Platelet transfusion refractoriness (PTR), in which platelet counts do not increase after transfusion, occurs in many patients who receive platelet transfusions. PTR is a clinical condition that may fatally harm patients. The causes of PTR can be divided into two types: immune and non-immune. Most causes of PTR are non-immune. Among immune causes, the most common etiology is human leukocyte antigen (HLA) class I molecules. PTR caused by anti-HLA antibodies is usually managed by transfusing HLA-matched platelet units. Therefore, it is important, especially for hemato-oncologists who frequently perform transfusion, to accurately diagnose whether the cause of platelet transfusion failure is due to alloimmune or non-immunological causes when determining the treatment direction for the patient. In this review, we cover the definitions, causes, countermeasures, and prevention methods of PTR.