Mesothelioma: What's New?

Introduction

Second revision of the scientific literature on malignant pleural mesothelioma (MPM).

What new discoveries, studies and research protocols have been developed during the last few months?

How is research progressing on mesothelioma, a subject close to our hearts?

PubMed, the free access database containing articles, references, abstracts, revisions, etc., about science and medicine, serves as the definitive starting point for this new revision.

We therefore consulted all the scientific literature published between January 1 and June 30, 2013.

Under the general topic of "Mesothelioma", we found the following for this period:

- 345 total publications
- By filtering the search to studies conducted in humans only, we narrowed it down to 75 studies during the last 6 months (not bad for a disease considered "rare" by some!)

Our revision does not claim to be a scientific review, but it offers patients, their families and general practitioners a concise idea of the latest scientific research on mesothelioma. This is not a critical analysis of individual articles, rather it is a recent snapshot of the most well-known scientific bibliography in the world. People who would like more detailed information can delve further into the topics by reviewing the references provided at the end of this short revision.

Diagnosis

Various research groups are looking for new biomarkers that can be used to diagnose MPM.

For example, claudin-4 is a protein involved in cellular junctions and is considered a useful immunohistochemical biomarker to distinguish between epithelioid mesothelioma and carcinoma metastases[i].

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Another biomarker being studied is BAP1, which is a deubiquitylase involved in the cellular cycle, gluconeogenesis, response to DNA damage, cellular differentiation and cell death. Researchers have discovered that a germline mutation of BAP1 may be associated with a "syndrome" that causes melanoma in young people and may lead to the development of mesothelioma, uveal and cutaneous melanoma, and perhaps other neoplasms in older people[ii]. Other noteworthy mesothelioma[iii] biomarkers currently under investigation include fibulin [iv v vi], PTEN[vii], GLUT, MCT-1 and MCT-4 [viii], IMP3[ix].

New technologies and methods are currently being defined for earlier and better identification of this disease[x], others could be developed in addition to those already existing to provide further information[xi].

Mesothelioma must be differentiated from other benign diseases such as fibrous pleuritis. Several researchers are focusing on this topic and have evaluated a biomarker that could distinguish between these two diseases[xii].

The distinction between mesothelioma and lung cancer is also important, especially because it leads to different treatment approaches; this topic is also being studied[xiii].

In addition to biomarkers, we must not forget the importance of differential diagnosis[xiv] and an accurate case history to determine the possibility of environmental exposure[xv xvi xvii xviii xix] so we can arrive at the most accurate and early diagnosis possible.

Therapy

Notwithstanding the increased survival rate obtained through multimodal therapy based on a combination of surgery and chemotherapy, we need new treatments to further improve the results.

With this in mind, new therapeutic approaches are appearing on the horizon for the treatment of MPM.

Several researchers have investigated the administration chemotherapy or other agents directly into the thoracic or pleural cavity[xx xxi xxii]. Effective results have not yet been obtained, however.

There have been a few case reports of spontaneous remission after intratumoral lymphocytic infiltration, which have increased the median survival rate.

Based on these reports, several researchers are investigating the results further. For example, studies on immunotherapeutic approaches for MPM are underway with the aim of obtaining better results than those offered by standard therapy[xxiii].

Various studies have shown that patients who develop post-operative empyema after pulmonary resection have an improved survival rate.

Based on this data, we can hypothesize about the importance of the immune system against the tumor and the need to find drugs that can increase the immune response against cancer[xxiv xxv xxvi].

Various studies have investigated the intrapleural injection of Calmette-Guerin bacillus as an adjuvant to surgery, but significant clinical benefits have not yet been obtained[xxvii].

Various studies have investigated the systemic administration of immunotherapy such as interleukin and interferon gamma. However, the results thus far have been no more effective than current therapy and it is important to evaluate the side effects to determine the risk versus the benefit of these treatments[xxviii xxix].

Several researchers have analyzed the possibility of administering immunostimulant cytokines into the intrapleural cavity to treat MPM. Their research has shown a significant tumoral response using both IL2 and IFN gamma. The treatment seems more effective in patients with early stage MPM and these results could be truly promising[xxx xxxi xxxii xxxiii xxxiv].

The search for an adequate, effective treatment for MPM continues and new methods for novel, more effective and less toxic approaches are under investigation.

Gene therapy and new, emerging technologies in particular are examining the use of “transfer” genes to potentially transport cancer drugs. Gene vectors have been researched in clinical and preclinical studies and are characterized by complex liposomes/DNA or modified viruses, including herpes, vaccinia and adenoviruses[xxxv xxxvi].

The results from these studies have been mixed and need further research, but they are promising and offer much hope for the future.

Several researchers[xxxvii] have documented a dose-dependent response to intrapleural administration. The case of two “long surviving” patients whose disease stabilized after 6 months was reported a few years later[xxxviii]. Also reported[xxxix] were complete responses to the treatment, partial responses and stable disease evaluations after therapy[xl xli xlii xliii].

There has been much discussion about “suicide gene therapy” and “cytokine gene therapy”.

“Suicide gene therapy” is a treatment characterized by the transduction of tumor cells with a gene codifying for an enzyme that induces sensitivity to the chemotherapy drugs normally used. In other words, a prodrug is transformed into a toxic metabolite by introducing an enzyme into the malignant cells, resulting in the death or suicide of the tumor cells[xliv xlv xlvi xlvii xlviii xlix l].

The rationale behind “cytokine gene therapy” is the fact that activated tumor cells cause the release of many immunostimulatory cytokines, which in turn leads to an immune response against cancer[li lii liii liv].

Local administration of these cytokines could certainly avoid the side effects that have been documented with systemic administration[lv lvi lvii lviii lix].

All these new treatments have led to improved patient survival and quality of life than in the past. New studies will certainly help offer patients new hope for the future.

Conclusions

This is the latest news on the scientific research being conducted to find new treatments for MPM. We must emphasize that these clinical studies need further investigation and more data before they can be translated into clinical practice.

Nonetheless, guidelines for the diagnosis and treatment of this disease are being used on a daily basis. Continual congresses and conferences allow physicians to remain up-to-date and exchange information about new scientific achievements. For example, recommendations on total MPM patient care were published following the "Second Italian consensus conference on malignant pleural mesothelioma"[lx].

We therefore propose that MPM patients consult clinical centers dedicated to this disease in order to receive care that is personalized and focused on the patient rather than just the disease, in the knowledge that there is an answer to the question posed at the beginning of this article: are scholars, scientists and researchers making progress in their work? Are they focusing on a subject that is close to our hearts? Are they studying mesothelioma?

The answer is yes.

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