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An innocent victim (fetal alcohol syndrome)

J. Cohen-Lévy

DESCRIPTION OF THE CASE

A young patient, 10 years of age (Fig. 1), was referred to us by her dentist for the correction of an excessive overjet, caused by finger sucking. She presented with delayed growth and short stature and was being treated for these conditions at a hospital facility. Initially it was difficult to examine her because she was very apprehensive. The extraoral examination revealed mildly atypical facial features: orbital hypertelorism (the distance separating the two eyes is greater than the width of an eye), narrow eye slits, flattened philtrum (Fig. 1). The intraoral examination showed a full Class II

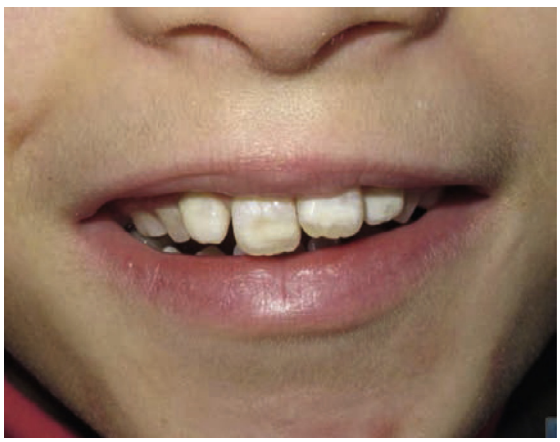

Figure 1
View of the lower third of the face. Indistinct philtral ridge/crest, thin and convex upper lip.

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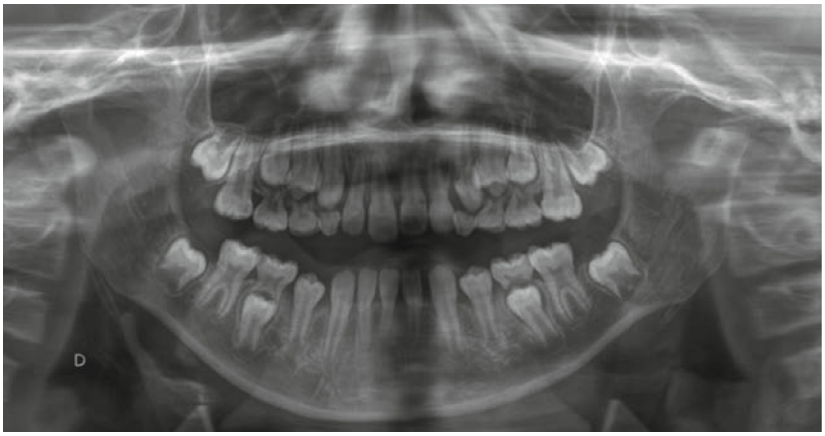

Figure 2
Panoramic view.

division 1, an undersized maxilla with a narrow and high arched palate. The enamel showed signs of hypoplasia on the permanent incisors, with whitish spots in a ring-like arrangement.

DESCRIPTION OF THE RADIOLOGICAL FILE

The file consists of a panoramic xray and a lateral cephalometric xray in occlusion, and shows dental abnormalities of number and shape, a dental age commensurate with the chronological age of the patient (Fig. 2): agenesis of a permanent mandibular incisor, presumably 32, taurodontism of the first molars, short and narrow appearance of the anterior roots, some of which present an image of crown-root kinking (21, 41, 42), and no visible image of the toothbuds of the third molars.

The forehead appears to be significantly rounded with a broad nasal bridge. The mandible presents signs of hyperdivergence and Björk posterior rotation, including a very thin mandibular symphysis and a virtually straight mandibular canal. The upper air ducts are narrow, due in part to the retraction of maxilo-mandibular bones, but also due to the relative hypertrophy of the adenoids (Fig. 3).

Two enotoses extend into the cranial vault, near the parietal bones, and have the characteristic appearance of an island of mature cortical bone found inside of cancellous bone. These benign lesions could be congenital in origin, reflecting a lack of resorption during ossification. A classic diagnosis is made based on the radiological findings alone and their asymptomatic nature: the dense and homogeneous appearance within the medullary bone, where fine extensions radiate to the periphery, in continuity with the adjacent trabeculae, sometimes resembling a ''brush border''. These images have to be

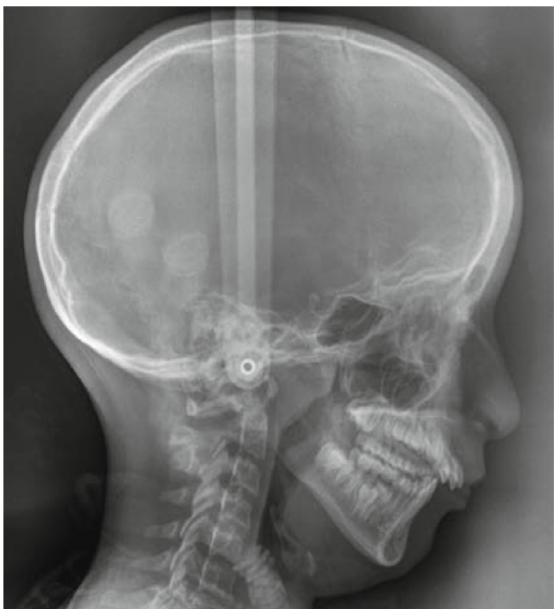

Figure 3
Lateral cephalometric xray view in occlusion.

examined carefully since they can occasionally mimic more aggressive processes (CT scan or a bone scintigraphy).

What diagnosis is called for?

Fetal alcohol syndrome (FAS) and more generally FASD (fetal alcohol spectrum disorders) refer to a whole range of developmental disorders caused by the mother's consumption of alcohol during pregnancy.

FAS, that presents the severest form of the syndrome, with a complete phenotype, was described as early as 1968 based on approximately a 100 cases[16] and later in 1973 in the international literature, where relatively

ARCHITECTURAL AND ORTHOGNATHIC CRANIOFACIAL ANALYSIS

LAST NAME: FIRST NAME: AGE: 10 years, 4 months SEX: f CRANIAL TYPE: ORTHOFRONTAL

POPULATION REFERENCE: Caucasian Date of xray: 01/09/2014 OPTIONS: F4 by NP calculated

SYNTHESIS

*The numbers provided in this table correspond to the **differences** between the optimal numbers and those of the patient.*

C1/F1 Cranial angle adapted (remember)		84°
MAXILLA		
Orientation	RETROMAXILLARY/MAXILLARY RETROGNATHIA	-4°
Height of the palate (Pu)	Collapse	1mm
Molar occlusal plane	Collapse	5mm
MANDIBLE		
Mental symphysis (position) In relation to the F1 line (cranial angle adapted)	RETROGNATHIC MANDIBLE	-5°
Vertical direction (Me)	Collapse	11mm
Ramus in relation to F3 Condylar head Position	RETRO-CONDYLAR	7mm
Posterior edge Orientation	Anterior tilting	3°
Measurements Ramus (height)	BRACHYRAMUS	-2mm
Angle	Open	14°
Body (length)	BRACHYCORPUS	-2mm
Total length (Cp-Me)	DOLICHOMANDIBULAR	2mm
MAXILLARY-MANDIBULAR Discrepancy		
Angle f1M/f1m	Skeletal Class II	2°
VERTICAL PROPORTIONS ON LOWER THIRD OF THE FACE		
ENA-Me Segment/Total osseous profile (N-ENA + ENA-Me)		59%
Difference	Anterior Vertical Excess	4%

Incisor measurements

i. Sup. Apical position PRO	3mm	Orientation LABIAL INCLINATION	8°
i. Inf. Apical position RETRO	-2mm	Orientation PALATAL INCLINATION	-12°
Mental-incisal height (ib-imt distance)			7mm
Auxological analysis (expressed potential)			
Actual ramus surface percentage in relation to the theoretical			77%
HYOID BONE			
Hy area in relation to V3 Collapse	▽ 9mm	△	

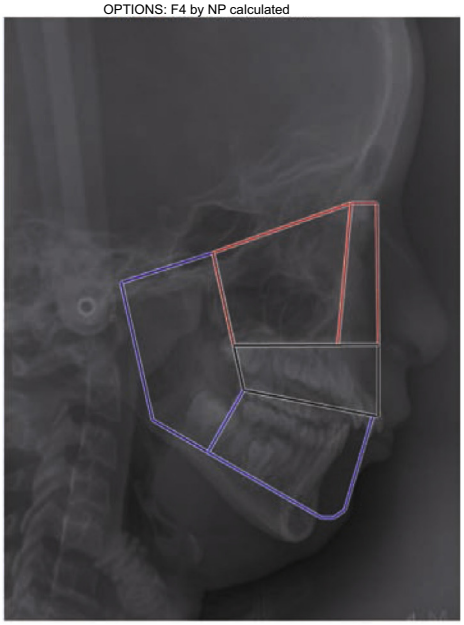

Figure 4
Delaire cephalometric analysis (Tridim® software).

specific diagnostic criteria were established, especially in regard to facial phenotype[13,28].

Epidemiological studies are particularly challenging, depending on the populations studied and on the socio-professional categories[17] involved, but researchers believe that the prevalence of FAS may be as high as 2 to 7 per 1000 in all populations and mixed ethnic groups. The highest prevalence of FAS and FASD has been reported in South Africa with a rate of 68 to 89 per 1000 births. With respect to the entire spectrum, FASD has been diagnosed infrequently and, based on a worst-case scenario, from 2 to 5% of children in the United States and in Western Europe may be affected. In France, INSERM[12] estimated that in 2001 the incidence of FAS was in the range of 0.5–3 per 1000 births, representing 700 to 2000 new cases a year.

Specific assessment criteria were adopted for the use of pediatricians[11]: the first list of criteria in 1996 by the IOM (Institute of Medicine, National Academy of Sciences) and a second list, called the ''Washington criteria'' that was established based on a study of more than a 1000 cases stemming from a network for prevention and diagnosis in the state of Washington, in the USA (2000).

FAS is accompanied by various malformations, cardiovascular and skeletal abnormalities, statural growth deficiency, with low weight and small size at birth (below or equal to the 10th percentile that persists during post-natal growth). A dysfunction of the central nervous system is a constant sign, accompanied by an overall cognitive deficit, ranging from slight to severe forms, deficits of the executive functions and mental disorders involving behavior and/or attention.

The facial anomalies[13] are correlated to the stage, the amount and the total duration of exposure to alcohol *in utero*. They fall into the following categories:

- **Cutaneous**
  - short palpebral fissures (length less than or equal to the 10th percentile; resulting in a narrow ''opening'' of the eyelids). Even if there are ethnic variations, especially with regard to the shape of the eyelids, a reduction in the orbital dimensions is systematically found[20];
  - short turned-up/snub nose, with an accentuated saddle nose;
  - long upper lip with thin vermillon border, a flattened or smooth philtrum (see Fig. 1);
  - minor anomalies of the pinna, that may be low set.

- **Skeletal**
  - microcephalia (head circumstance lower or equal to the 10th percentile found in the most severe forms);
  - low forehead, with frontal bossing due to maxillary retrusion;
  - mandibular micrognathia and maxillary hypoplasia, that lead to collapsed midface.

- **Other anomalies**
  - nail dysplasia[6] (20% of FAS cases).

These facial abnormalities that are recognizable at birth tend to be less apparent with growth[21]. Therefore, a digitized Procrustean analysis of the facial points, performed using a 3D

surface scanner[22], allowed practitioners to detect children with FAS from a control population in more than 95% of cases by age 5, whereas the number lowered to 80% by age 12.

A number of clinical studies provide a detailed description of the teratogenic and neurotoxic effects of alcohol (ethanol) on the embryo and the fetus, and animal models have been developed, on the zebra fish, rodents[27] and some primates (*Macaca nemestrina*[18,26]).

The pathogenesis of FAS is due to the apoptosis of certain cellular populations during the 12 hours following the ingestion of ethanol; some cells are particularly sensitive to it, such as those that spring from the neural crest cells, while others are more resistant (based on genomic analyses). Although the teratogenic effects of alcohol are significant during the course of the first weeks of development (embryogenesis), there are also others in the course of the last trimester, that induce an apoptosis of neurons and of oligodendrocytes. This disruption in development explains some of the problems with behavior and learning that show up later in a child exposed to alcohol *in utero*, even if some of the characteristic syndromic features are absent[7].

Some molecules, such as antioxydants, retinoids, the *sonic hedgehog* protein, and the SAL and NAP peptides[29], may diminish or on the contrary exacerbate the teratogenic effects of ethanol.

Using a mouse model, a team of researchers was able to demonstrate that anomalies of the craniofacial bones were a reliable and sensitive marker for FAS[27]. The analysis of face and profile cephalometric points on nonsyndromal subjects with a lower IQ and learning difficulties may allow clinicians to identify children who had been heavily exposed to alcohol *in utero* (analysis with 3D facial photographs[30]).

Some reports on clinical cases have described patients with a specific defect in the skeletal and craniofacial midline, originating from the disruption of the ordered development of midline mesoderm in the periocular and nasal region[23], and have connected it to a greater frequency of agenesis of the corpus callosum in the brain.

The overall symmetry and dental symmetry have likewise been affected[14]; to such an extent that a publication on ''fluctuating'' odontometric asymmetry[15] suggested that it may be a marker for FAS, since the mother's alcoholism constitutes a disruptive agent in the odontogenesis at the stage at which the dental organs are still only soft tissue.

WHAT ARE THE REPERCUSSIONS ON ORTHODONTIC TREATMENT?

Knowing about this syndrome and its lesser forms is important for the orthodontist, and even more so given that the degree of the growth deficit and of the intellectual disability is directly linked to the severity of the craniofacial anomalies[28]. Subjects with this syndrome, present with a high prevalence of dental

anomalies and speech pathologies that frequently require early intervention[5]. A high rate of temporo-mandibular joint disorders has also been reported[5].

Communication with other medical specialists is necessary and specific.

- The majority of these children have disorders in the ENT area and vestibular dysfunction is common[5]. In the case presented above, we see hypertrophy of the adenoids on the lateral xray, that contributes to low lingual posture (mouth breathing caused by upper airway obstruction). An association with sleep apnea should be investigated, because it has been described[31], in connection with retraction of the midface.
- A high rate of non-nutritive sucking (thumb or digit sucking, tongue suction) has been shown in these patients, that causes a labial inclination of the upper incisors and a counter-clockwise tilting of the palatal plane. Getting these children to willingly cooperate and comply with wearing removable appliances may be particularly difficult.
- An Australian study showed significantly increased rates of gingivitis and periodontal diseases (adjusted OR (odds ratio) of 1.67, 95% confidence level at 1.12–2.01), as well as for other diseases of the lips (odds ratio 1.56) and of the oral mucosa.
- Dental eruption may be slightly delayed and anomalies of the enamel are common[28].
- In terms of cephalometrics[8,9,22], FAS patients present with an overall underdevelopment of cephalic dimensions, an asymmetry of upper and middle thirds of the craniofacial complexes, and telecanthus in some instances, with the characteristic long face and large gonial angle[19].

CONCLUSION

Insofar as there is a dose-response effect between the consumption of alcohol and its teratogenic effects on the fetus, and given that experimental studies have demonstrated alcohol's toxicity on developing nerve cells, we should announce a zero tolerance for alcohol use during pregnancy.

Conflicts of interest: The author declares no conflict of interest.

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