Surgical excision led to complete resolution without any topical antifungal therapy and no recurrence was noted till 1 year of follow-up.

DISCUSSION

Ocular mycoses in children are commonly seen in the form of fungal keratitis or keratoconjunctivitis, and most can be attributed to an exogenous source with an antecedent history of trauma, surgery or use of topical steroids.[1,2] Even though fungi have been isolated from healthy conjunctival sacs, with a reported incidence of 2.9%–27.4% across various age groups, their frequency is found to be much lower (0.8%–2%) between 0 and 9 years of age.[3–5] Mycotic flora of healthy ocular surface is mainly considered as transient aerial contaminants that can act as potential pathogens in the presence of altered tissue resistance. *Aspergillus* is a common mould present in the environment and has been reported to be the most commonly isolated fungus from eyes with no pre-existing diseases.[5] In the presence of predisposing factors such as trauma and immunosuppressed states, *Aspergillus* species can cause a wide array of sight-threatening ocular infections (e.g. keratitis, endophthalmitis, scleritis and orbital cellulitis). Chen *et al*. reported a case of conjunctival aspergilloma presenting as chronic refractory conjunctivitis in an immunocompetent woman and proposed opportunistic subconjunctival seeding of the fungus as the factor responsible.[6] We suspect a similar causal factor in our case. Tropical/subtropical countries with higher temperature and humidity have increased rates of fungal isolation, and contamination of external eye can occur more frequently during summer and harvesting season when more fungal spores are present in the environment. Arora and Tyagi reported that in India, a majority of the fungal infections were in agricultural workers.[5]

In our patient, the exact inciting cause for the fungal conjunctivitis could not be determined, but he was at an increased risk of developing the infection secondary to environmental factors. Coming from a rural area of a tropical country and agricultural background, the chance of exposure to fungal contaminants was high and even accidental rubbing of the eye could have been responsible for subconjunctival seeding and eventual development of aspergillosis. The presence of multiseptate filamentous hyphae on silver methenamine stain helped in providing a definitive diagnosis. Hence, we believe that this report will increase awareness for general practitioners to keep in mind the rare but possible differential diagnosis of conjunctival aspergillosis besides other more common causes of a conjunctival mass in a child.

To the best of our knowledge, this is the first report in a child of conjunctival aspergillosis presenting as a pedunculated polyp which was adequately managed by surgical excision without the need for antifungal therapy.

Conflicts of interest. None declared

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Severe autoimmune-mediated thrombocytopenia in an elderly woman

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ABSTRACT

The efficacy of immunotherapies that use antibodies to block programmed cell death 1 (PD-1) has been extensively investigated for lung cancer. Along with reactivation of the patient's immune response to tumour cells, immune-related adverse effects with anti-PD1 therapy have been reported. We report an 80-year-old woman who had suffered from a primary lung adenocarcinoma pre-treated with pembrolizumab and was admitted to our hospital with serious autoimmune-mediated thrombocytopenia induced by pembrolizumab.

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INTRODUCTION

The efficacy of immunotherapies that use antibodies to block programmed cell death 1 (PD-1) has been extensively investigated for advanced/metastatic non-small cell lung cancer (NSCLC). Monoclonal antibodies that block PD-1 provide substantial benefit, prolonging both progression-free and overall survival. However, along with reactivation of the patient's immune response to tumour cells, immune-related adverse effects (iRAEs) with anti-PD1 therapy have been reported.[1] Haematological iRAEs have been described occasionally. These include immune thrombocytopenia, autoimmune haemolytic anaemia, agranulocytosis or pure red-cell aplasia.[2,3] Severe forms of autoimmune-mediated thrombocytopenia have been reported rarely.

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THE CASE

An 80-year-old woman who was diagnosed with primary lung adenocarcinoma (pT1bN2M1a, stage IVA) under treatment with pembrolizumab (Keytruda, on day 11 after initiating pembrolizumab infusion) was admitted to our hospital with severe thrombocytopenia. She had been previously diagnosed with old myocardial infarction and hypertension, without a history of autoimmune or coagulation disorders. Prior to treatment with pembrolizumab, the platelet count was 203×10^9/L. On admission, the bone marrow aspirate done in another hospital revealed normal plasticity with no obvious morphological abnormalities, phagocytosis or malignant invasion. The number of megakaryocytes was 68 cells/ml. Although megakaryocyte numbers were maintained, the cells were relatively small and immature, and platelets infrequently adhered to them. Laboratory testing showed a platelet count of 13×10^9/L, white blood cell count of 6.09×10^9/L, haemoglobin 9.8 g/dl, prothrombin time 14.6 seconds and international normalized ratio of 1.14. On examination, the patient had purpuric rash on the trunk and both upper limbs. She received intravenous immunoglobulin 10 g/day for 3 days, methylprednisolone 80 mg/day for 20 days, thrombopoietin-receptor agonist 15 000 μ/day, for 20 days and 10 units of platelets (Fig. 1). The patient had no improvement in the platelet count. Three days after administration of the immunoglobulin, the patient developed acute left heart failure and progressive decrease of blood pressure and was unable to tolerate rituximab treatment.

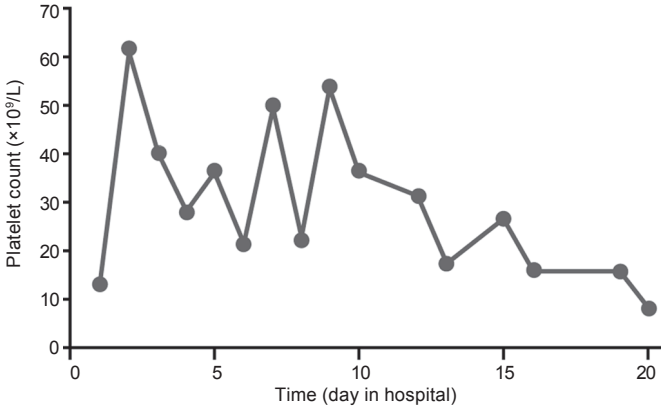

FIG 1. Changes in platelet count during hospitalization.

DISCUSSION

Programmed cell death 1/PD-L1 inhibitors have revolutionized the treatment of malignancies. However, they can trigger various iRAEs, such as interstitial pneumonitis, colitis with gastrointestinal perforation, type 1 diabetes, severe skin reactions, immune thrombocytopenia (ITP), neutropenia and sepsis after corticosteroid therapy, encephalopathy and neurological sequelae, Guillain–Barré syndrome, myelitis, myasthenia gravis, myocarditis and cardiac insufficiency, acute adrenal insufficiency and nephritis.[4]

Immune thrombocytopenia is acquired thrombocytopenia caused by autoantibody and T cell-mediated platelet destruction and impairment of thrombopoiesis. For patients with NSCLC, PD-1/PD-L1 inhibitors are generally safer and better tolerated than cytotoxic chemotherapy, though a 0.7% incidence of thrombocytopenia has been reported.[5] In a retrospective chart review of 2360 patients with melanoma treated with immune checkpoint inhibitors, <1% experienced thrombocytopenia, and of these, most showed spontaneous resolution and did not require treatment.[6]

In our patient, thrombocytopenia developed shortly after initiating systemic therapy with pembrolizumab, and infusion of platelets, glucocorticoids, gamma globulin and recombinant human thrombopoietin was not effective. In some instances, therapy with pembrolizumab aggravated thrombocytopenia and induced or increased the production of platelet-specific IgG autoantibodies. Due to the clinical course and the laboratory results, it is likely that thrombocytopenia was caused by PD-1 inhibitor-induced platelet autoantibodies through autoimmune activation.

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Conflicts of interest. None declared

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