INTRODUCTION
Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are associated with short-term therapy with phenytoin, phenobarbital, and carbamazepine. The association with valproic acid seems to be confounded by concomitant short-term therapy with other causal agents. The period of increased risk is largely confined to the first 8 weeks of treatment.1,4 SJS and the related disease TEN are life-threatening reactions of the skin to particular types of medication.2,3 The purpose of this case report is to highlight a phenytoin-induced TEN case in an intensive care unit in Turkey.

CASE REPORT
A 59 years old male patient was suffering from cerebral haemorrhage presented toxic epidermal necrolysis following phenytoin intake. He had diabetes mellitus, hypertension, chronic obstructive pulmonary disease, coronary artery disease, and a history of previous coronary artery bypass grafting. He was operated for middle cerebral artery M1 segment aneurysm, after operation, he was admitted into the intensive care unit. He was mechanically ventilated in the intensive care. Phenytoin therapy was started after the operation because of tonic-clonic seizures. Eighteen hours after the initiation of phenytoin treatment, maculopapular exanthema emerged on the skin of upper thoracal region. It spread out to whole trunk, limbs and face. It covered over 50% of the body surface area in 10 minutes. Nikolsky's sign became positive. On the 5th day, the appearance of skin lesions turned into giant bullae. Ocular, oral and genital mucosa erosions developed, leaving upper layer of skin in the remainder areas as red. His vital signs were: blood pressure 56/29 mmHg, heart rate 123 beats/minute, respiration rate 28/minute and body temperature was 39°C. Laboratory results revealed a white blood cell count of 1,700/mm³ (neutrophils 18.4%, lymphocytes 44%, eosinophils 18.2); a platelet count of 97,000/mm³; an erythrocyte sedimentation rate of 69 mm/ after first hour; a serum C-reactive protein concentration of 20 mg/dl; serum aspartate aminotransferase and alanine aminotransferase concentrations of 92 U/l and 110 U/l, respectively; a blood urea concentration of 221 mg/dl; a serum creatinine concentration of 2.27 mg/dl; serum sodium and potassium concentrations of 137 mEq/l and 4.9 mEq/l, respectively; a total protein serum concentration of 4.6 g/dl; and a serum albumin concentration of 1.8 g/dl. Skin biopsy was harvested two times at 7 days intervals and histopathological examination revealed dense dermal infiltration, basal vacuolar change, subepidermal bullae, lymphocytes, eosinophils and neutrophils were present (Figures 1 - 4).

High-resolution sequence-based HLA typing HLA-A*3101. Bilateral diffuse pulmonary infiltrates appeared on chest radiography. He also had purulent respiratory secretion. Multi-drug resistant Acinetobacter baumannii was isolated from endotracheal aspirate, blood and skin. Antibiotic susceptibility testing results revealed that the bacteria was sensitive to colistin. Although the patient was treated with colistin, methylprednisolone, intravenous immunoglobulin, fluids, topical antibiotics as well as the debridement of necrotic areas surgically, he died on the 9th day after the appearance of skin lesion.
DISCUSSION

There were extensive epidermal detachment, superinfection, alteration of immunologic functions, hematologic abnormalities and visceral involvement in this case. To a specific Score for TEN (SCORTEN) of the case is evaluated at admission day.3 His SCORTEN value was 7. The hospital mortality rate is approximately 80%.4 Ventilator-Associated Pneumonia (VAP) due to a multi-drug resistant Acinetobacter baumannii is one of the most lethal complications, which is associated with an increased lenght of stay in the intensive care unit. Various underlying conditions like head injury, cerebral hemorrhage and chronic obstructive pulmonary disease were found to be associated with Acinetobacter VAP.5,6 In this case, the existence of the cerebral hemorrhage, chronic obstructive pulmonary disease, diabetes mellitus, long-term mechanical ventilation and hospital nosocomial outbreak of Acinetobacter may contribute to VAP.

There is a strong association between HLA-B*1502 allele and carbamazepine-induced Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS-TEN) in the Han Chinese populations.7 Human Leukocyte Antigen (HLA) allele, HLA-A*3101, which has a prevalence of 2 - 5% in Northern European populations, was significantly associated with the hypersensitivity syndrome. The presence of the HLA-A*3101 allele was associated with carbamazepine-induced hypersensitivity reactions among subjects of Northern European ancestry. The presence of the HLA-A*3101 allele increased the risk from 5.0% to 26.0%, whereas its absence reduced the risk from 5.0% to 3.8%.5,9 The presence of the HLA-A*3101 allele was associated with the hypersensitivity syndrome (P=3.5 x 10^-9), which has a prevalence of 2 - 5% in Northern European populations. An independent genomewide association study of samples from subjects with maculopapular exanthema also showed an association with the HLA-A*3101 allele (P=1.1 x 10^-9). Follow-up genotyping confirmed the variant as a risk factor for the hypersensitivity syndrome (odds ratio, 12.41; 95% confidence interval [CI], 1.27 - 121.03), maculopapular exanthema (odds ratio, 8.33; 95% CI, 3.59 - 19.36), and SJS/TEN (odds ratio, 25.93; 95% CI, 4.93 - 116.18) of TEN is 25 - 35%; it can be even higher in elderly patients and those with a large surface area of epidermal detachment.9,10

Before starting treatment with anticonvulsants patients should be screened for HLA alleles, so that the medication of anticonvulsants could be individualized. If HLA screening for HLA alleles became common, phenytoin associated SJS/TEN incidence might be reduced.

REFERENCES


