Rare disease

Severe obstructive sleep apnoea due to adenotonsillar hypertrophy after liver transplantation

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Summary

Epstein-Barr virus-related adenotonsillar hypertrophy is a precursor to post-transplantation lymphoproliferative disorder. We report a case of a 4-year-old child with severe obstructive sleep apnoea, who had liver transplantation at the age of 7 months. She had gross lymphoid hypertrophy in the oropharynx and supraglottis. We performed an adenotonsillectomy and aryepiglottoplasty which improved her symptoms. We emphasise the importance to consider the diagnosis of post-transplantation lymphoproliferative disorder in post-transplantation immunosuppressed patients who present with adenotonsillar hypertrophy.

BACKGROUND

Post-transplantation lymphoproliferative disorder (PTLD) is an important cause of mortality and morbidity after solid organ transplantation.^{1 2} In the paediatric population, PTLD may present with signs and symptoms of adenotonsillar enlargement. The diagnosis of PTLD should be considered in immunosuppressed paediatric patients who present with adenotonsillar hypertrophy.

In one UK study, the incidence of adenotonsillar hypertrophy in liver transplant recipients was 28%³ as compared with 2–3% in normal paediatric population.⁴ Young age and Epstein-Barr virus (EBV) seronegativity seem to confer increased risk of adenotonsillar hypertrophy in paediatric patients undergoing solid organ transplants.⁵ The main reservoir for replicating virus is the epithelial cell of the Waldeyer ring.⁶ There is strong evidence to suggest that the donor organ is often the source of primary EBV infection.⁷

CASE PRESENTATION

A 4-year-old girl was referred for ear, nose and throat (ENT) opinion in view of mouth breathing, sleep disturbance and upper airway noises. She had liver transplantation at the age of 7 months for haemangioendotheloma type 1. She was on long-term immunosuppression with tacrolimus and prednisolone.

On examination, she appeared generally well but was grossly mouth breathing and had severe fissured cheilitis (figure 1). She was also noted to have mildly enlarged lymph nodes in axillary, inguinal and submandibular regions in addition to quite marked tonsillar hypertrophy. Her chest was clear and abdomen was soft with palpable spleen tip. She had no severe infections in the past. She had been fully immunised. She was found to be allergic to bananas recently. There was no family history of atopy or autoimmune diseases.

INVESTIGATIONS

On investigation, her full blood count and liver function test was normal and autoimmune profile was negative.

Her EBV immunoglobulins G was positive and EBV Immunoglobulins M was negative. Her EBV PCR levels ran between 150 and 250×10⁵ copies/ml.

Sleep study covering 6 h of sleep revealed severe obstructive sleep apnoea (OSA). Her mean SpO₂ was about 79.43% throughout the study. The lowest SpO₂ recorded was 34%. The average desaturations (>4%) were 112 times/h for an average period of 14 s and a maximum of 87 s. Her apnoea hypopnoea index was 32. Her respiratory arousal index was 6.3/h and respiratory rate was in the order of 45–55 breaths/min. Her mean PCO₂ during the study was 5.73 kPa and the maximum was as high as 10.13. These results suggested that the airway obstruction was severe enough to result in respiratory failure.

DIFFERENTIAL DIAGNOSIS

A range of nasal and pharyngeal airway obstruction may contribute to OSA.⁴

Oropharyngeal causes include enlarged tonsils, retrognathia, macroglossia and glossoptosis. Nasal and

Figure 1 Fissured cheilitis.

Figure 2 Enlarged tonsils.

nasopharyngeal causes include rhinitis, enlarged adenoids, septal deviation and nasopharyngeal masses such as tumour and lymphoma (as was suspected in this case).

Systemic diseases known to cause OSA include cerebral palsy, sickle cell disease, glycogen storage diseases and achondroplasia. Downs, Prader-Willi, Treacher-Collins, Apert and Crouzon's are all syndromic causes of OSA.

TREATMENT

In view of her significant sleep apnoea, she was listed for adenotonsillectomy with a planned postoperative paediatric intensive care unit (PICU) bed. Examination under anaesthetic confirmed that she had fissuring of her lips and a soft palate. She had enlarged adenoids, Grade 3 tonsillar hypertrophy (figure 2), hypertrophy of the tongue and massive hypertrophy of the lymphoid tissue of tongue base (figure 3) and supraglottis (figure 4). Adenotonsillectomy was performed and sent for histopathology to rule out lymphoma. Multiple biopsies were taken from tongue base, buccal mucosa and supraglottis. Unilateral limited aryepiglottoplasty was also performed to improve the airway. Postoperatively, she was sent intubated to the paediatric intensive care unit. She was extubated 24 h later and her postoperative recovery was uneventful. She was discharged from hospital the next day.

Figure 3 Tongue-base lymphoid hypertrophy.

Figure 4 Hypertrophied mucosa over arytenoids.

OUTCOME AND FOLLOW-UP

On a follow-up visit, her mother reported a remarkable improvement in her sleeping pattern at night. The histopathology of the specimens was reported as active chronic inflammation and lymphoid hypertrophy. There was no evidence of EBV on immunocytochemistry and no evidence of lymphoma.

DISCUSSION

There are few reports of severe OSA related to PTLD although solid organ transplantation can lead to lymphoid tissue hypertrophy.⁸

Rombaix *et al*⁹ have described two patients with EBV-driven PTLD who presented with stridor. In both cases, the enlarged lymphoid tissue decreased dramatically with a rapid reduction in immunosuppression and consequently the recovering of a natural immune response against EBV infection.⁹

EB virus-related lymphoid hypertrophy may first present as adenotonsillar enlargement. The role of EB virus in the development of PTLD is not unknown.^{8–10} Nearly 90% of cases of PTLD are triggered by primary EB virus infection.⁷ The use of potent immunosuppressants after transplantation has led to an increase in the incidence of PTLD.^{7–10} EB virus infects B lymphocytes and causes polyclonal activation and proliferation. In immunosuppressed patients, the T-lymphocyte response is limited and EB virus-induced polyclonal B-cell proliferation may proceed unchecked.

Those patients who are seronegative for EBV at the time of transplantation with EBV seropositive donors are at a high risk of developing PTLD. In the presence of immunosuppression, these patients are more likely to develop a primary EB virus infection from the donor organ.⁸ Adenotonsillar tissue is a potential site for EB virus-related lymphoid hypertrophy.

A 2010 review of tonsillectomy for PTLD patients has shown tonsillar hypertrophy, male gender and young age at transplantation are associated with higher rates of PTLD and these risk factors should be borne in mind when assessing possible patients.¹¹ Shapiro *et al*¹² echo these findings and confirm younger patients and EBV seronegativity confer increased risk for adenotonsillar

hypertrophy in paediatric patients who have undergone solid organ transplantation.

As the prevalence of EB virus-related tonsillar hypertrophy is high in post-transplant patients, even asymptomatic adenotonsillar enlargement in these patients must be addressed aggressively and investigated.^{8 13 14} A Miami study has shown flow cytometry to be the most effective diagnostic modality in the evaluation of PTLD.¹³

There is no agreed gold-standard treatment or guideline for managing PTLD; however, the few cases that are described have all performed adenotonsillectomy followed by reduction of immunosuppressant.^{11–15} This was the treatment modality employed for our patient with success. We urge a multidisciplinary discussion between ENT surgeons, paediatricians and the transplant team with the eventual outcome of surgery and immunosuppressant reduction.

Learning points

- ▶ Post-transplantation lymphoproliferative disorder is an important cause of mortality and morbidity after solid organ transplantation.
- ▶ Epstein-Barr virus-related adenotonsillar hypertrophy is a precursor to post-transplantation lymphoproliferative disorder.
- ▶ It is important to consider the diagnosis of post-transplantation lymphoproliferative disorder in post-transplantation immunosuppressed patients who present with adenotonsillar hypertrophy.

Competing interests None.

Patient consent Obtained.

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