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Case Report

A Problem of Late Diagnosis: Case Report with Polypharmacy

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Summary

A 49-years old, HLA-B27-negative female patient presented with inflammatory low back pain since age of 26 years and "failed back surgery syndrome" since age of 39 years. She recurrently suffered from additional arthritis, enthesitis and tenovaginitis, leading to imaging-based diagnosis of spondyloarthritis with a diagnostic delay of 23 years. NSAIDs and glucocorticoids rapidly improved her symptoms, and 11 out of the more than 18 initial tablets and capsules for pain management, central nervous disease and possible side-effects could be reduced within the following 14 months after diagnosis. Accordingly, medication costs for management of pain and gastrointestinal side-effects were reduced by a calculated 1.63 - 2.27 € per day (=595.00 - 828.55 € per year).

Polypharmacy in an undiagnosed pain patient should be considered as a red flag indicating the need for a multidisciplinary diagnostic approach. Treatment of an underdiagnosed rheumatic disease may effectively reduce polypharmacy.

Keywords: Polypharmacy; Early-diagnosis; Spondylarthritis

Background

Spondylarthritis (SpA) is a chronic immune-mediated rheumatic disease with a European prevalence between 0.2-1.6 % [1]. As both functional and structural changes have an important impact on pain and reduction of life quality [2], early diagnosis is important. Non-steroidal antirheumatic drugs (NSAIDs) are recommended as first line treatment to achieve remission or at least low disease-activity [3]. COX2-selective NSAIDs are available for patients prone to gastrointestinal side-effects, with at least comparable efficacy to conventional NSAIDs [4]. Celecoxib, one of the COX2-selective NSAIDs, was shown to retain structural disease progression when applied continuously compared to on request [5]. Etoricoxib, another COX2-selective NSAID, showed an even superior analgesic effect in rheumatoid arthritis when compared to naproxen, a non-selective COX-inhibitor [6]. Side-effects and lack of efficacy of unspecific NSAIDs may lead to extended treatment of SpA using the more potent biologicals (like inhibitors of TNF-alpha and interleukin-17) [7].

Polypharmacy is defined by the number of medications applied (usually above 4) or their inappropriateness [8]. Polypharmacy may result in unwanted drug interactions [9], and/or lead to an increase of adverse and serious adverse events, with more frequent admissions to hospitals, thus extending the costs of health care [10].

This case shows an impressive reduction of analgesic medications after late diagnosis of SpA and treatment with NSAIDs.

Case Presentation

This 49-year-old woman was referred to the outpatient clinic for rheumatology because of persisting diffuse pain. Erythrocyte sedimentation rate and C-reactive protein levels were repeatedly tested normal. She took 28 +½ +⅓ tablets or capsules at her 1st visit (Table 1), thus clearly fulfilling the criteria for polypharmacy.

First visit

The patient described lumbosacral pain radiating on the back side of the leg down to the knees. The maximum of pain happened at night-time and interrupted her sleep between 2.00 to 3.00 a.m. Pain worsened when sitting for a longer period of time and improved with movement. The first symptom of such inflammatory back pain was 23 years ago – at age of 27 years, with insidious onset.

Eleven years before this first visit, she had ongoing pain after surgical intervention with spondylodesis of L3-S1, diagnosed as "failed back surgery syndrome". Pain was insufficiently managed with more than 18 tablets and capsules other than NSAIDs (Table 1).

At clinical examination, she had swelling over the left trochanter and pulling pain in the hip joint. The finger-to-floor-distance was 35cm. Previously performed Magnetic Resonance Images (MRIs) showed the fused L3-S1 vertebrae, alongside with an effusion in the sacroiliac joint and edema in the sacrum and caudal ilium. Elevation of shoulders was only possible

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after passive mobilisation. The MRIs of shoulders and arms revealed several effusions of joints and tendons.

Examination further revealed muscular dysbalances in the neck and thighs. For the past 2 years, the patient suffered from intense headache. Comorbidities included obesity (with body mass index of 33.1 kg/m2), osteoarthritis of the knees with rupture of the anterior cruciate ligament, diabetes mellitus type II, and a bipolar affective disorder. At age of 42 years, she suffered from a transient ischemic attack and was tested with an elevated lipoprotein (a) level of 381.9 nmol/l. Her history further included several abdominal surgeries including stomach adjustments, as well as a meniscus surgery in the right knee. She had never smoked and does not drink any alcohol.

With inflammatory back pain since age of 26 years, diagnosis of "failed back surgery syndrome" at age of 39 years and other findings, including typical MR-images, diagnosis of axial SpA was considered despite HLA-B27 negativity, and naproxen, a non-selective NSAID, recommended for inflammatory back pain and low-dose corticosteroids (methylprednisolone) because of the effusions of joints and tendons. A proton pump inhibitor was recommended as ulcer prophylaxis.

Second follow-up, 4 months after first visit

Under treatment with naproxen and methylprednisolone, sleep disturbances, hip and lumbosacral pain improved, so physiotherapy could be started to treat the muscular dysbalances. After 2-3 weeks of treatment with the non-selective NSAID, however, gastrointestinal side-effects occurred, and the patient stopped naproxen and methylprednisolone as well as physiotherapy. She restarted her previous analgesics metamizole and hydromorphone, but without the positive effect of naproxen. She had also stopped physiotherapy and now presented again with increased pain symptoms.

At this visit, with characteristic inflammatory low back pain, responsive to NSAIDs and the typical MR-images, diagnosis of axial SpA was confirmed. The shared decision was made to start with the COX2-selective NSAID etoricoxib because of her gastrointestinal complaints.

Third follow-up, 6 months after first visit

She presented with still ongoing symptoms, and increased pain without swelling of joints. Again, analgesics without NSAIDs were not successful, as payment of etoricoxib had not been approved by the insurance company. Etoricoxib is routinely refunded only for painful osteoarthritis in patients older than 65 years, with gastric ulcer in the history, or under anticoagulation. A second prescription for etoricoxib was made after successful negotiation with the insurance company.

Fourth and fifth follow-up, 12 and 18 months after first visit

After diagnosis of SpA and 1 year of treatment with the COX2-selective NSAID, pain-related medication other than NSAIDs had been slowly reduced by 10 tablets, and pantoprazole was stopped (Table 1). Physiotherapy and dietary efforts for weight loss were still ongoing.

Discussion

This woman was newly diagnosed with SpA at age of 50 years, after 23 years of pain symptoms without diagnosis. Even surgery was performed but ineffective, with subsequent diagnosis of "failed back surgery syndrome". The diagnostic delay is remarkable, as literature reports a mean delay of "only" 6.8 years

Table 1: List of more than 18 daily analgesics, central nervous and other medications before, and after diagnosis of spondyloarthritis with start of etoricoxib 60mg in the evening (+1 tablet). 11 tablets or capsules were reduced during 3rd and 6th visit (depicted in bold letters). Additional 10 tablets (cardiovascular, antidiabetic and thyroid medications) are not listed and remained unchanged. ret, retard preparation.

	Medication	1 st - 3 rd visit	6th visit
Analgesics	Hydromorphon ret 4 mg	1/1/1/0	1/1/**0**/0, **reduced**
	Hydromorphon ret 2 mg	1/0/1/0	**0**/0/1/0, **reduced**
	Hydromorphon 2.6 mg	1/0/1/0	**stopped**
	Metamizole 500 mg	1/1/1/0	**stopped**
Nervous system	Escitalopram 5 mg	2/1/0/0	**2/0/0/0, reduced**
	Valproic acid ret	3x500mg	**2x150mg, reduced**
	Quetiapine 25 mg	0/0/0/½	unchanged
	Trazodone ret 150 mg	0/0/0/⅓	unchanged
Others	Pantoprazole 40 mg	1/0/1/0	**stopped**
Daily tablets		18+½+⅓	minus 11 tablets

[11]. The number of analgesic medications other than NSAIDs clearly fulfilled the definition of polypharmacy at least since age of 42 years, when she already took 21 different medications. Now, at age of 50 years, she took 28 +½ +⅓ tablets or capsules at her 1st visit (table 1). After diagnosis of SpA, only one tablet was added for treatment of the underlying disease with the consequence, that after only 6 months both pain medication and ulcer prevention could be reduced by 11 tablets or capsules (table 1), anticipating advantages for the patient with reduced risk for side-effects and interactions. Polypharmacy coincides or may even increase morbidity and mortality especially in elderly patients and should therefore be avoided [12].

This report shows multiple aspects of quality of care: First, patients with insufficient treatment of chronic pain should be assessed in multidisciplinary settings; second, diagnostic delay of SpA should be as short as possible, confirming the adequate need of rheumatological services; besides, polypharmacy can be an important hint for further assessments and the need of an underlying diagnosis for chronic pain.

Of note, the daily costs of medication for the management of pain and gastrointestinal side-effects could thus be reduced by 1.63-2.27 € per day, which sums up to 595.00-828.55 € per year (according to pricing lists of Diagnosia & Enterprise with cost reduction of 2.61-3.19 €, and additional cost of 0.92-0.98 € per day for etoricoxib, dated May 22, 2020). This analysis does not include any indirect costs for reduced work capabilities or other compensations.

The limitation of this case report is that the patient had multiple comorbidities like obesity, diabetes mellitus type II, osteoarthritis and a bipolar affective disorder. The correlation between number of medications and number of comorbidities is well established, and was recently confirmed for rheumatoid arthritis as another chronic immune-mediated rheumatic disease [13]. As a consequence, some medications like valproic acid were not originally prescribed for pain management, but doses could be reduced by psychiatrists in parallel with effective pain management.

In conclusion, this report supports the need of diagnosis in multidisciplinary settings especially for patients with polypharmacy.

Take Home Messages

- Polypharmacy may be high in pain patients without underlying diagnosis. In these patients, a multidisciplinary diagnostic approach including a rheumatologist can be successful.
- The diagnostic delay for spondyloarthritis can be still prolonged over years, despite all efforts made to allow earlier diagnosis and treatment.
- Effective treatment of spondyloarthritis can improve pain, disease activity and life quality with reduced number of medications, thus reducing polypharmacy and saving money in health care systems over the long-term.

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