The Double Jeopardy of Leukemia and Dengue: A Report of Three Cases
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Abstract:
Dengue is predominantly a self-limiting illness. The association of dengue with new onset of leukemia has been rarely reported. We describe herein a series of three patients diagnosed with acute lymphoblastic leukemia, chronic myeloid leukemia, and acute promyelocytic leukemia who presented with concurrent dengue infection at a tertiary care institute in the southwestern coastal region of India. In spite of the different types of leukemias, we observed similar trends in their blood parameters, which were comparable with those of nonleukemic dengue patients. The transfusion profile of each of these patients is described. We could conclude that even in the presence of leukemia, dengue tends to be self-limited. No such comparative case reports have been published so far, and with an increasing incidence of dengue in the world, the occurrence of the two might not remain a remote possibility.

Keywords:
Dengue, leukemia, lymphoblastic, myeloid, promyelocytic

Introduction
Dengue has become ubiquitous with the World Health Organization, estimating 3.9 billion individuals at risk.[1,2]

Classical dengue is a self-limiting disease. The risk of dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) is the highest. During days 2 to 10 of illness, and this period is considered critical. Synchronous diagnoses of dengue and leukemia are rarely reported; hence, the effect of one on another remains unexplored.[3,4]

Case Reports
Case 1
A 32-year-old male presented with fever of 5 days, melena, hepatosplenomegaly, and petechial rashes. The patient tested positive for immunoglobulin M (IgM) and IgG anti-dengue using the enzyme-linked immunosorbent assay. A diagnosis of DHF was considered. Laboratory investigations on the day of admission (Day 6) and subsequent days are presented in Table 1. Peripheral blood smear examination (PBSE) later in the day revealed atypical lymphocytes as well as 31% blasts. The diagnosis of acute lymphoblastic leukemia (ALL) was confirmed by flow cytometry. Serum transaminase levels were mildly elevated. The patient received eight units of random donor platelets (RDP) on the day of admission (day 6) and 2 units RDP on day 16 and required no further transfusions throughout the induction phase of chemotherapy.

Case 2
A 61-year-old female presented with a fever of 5 days duration and had massive splenomegaly. Investigations on the day of admission and up to a week thereafter are represented in Table 2. PBSE showed the features consistent with chronic myeloid leukemia (CML) which was confirmed by the presence of P210 transcript. The patient...
became afebrile on day 10. She went on to have an unexceptional course during the treatment.

**Case 3**
A 54-year-old male presented with excessive bleeding following tooth extraction. On the day of the presentation, the patient was seronegative for dengue. Hematological investigations throughout his admission are presented in Table 3. PBSE on the day of admission revealed leukoerythroblastic picture with 10% atypical cells. A diagnosis of acute promyelocytic leukemia (APML) was confirmed by the detection of PML/Rara transcript. He was started on arsenic trioxide on day 8 of admission and developed fever on day 11 (day 1 of illness). Fever continued unabated for 4 days. On day 8 of illness, he developed abdominal pain, acute breathlessness, and fall in blood pressure. Liver dysfunction became evident. The patient developed ascites and pleural effusion both of which are features of Dengue Shock Syndrome. The diagnosis of DSS was however not thought of until the patient developed marked refractory thrombocytopenia and repeat test for dengue turned out to be positive. Prothrombin time and activated thromboplastin time and D-Dimer assays remained normal despite low fibrinogen levels. The patient died on the very same day.

**Discussion**
Anemia, thrombocytopenia, leukopenia/leukocytosis with fever, and bleeding manifestations are the elements encountered in leukemias and dengue and can present a diagnostic dilemma.

The molecular pathogenesis of ALL, CML, and APML are different. However, during dengue, they showed similar trends in blood parameters. In all three cases, a gradual drop in white cell count (WCC) and platelet count (PC) was noted after 4–6 days of illness [Figures 1 and 2], i.e., during the critical period and the fall in PC was

### Table 1: Hematological parameters of Case 1 from day 6 to day 13

| Day | Tr (units) | Hct (%) | Hb (g %) | WCC (x10⁹/L) | Plt (x10⁹/l) | Bl (%) |
|-----|------------|---------|----------|--------------|--------------|-------|
| 6   | 8 RDP      | 33.5    | 11.1     | 11           | 9            | 31    |
| 7   |            | 28.1    | 9.5      | 4.9          | 55           | 36    |
| 8   |            | 26.4    | 8.9      | 5            | 38           | 35    |
| 9   |            | 27.5    | 9.2      | 8.4          | 38           | 20    |
| 10  |            | 27.9    | 9.2      | 44.2         | 28           | 71    |
| 11  |            | 24.6    | 8.2      | 88.8         | 25           | 79    |
| 12  |            | 20.5    | 7.7      | 89.5         | 20           | 80    |
| 13  |            | 6.6     | 6.7      | 19.9         | 18           | 28    |

Day=Day of illness; Tr=Transfusion profile; Hct=Hematocrit; Hb=Hemoglobin; WCC=White cell count; Plt=Platelet count; Bl=Blast percentage; RDP=Random donor

### Table 2: Case 2 hematological parameters of Case 2 from day 6 to day 12

| Day | Tr (units) | Hct (%) | Hb (g %) | WCC (x10⁹/L) | Plt (x10⁹/l) | Bl (%) |
|-----|------------|---------|----------|--------------|--------------|-------|
| 6   |            | 30.8    | 10       | 45.8         | 407          |       |
| 7   |            | 29.3    | 9.5      | 39.1         | 338          | 5     |
| 8   |            | 32.2    | 10.1     | 41.9         | 361          | 5     |
| 9   |            | 29      | 9.7      | 39.2         | 320          | 4     |
| 10  |            | 29.5    | 9.3      | 40.7         | 330          | 7     |
| 11  |            | 29.2    | 9.3      | 49.2         | 354          | 5     |
| 12  |            | 28.9    | 9.3      | 53.2         | 365          | 7     |

Day=Day of illness; Tr=Transfusion profile; Hct=Hematocrit; Hb=Hemoglobin; WCC=White cell count; Plt=Platelet count; Bl=Blast percentage; RDP=Random donor

### Table 3: Laboratory parameters of Case 3

| Day | Tr (units) | Hct (%) | Hb (g %) | WCC (x10⁹/L) | Plt (x10⁹/l) | Bl (%) |
|-----|------------|---------|----------|--------------|--------------|-------|
| 2PRB | 12.8      | 4.5     | 1.9      | 24           |
| 4RDP | 25.2      | 9       | 3.3      | 33           |
| 22.9 | 8.1       | 3.1     | 26       | 11           |
| 8.7  | 2.2       | 23      | 12       |
| 3RDPF  | 7.9 | 2     | 17       |
| 3FFP | 21.6      | 7.7     | 3.3      | 25           |
| 19.6 | 6.7       | 3.7     | 33       |
| 2CRY | 25.1      | 8.8     | 5.6      | 39           |
| 4RDP | 25.2      | 8.8     | 3.9      | 15           |
| 2PRBC | 22.3   | 7.7     | 3.4      | 36           |
| 2PRB | 20.6      | 7.3     | 4.2      | 28           |
| 2CRY | 20.8      | 7.1     | 11       | 36           |
| 2PRB | 23.4      | 8       | 16.2     | 40           |
| 4RDP | 26        | 8.7     | 13.3     | 9            |
| 2PRB | 24.9      | 8.5     | 10.7     | 10           |
| 4RDP | 21.2      | 7.3     | 8.4      | 7            |
| 2CRY | 22.8      | 7.8     | 9.4      | 19           |

Day=Day of illness; Tr=Transfusion profile; Hct=Hematocrit; Hb=Hemoglobin; WCC=White cell count; Plt=Platelet count; Bl=Blast percentage; PRBC=Packed red blood cells; RDP=Random donor platelet; FFP=Fresh-frozen plasma; CRY=Cryoprecipitate
consistent despite RDP transfusion in cases 1 and 3. The trends of WCC and PC observed here are very similar to those of nonleukemic dengue patients observed by Chaloemwong et al. [5]

The interesting phenomenon in fall of blast counts which in all three cases hit nadir on day 9 rather confirms the marrow suppressive nature of dengue [Figure 3].

Hemoglobin and hematocrit paralleled each other and at no point showed a warning sign of DHF or DSS. Elevated transaminase levels which is a strong predictor for DSS was seen only in case 3. [6] Garcia et al. reported refractoriness of the PC in acute myeloid leukemia with dengue. Our observation was similar in Case 3. Commencement of chemotherapy after hematological recovery from dengue (critical period) in Case 1 might be the cause of why he required lesser number of transfusions as opposed to Case 3. Furthermore, in APML, loss of the promyelocytic-leukemia-gene product, which is an important restriction factor against dengue viruses, may have blunted the host defense [7]

**Conclusion**

Dengue must be tested for in patients with leukemia who have cytopenia that are unresponsive to transfusion. Blood parameters irrespective of the type of leukemia show comparable trends during dengue episodes. The critical period for dengue is during 4–10 days of illness, and prompt diagnosis of both diseases with supportive treatment determine the outcome.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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