Microscopic Findings of Sheet-Type Collagen Applied to Air Leaks after Pulmonary Resection

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Purpose: It has been reported that Integran®, a sheet-type absorbable topical collagen hemostat, is feasible for preventing pulmonary fistula after lung surgery. The most favorable aspect of Integran® is that it contains no blood products. However, the microscopic findings of post-surgery application of Integran® to the lung are not known. We identified 2 such cases of Integran® application, which were carried out a few years earlier, and described the microscopic findings.

Method: In case 1, a 53-year-old man underwent video-assisted left upper lobectomy for primary lung cancer. Integran® was applied to the left lower lobe. Completion left pneumonectomy was performed after 2 years and 1 month due to recurrence. In case 2, a 77-year-old woman underwent video-assisted right middle lobectomy for primary lung cancer. Integran® was applied to the right upper lobe. Completion right upper lobectomy was performed after 1 year and 8 months due to recurrence.

Results: The repaired visceral pleura of the 2 patients were covered with proliferated collagen fibers. However, there was little infiltration of inflammatory cells and fibroblasts.

Conclusion: The microscopic findings revealed that the ability of Integran® to generate inflammation or adhesion is weak, but it has the ability to repair damaged visceral pleura.

Keywords: air leak, sheet-type collagen, Integran®, sealant, lung surgery

Introduction

Various sealants for air leaks after pulmonary resection have been reported.1–3) A bioabsorbable polyglycolic acid (PGA) mesh sheet soaked in fibrin glue is one of the most prevalent sealants. However, the most unfavorable aspect of this sealant is that the fibrin glue is derived from blood products. Miyamoto et al. reported that Integran® (Integran®, Nippon Zoki Pharmaceutical Co. Ltd., Osaka, Japan, and KOKEN Co. Ltd., Tokyo, Japan), a sheet-type absorbable topical collagen hemostat, was feasible for preventing pulmonary fistula after lung surgery.4) However, the microscopic findings of lung tissue to which Integran® was applied are not known. We have identified 2 cases, in which Integran® had been applied to the visceral pleura a few years prior, and describe the microscopic findings of these specimens.

Materials and Methods

In case 1, a 53-year-old man underwent video-assisted left upper lobectomy for primary lung cancer. Integran® (100 × 50 mm and 0.2-mm thick) was divided into 6 pieces and applied to the left lower lobe. Completion of a left pneumonectomy was performed after 2 years and 1 month due to the recurrence of lung cancer, and a lung specimen, to which Integran® had been applied, was obtained.
In case 2, a 77-year-old woman underwent video-assisted right middle lobectomy for primary lung cancer. Integran® was applied to the right upper lobe. Completion right upper lobectomy was performed after 1 year and 8 months due to recurrence. We obtained a specimen of the lung to which Integran® had been applied.

In both cases, the sites to which Integran® had been applied were identified by reviewing the video recording of their earlier operation.

**Results**

In case 1, adhesion was not found between the parietal and visceral pleura but was present at the hilum of lung.

In case 2, adhesion was not detected between the parietal and visceral pleura. The visceral pleura to which Integran® had been applied appeared white and thickened. Membranous adhesion was observed in the surrounding area.

The microscopic findings from the specimens, with and without Integran®, are illustrated in Figs. 2 and 3. In both cases, the visceral pleura to which Integran® had been applied were covered with proliferated collagen fibers. However, there was little infiltration of inflammatory cells and fibroblasts.

**Discussion**

The raw material used to produce Integran® is atelocollagen derived from the dermis of Australian calves by enzyme solubilization and purification. The product contains no protein other than atelocollagen; therefore, it has low antigenicity. The purified atelocollagen is subjected to spinning and chemical cross-linking using a polyepoxy compound to convert it into an insoluble and physically stable fiber. It is commonly used as a hemostat in the medical field. Miyamoto et al. reported that the use of Integran® was feasible for preventing pulmonary fistula after lung surgery.

When we carry out reoperations, we sometimes find severe adhesion in the area to which a PGA mesh sheet had been applied. Nakamura et al. reported the microscopic findings of PGA sheets that had been applied to the lungs 4 weeks earlier. According to their report, there was robust adhesion between the parietal and visceral pleurae that required a pleurectomy for lobectomy. However, in reoperation where Integran® had been applied earlier, we found that the adhesion generated by Integran® was gentle in comparison to that of a PGA mesh sheet soaked in fibrin glue. Okubo et al. reported that cotton-type collagen insertion at mediastinoscopy for lung cancer separated the mediastinal nodes from the trachea and made the node dissection easier. Hexig et al. reported that cytotoxicity was detected for oxidized...
cellulose (Surgicel®) and microfibrillar collagen (Avitene®), but not for Integran®. The biocompatibility of Integran® was good.7)

The ability of Integran® to be used as a sealant is believed to be as follows. Integran® that is applied to the damaged visceral pleura absorbs blood, swells, and adheres closely to the damaged visceral pleura. Thereafter, Integran® contributes to repair of the damaged visceral pleura. However, Integran® causes little infiltration of inflammatory cells and fibroblasts. As the result, adhesion generated by Integran® itself is gentle. Incidentally, the earlier operations for the present 2 cases were carried out under video-assisted thoracic surgery, so adhesion between the parietal and visceral pleura were not generated. Severe adhesion is not required for sealants. Furthermore, severe adhesion makes reoperation difficult.5) One of the useful aspects of Integran® is that it contains no blood products. Another useful feature is that the ability of Integran® to generate inflammation or adhesion is weak. However, Integran® is able to repair damaged visceral pleura. We believe that these characteristics of Integran® make it favorable for use as a sealant after pulmonary resection.
Conclusion

The microscopic findings revealed that the ability of Integran® to generate inflammation or adhesion is weak, but it has the ability to repair damaged visceral pleura.

Disclosure Statement

The authors declare no conflicts of interest.

References