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Fish Skin for Burns

The annual burn incidence rate in the US is approximately half a million people, including 40,000 hospitalizations as a result of burn-related injuries and 3400 deaths. The main treatment for deep dermal and full thickness burn injury is early excision and coverage with autologous split skin grafting or flaps. This avoids common complications like sepsis, multi-organ failure, and acute kidney injury.

When the wound is extensive, availability of autologous skin becomes a problem, and allogenic and xenogeneic skin for temporary coverage after excision will be needed. A variety of dressings are currently available for superficial partial-thickness burns such as silver-impregnated, alginate, hydrocolloid, hydrogel, silicone-coated nylon, polyurethane film, or biosynthetic dressings without a gold standard being defined.

As a matter of review, autografts are skin grafts that are transferred from the same person with the wound but a different healthy location, allografts are skin grafts transferred from a different person used as a donor (cadaver), and xenografts are transferred from an animal such as pigs, cattle, or fish. Xenografts are termed cellular and/or tissue-based products.

Human cadaver and pig skin are the major source of temporary coverage for deep and full thickness burn injury. Application of human and pig skin grafts carries a risk of auto-immune response along with a risk of viral and bacterial disease transmission. Skin from a cadaver has a limited supply and is expensive.

An alternative for grafting extensive areas of burned skin is using acellular fish skin (xenograft). Acellular fish skin has been described as effective, safe, efficient skin substitute free of the risk of transmission of viral disease and auto-immune reactions. Acellular fish skin has also been utilized with success in the healing process of acute and chronic wounds like diabetic foot ulcers and non-healing leg wounds.

The most exceptional property of acellular fish skin grafts that makes it efficacious is its lipid profile. Fish skin is rich in Omega-3 polyunsaturated fatty acids, eicosatetraenoic acid, and docosahexaenoic acid, which are highly effective as antimicrobial agents even against methicillin-resistant Staphylococcus aureus, and in modulating the inflammatory response of the acute wound healing stage.

Fish skin maintains its three-dimensional structure and is highly porous, providing an extracellular matrix composed of glycosaminoglycans, proteoglycans, fibronectin, and

growth factors which allows the migration of autologous cells to promote the proliferative and epithelialization phases of the burn healing process.

Acellular fish skin grafts are also very porous, having about 16.7 large diameter apertures for every 100 µmm allowing it to properly adhere to human skin and promote the passage of human fibroblasts, which are known to play an important role in effective wound healing.

Fish skin is stored at room temperature, has a shelf life of three years, and is marketed as an off-the-shelf product. This characteristic makes fish skin ideal in the setting of combat casualties where cadaver or pig skin is not practical due to the short shelf life.

The fish graft contracts slightly after salination and insertion into the wound bed, so it is recommended that pre-wetting takes place before the product is applied so that shrinkage occurs before applying it to the burn patient. Acellular fish skin graft is harvested from two major species such as the Nile Tilapia or the North Atlantic cod.

Applications for the use of fish skin graft include burn skin reconstruction, chronic and oral wound, hernia repair, breast reconstruction, and dura mater reconstruction. Acellular fish skin presents an effective treatment option in burn management since studies indicate accelerated wound healing, pain, and discomfort reduction, decrease in necessary dressing changes, as well as treatment-related costs.

The novel approach of acellular fish skin xenografts may represent an effective, low-cost alternative for the management of deep and full thickness burns since existing evidence indicates accelerated wound healing, reduction of pain and necessary dressing changes, as well as improved long-term outcomes. Wounds managed with fish skin graft have better functionality long-term and aesthetically superior when compared with those managed using other cellular tissue-based products.

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PICA

The term Pica is derived from a brown-billed magpie bird, famous for its habit of indiscriminate gathering and eating a variety of objects to satisfy its hunger and curiosity. In the medical argot, Pica refers to the persistent, compulsive craving for and the ingestion of substances usually considered inedible.

The behavior of a patient with Pica is discordant with cultural practices and continuous beyond the normal developmental phase of occasional indiscriminate and experimental mouthing and swallowing over a period of at least one month. Pica occurs worldwide with a prevalence greatest in children eighteen months to six years. It is more common in blacks than whites and more common in boys than girls.

20-30% of all children from one to six years of age have practiced Pica. In the USA, less than 10% of children older than 12 years of age meet the diagnostic criteria for Pica. Pica is more common than generally appreciated, with prevalence higher in Africa compared to the rest of the world. It is also more common among low socioeconomic level children and pregnant women.

Among the etiology and pathogenesis of Pica are hunger, disturbance in the mother-child relationship, relief of anxiety by oral gratification, and an infantile hand-to-mouth behavioral response to family stress or as an expression of oral fixation. Others believe it is an attention-seeking device. Pica is common in mentally handicapped children, and the prevalence correlates with the severity of mental retardation. It is also more common in those with autistic spectrum disorder, attention deficit, schizophrenia, obsessive-compulsive disorder, and depression.

There is an association between Pica and iron deficiency. Children with sickle cell anemia are at greater risk for developing Pica. Children with Pica are highly selective, and the ingested material depends on the availability in the environment as well as conscious selection factors. Substances that may be craved by children with Pica include clay (geophagia), raw starch, dirt, ice, raw potatoes, hair (trichophagia), fibrous plant roots, sand, pebbles, glass, soap, feces (coprophagia), vomitus, and the list goes on. By far, the most common are clay and raw starch.

In the majority of cases, the physical exam is normal. Other signs of Pica include pallor, anemia, anorexia, easily fatigability, malnourishment, developmental delay, abdominal discomfort, or pain if large quantities of inedible substances are ingested. Bezoars may lead to intestinal obstruction needing surgical evaluation.

General labs are indicated, including blood lead levels, along with simple abdominal films looking for filling defects or radio-opaque material in the gastrointestinal tract. Complications depend on the substance ingested. Ferrous deficiency anemia is a common complication since the binding of the ingested clay to the iron causes an inability to be absorbed properly. This is particularly important in pregnant women after geophagia.

Pica is a risk factor for accidental ingestion of toxic substances such as lead in pencils and toys. Malnutrition results from Pica. Other electrolyte abnormalities identified in children with Pica include zinc deficiency, hypokalemia, hyperkalemia, hyperphosphatemia, and metabolic alkalosis. Other complications include parasitic infestation, tooth abrasion, constipation, and bowel obstruction. Complications from bowel obstruction and perforation from masses of consumed matter in the stomach and intestine might need surgical intervention.

There is no gold standard for the management of Pica. Management of Pica includes training and supervision while eating, attention to individual emotional needs and stress, behavioral therapy, family counseling, and psychotherapy.

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Rhabdoid Tumors

Rhabdoid tumors (RT) are rare and highly aggressive malignant tumors of embryonal origin typically diagnosed in early childhood. Initially diagnosed in 1978 as a RT of the kidney, subsequent cases identified tumors with similar histology in soft tissue and central nervous system (CNS). In 1995 an atypical teratoid/rhabdoid tumor was described in the CNS. RT are often diagnosed in late stages carrying a poor prognosis.

These tumors are known for being particularly aggressive and fast-growing. The three most common site for RT are the kidney, CNS, and soft tissue (Extrarenal). Frequent sites for extrarenal RT include skin, liver, and lung, although tumors in almost all soft tissue have been reported. Peak incidence of RT is between one and 4 years of age. Classic RT have been diagnosed also in adults.

Atypical teratoid/rhabdoid tumor (AT/RT) is a rare and aggressive type of embryonal tumor of the CNS occurring in children. AT/RT represent brain tumor in early childhood, which is the most common CNS primary malignant tumor in children less than 6 months of age. Spinal AR/RT has the following characteristics: children has cauda equina syndrome (lower back pain, muscle weakness and numbness in the lower limbs, loss of sensation in the saddle area, bladder and bowel dysfunction, and sexual dysfunction), the mass invaded the thoracolumbar spinal junction, and the extramedullary space of multiple segments grew along the spinal longitudinal axis; bleeding mass was revealed in MRI imaging; meninges, nerve root, and sacral canal metastases occurred.

The gold standard for the definitive diagnosis of AT/RT is biopsy combined with immunohistochemistry. The loss or inactivation of the SMARCB1/hSNF5/INI tumor suppressor gene has been identified as the hallmark genetic defect in RT. This mutation can arise somatically or more commonly inherited in the germline (> 35% of tumors). Loss of expression of this protein permitted the development of an immunohistochemistry assay that help make the clinical diagnosis of RT. RT are associated with a high rate of low birthweight and preterm birth, with a higher likelihood of later gestational age. A large number of multiple birth and twin pregnancy among case families with RT has been identified.

Histologically RT contains characteristic filamentous cytoplasmic inclusions, large nucleoli, and abundant eosinophilic cytoplasm. A variety of neural, epithelial, mesenchymal, or ependymal patterns may also be present. CNS RT comprise rhabdoid cells and areas of primitive neuroepithelial tissue resembling primitive neuroectodermal tumor. The cell of origin of RT is a primitive stem cell possibly derived from the neural crest.

Symptoms depend on the location of the tumor. Kidney tumors may cause a mass or swelling in the abdomen, while brain tumors can cause increased head size, developmental delays, or symptoms related to increased pressure in the brain. Diagnosis typically involves imaging studies like MRI or CT scans, followed by a biopsy to confirm the type of tumor. Brain and spine imaging studies should always be performed in newly diagnosed children with renal or extrarenal RT.

Management of RT include a combination of surgery, chemotherapy, and radiotherapy. The approach depends on the size, location, and extent of the tumor, as well as the age and overall health of the child. There are slight differences in management between COG, Dana Farber, and the European consortium mostly regarding induction chemotherapy and consolidation therapy. The early use of radiotherapy is controversial in young patients due to side effects of irradiating the spine.

The prognosis for selected patients, in particular those with localized RT associated with an older age and lower stage disease has improved somewhat, though the overall outcomes of RT remain poor despite maximized therapy intensity needing better targeted novel therapy largely focused on the biology of SMARCB1. RT has been found to be sensitive to the protein-translation inhibitor Homoharringtonine which could have a therapeutic potential.

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