of CML. Each fusion RNA gives rise to a different tyrosine kinase that may have a significant impact on the disease biology. Knowledge of the transcript type rules out any ambiguity when following a patient through therapy or in filling gaps in treatment strategy. Among the rare BCR-ABL fusion transcripts, e13a3 occurs in overall 9% cases. Interestingly, the 'a3 variants' without the a2 exon is higher in males than in females. Indian population data on rare BCR-ABL fusion variants is scant and needs a systematic approach. One study by Arun et al. 2016 reported the incidence of rare transcript variants in 1260 patients with 0.3 % carrying the e14a3 variant and none carrying e13a3. The biological significance of the 'a3 variants' is unclear, as the absence of exon 2 leads to deletion of the N terminal of SH3 domain of the tyrosine kinase protein ; resulting in a possible aggressive leaukomogenesis or the opposite, reduction of activating signal. Current evidence leans towards better prognosis for patients carrying e13a3 variant. Our patient suffered through an aggressive disease form and whether carrying the e13a3 BCR-ABL fusion variant was the cause or it would have been a beneficial feature for targeted therapy would remain an enigma.

CONCLUSION

The above case study highlights the importance of a comprehensive analysis and the use of multiple techniques such as flow cytometry, cytogenetics, qRT- PCR and sequencing for the identification of rare variants which occur at a very low frequency. In this particular case, if we had not performed cytogenetic analysis, the RT-PCR would be reporting a false negative for the patient leading to a missed diagnosis. Given the rarity of such case reports in India, adding to literature could directly benefit the evidence based management of CML