

Osteonecrosis of the jaw (ONJ) in patients treated with Bisphosphonates (BP): the experience of the "Rete Oncologica di Piemonte e Valle D'Aosta" (North-Western Italy)



Discovery of a New Disease

"If you think you've discovered a new disease, you probably haven't reviewed the literature thoroughly enough." (Anonymous)

The Three Stages of a Scientific Theory

Stage 1: It is scoffed at and met with disbelief.

Stage 2: It is accepted as true but insignificant and trivial.

Stage 3: It is thought to be correct and even revolutionary. In fact, those who criticized it most now claim that they invented it and are the experts.
(Anonymous)

(Cited by Robert E. Marx, "Oral & Intravenous Bisphosphonate-Induced Osteonecrosis of the Jaws", Quintessence Books, 2007)

Background

Bisphosphonates (BPs) are very useful drugs for treatment of myeloma, metastatic bone cancers, osteoporosis, Paget's bone disease.

Reports of cases of ONJ in cancer patients (pts) treated with BPs, mainly with Pamidronate (P) and Zoledronic Acid (Z), are increasing since 2003. Other cases have been signalled after long-term oral BPs.

"Frequency" of ONJ in case series ranged between <1% and >12% of cancer patients treated with BPs.

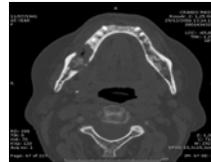
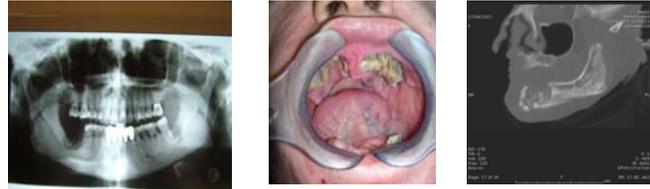
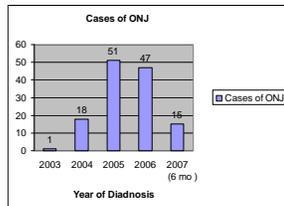
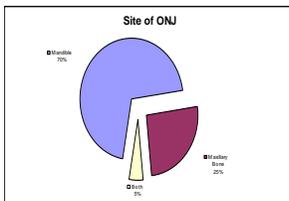
Material and Methods

On November 2005, after a workshop held in Alessandria, a regional ONJ Study Group (including oncologists, haematologists, maxillofacial surgeons, odontostomatologists, epidemiologists) was constituted; it diffused information and guidelines for diagnosis and prevention of ONJ, by mails, documents, meetings and newsletters, due to enlarge awareness of ONJ among specialists and dental practitioners. A case data collection form was mailed to all regional specialist care centers.

Results

We identified (on June 2007), among 172 segnalated patients, 163 well-documented cases of ONJ after cross-checking reports from centers of maxillofacial surgery / odontostomatology (19), medical oncology (25) and haematology / internal medicine (15). Pts were affected by breast cancer (61), myeloma (54), prostatic cancer (21), other types of cancer or unspecified (19), osteoporosis or Paget's disease (8). Pts characteristics: Sex : 59/104 M/F ; median age 68 yrs (range 42-91). BP treatment (among 148 cases, with available data) : Z in 101, P "switched" to Z in 27, P alone in 10, alendronate / risedronate / clodronate in 10.

Clinical findings (exposed bone or infections, pain, mobile teeth, soft-tissue swelling, nonhealing fistulas) and dental comorbidities or precipitating events (as teeth extraction, periodontal surgery, dental implants, or traumatic use of dentures) were those described in recent ONJ literature.



From AM Donoghue, MJA, Aug 2005

Images: courtesy by A.Fasciolo, M.Scoletta, F.Goa, G.Poglio, A.Diaspro, M.Migliario, P.Russo, O.Testori, V.Fusco.

Conclusions

Even if probably a considerable part of observed cases have not been reported to our data base, the 163 cases, collected in 3.5 years in a population of 4.3 million, are more than expected on the basis of some published estimations of incidence, for example those based on data concerning Australia (158 cases in 2 years in a population of 20.3 million: 114 cancer pts, 44 with osteoporosis/Paget's disease) or even only South Australia (25 cases, out of 1.5 million: 11 cancer pts, 14 with osteoporosis/Paget's disease) (Mavrokokki T et al, J.Oral Maxillofac. Surg. 2007).

Our oncology network recommended screening of all pts under treatment with BPs, with panoramic X-rays and referral center visit (w/o CT or MR scan in selected cases) and careful evaluation of pts candidate to be treated with BPs (with pretherapy dental care if necessary).

A case-control study has been planned to search possible risk factors of ONJ (treatment- and clinical history-related). Prospective evaluation of incidence in future, after pretherapy dental care policy and avoiding (as possible) surgical dental procedures during BP treatment, is warranted.

Trials about timing, duration, schedules of BP treatment are needed.

The goal is optimize cost-effectiveness of BPs, preventing and minimizing a possible debilitating long-term side effect of a class of drugs otherwise very useful for cancer patients.

Collaborating Centres

Centers of Odontostomatology/ Max-Facial Surgery

Torino - Patol. Orale (Mozzati, Scoletta)
Novara Odont (Foglio Banda, Migliario)
Mauriziano-Candilo (Goia, Basano, Gilardino, Chianelli)
Torino-Chir. Max. Face (Berrone, Ronieri, Diaspro)
Orbassano - S. Luigi (Pomatto, Barberis)
Torino - S. Giovanni Bosco (Beatrice, Caldarelli, Madona)
Verbania (ASL) (Lui, Milan)
Aosta (Ferrero, Gini)
Fassano (Genasio)
Biella (Cin)
Torino - Osp. Martini (Succo, Carbonaro)

Alessandria (Sorrentino, Fasciolo)
Novara ChMax (Benech, Poglio, Stellini)
Cuneo (Ruffino, Spada)
Asti (Polastri, Curtoni)
Vercelli (Falca)
Ivrea (Bagni, Prosa)
Cirié (Guiso)
Torino - Pat. Orale (Gandolfo, Arduino)

Centers reporting cases of ONJ in haematologic patients

Novara - Ematologia (Gaidano, Rossi)
Torino - Cardiolo (Aglietta)
Alessandria (Levis, Baraldi)
Torino Coes (Becchadone, Falco)
Torino Coes (Gallo, Pregno, Benevolo)
Cirié (Freilone)
Cuneo (Grasso)
Asti (Marchetti)

Torino - Maurizioano (Poccardi)
Novara - Cl. Medica (Avanzi)
Orbassano - S. Luigi (Saglio, Guglielmelli)
Casale M. - Oncologia (Botta, Muzio)
Vercelli - Oncologia (Demarino)
Savigliano - Medicina
Biella (Tonso)

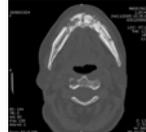
Epidemiological team

CPO Torino - Merletti, Ciccone, Galassi, Richiardi

Centers reporting cases of ONJ in oncologic patients

Torino - COES (Bertetto, Cuffreda, Donadio, Vandone)
Orbassano - S. Luigi (Doglietti, Berruti, Gorzegno, Tuca)
IRCC Candilo (Aglietta, Ortega, Vormola)
Alessandria (Bottaro, Fusco, Siffredi, Loidaris, Pertino)
Novara (Alabisa, Mirella, Forri, Berrone)
Torino - SGAS (Airoldi)
Casale (Botte, Muzio)
Navi Ligure (Castagneto, Stevani)
Cirié (Grassi, Montuccchio)
Alba-Bra (Foggiuolo, Franchini)
Verbania-VCO (Cozzi, Amodei)
Vercelli (Demarino, Manachino)
Borgomanero (Romanello)
Ivrea (Bretti, Velloni)
Torino - S. Anna (Durando)
Torino - S. Giovanni Bosco (Vietti Ramus, Tonda, Addeo)

Chivasso (Bertoldo)
Toriona (Simoni, Cosentino)
Cuneo (Marlano, Garrone, Occealli, Violante)
ASL8 (Dongiovanni, Ardina)
Biella (Clerico, Vincenti)
Torino - Ortholog (Rusconi)
Asti (Testone, Ferrero, Cesta)
Aosta (Nimico, Alvaro)
Torino - Amedeo di Savoia (Pontiglio)



15.07.2004 → 11.03.2005